



ADDRESS

Timisoara, Romania
Gospodarilor Street, nr. 42
Tel: +4-0256-439441
cod 300778
e-mail: boiaeugen@yahoo.com

JURNALUL PEDIATRULUI – Year XX,
Vol. XX, Nr. 79-80, july-december 2017
www.jurnalulpediatrului.ro
ISSN 2065 – 4855

REVISTA SOCIETĂȚII ROMÂNE
DE CHIRURGIE PEDIATRICĂ
www.srcp.ro

EDITOR IN CHIEF

Eugen Sorin BOIA

CO-EDITORS

Radu Emil IACOB

Liviu POP

Maria TRAILESCU

SECRETARY

Radu Emil IACOB

Vlad Laurentiu DAVID

EDITORIAL BOARD

O Adam

Valerica Belengeanu

Marioara Boia

Rodica Elena Cornean

A Craciun

M Gafencu

Daniela Iacob

Otilia Marginean

A Pirvan

CM Popoiu

Maria Puiu

R Spataru

I Velea

EDITORIAL CONSULTANTS

M Ardelean – Salzburg, Austria

Valerica Belengeanu – Timisoara, Romania

Jana Bernic – Chisinau, Moldavia

ES Boia – Timisoara, Romania

Maria Bortun – Timisoara, Romania

V Fluture – Timisoara, Romania

S Garofallo – Milano, Italy

DG Gotia – Iasi, Romania

C Ilie – Timisoara, Romania

Tamás Kovács – Szeged, Hungary

Silvo Lipovšek – Maribor, Slovenia

E Lazăr – Timisoara, Romania

J Mayr – Basel, Switzerland

Eva Nemes – Craiova, Romania

Gloria Pelizzo – Pavia, Italy

L Pop – Timisoara, Romania

I Popa – Timisoara, Romania

Maria Puiu – Timisoara, Romania

J Schalamon – Graz, Austria

I Simedrea – Timisoara, Romania

Rodica Stackievicz – Kfar Sava, Israel

H Stackievicz – Hadera, Israel

Penka Stefanova – Plovdiv, Bulgaria

C Tica – Constanta, Romania

Gabriela Zaharie – Cluj-Napoca, Romania

CONTENTS

1. PHYSIOPATHOLOGY AND TREATMENT IN NON-CYSTIC BRONCHIECTASIS

Adina M. Țurcanu, Otilia Frăsinariu, Traian Mihăescu.....3

2. CYSTIC FIBROSIS MANAGEMENT AT PUBERTY AND THE PROBLEMS OF ADOLESCENT – ADULT TRANSITION PERIOD

Liviu Pop, Ioan Popa, Marilena Lăzărescu.....7

3. NEONATAL CEREBRAL MONITORING IN THE POSTNATAL TRANSITION PERIOD

Nastase Leonard, Stoicescu Silvia Maria.....11

4. RASPBERRY PI AS A FRAMEWORK FOR A PAIN SIGNALING SYSTEM IN THE NEONATE

Alexandra Nyiredi, Daniela Iacob, Emil-Radu Iacob, Andrei Lihu, Constantin Ilie.....15

5. NEONATAL NEUROLOGICAL OUTCOME OF SMALL FOR GESTATIONAL AGE VERSUS PREMATURE INFANTS

Teofana Bizerea, Ramona Stroescu, Constantin Ilie, Claudiu Angelescu, Ștefana-Gheorghina Dezsi, Otilia Mărginean.....18

6. NEUROFIBROMA OF THE THIGH WITH COMPRESSION OF THE SCIATIC NERVE IN A CHILD

Narcis Flavius Tepeneu.....23

7. OTITIS MEDIA IN CHILDREN-RISK FACTORS AND COMPLICATIONS

Ana-Simona Drochioi, Magdalena Iorga, Mihaela Corlade-Andrei, Elena-Madalina Pitorac, Dana-Teodora Anton-Păduraru.....27

8. BLUNT ABDOMINAL TRAUMA IN CHILDREN – A PRACTICAL REVIEW

Flavius Bulgaru, Constantin Tica, Florin-Daniel Enache.....33

9. IDIOPATHIC INTRINSIC PYLORIC STENOSIS – A VERY RARE CAUSE OF GASTRIC OUTLET OBSTRUCTION IN SMALL CHILDREN

Lucian Vida, Aurel Mironescu, Șerban Rogoz.....39

10. ULTRASOUND DIAGNOSIS AND CORRELATION BETWEEN OBSTETRICAL TRAUMA AND NEUROLOGICAL DISORDERS

Marioara Boia, Daniela Cioboata, Florina Doandes, Nicoleta Lungu, Oana Costescu, Aniko Manea.....43

11. A 10 YEARS SBS RETROSPECTIVE STUDY OF NEONATES AND CHILDREN

Henry Osakwe, Adrian Pavel, Maria Trailescu, Elisa Mussuto, Calin Popoiu, Eugen Boia.....48

MANUSCRIPT REQUIREMENTS.....54

PHYSIOPATHOLOGY AND TREATMENT IN NON-CYSTIC BRONCHIECTASIS

Adina M. Țurcanu^{1,2}, Otilia Frăsinariu^{1,3}, Traian Mihăescu^{1,2}

Abstract

Non-cystic bronchiectases are an underdiagnosed pathology that is oftentimes classified as idiopathic. Identification of risk factors and determination of an accurate diagnosis are paramount in order to improve patient outcomes. Infectious exacerbations are often incorrectly treated, which leads to the onset of antibiotic resistance and microbial colonization. Determination of the pathogen agent that caused the infectious episode and its subsequent course of treatment must be carried out via specialized paediatric medical facilities or paediatric pneumology departments. Long term monitoring of the pulmonary function and clinical status in these patients is essential, as it reduces adult age mortality.

Keywords: non-cystic bronchiectases, child, antibiotics

Introduction

Bronchiectases were first described in 1819 by Laenec and before the age of antibiotics they were seen as a high mortality disease due to the associated respiratory failure and complications.

Bronchiectases are defined from an anatomical point of view as irreversible and abnormal dilations of various calibres (particularly medium sized ones) in the bronchial lumens, being located exclusively in a pulmonary lobe/segment, but also diffusely.¹

The underlying causes of bronchial tree damage includes major pathological modifications, particularly the alteration of the elastic and muscular components in the bronchial wall, secondary to chronic inflammation, and other endogenous and exogenous factors. Concurrently, mucosal edema and ulceration are also described. In its turn, healthy pulmonary tissue exerts contracting forces that deform the bronchia. The possibility of having other associated pulmonary pathologies such as fibroses, foreign bodies or tumoral formations should also be taken into consideration, as they can exert traction forces in certain areas of the parenchyma and contribute to the formation of bronchiectases.

The association with the centripetal and centrifugal forces exercised on the bronchial structure leads to modifications in its calibre, being able to become up to three or four times larger than the sizes deemed normal.

Stagnation of bronchial secretions and puss clogs that can form in case of microbial superinfections also contribute to the deformation of structures, maintenance of chronic inflammation and disease progression.²

Contents

Cough is a very frequent symptom in childhood. Literature data state that a third of children present with intermittent coughing on a monthly basis, and some parents describe it as chronic. To describe this symptom we used a series of terms, including «pre-bronchiectases», so as to highlight the importance of any potential changes that can be detected on the HRCT (fig.1). Persistence of the symptomatology for more than three week evidently requires the commencement of certain investigations in order to establish a diagnosis and prevent complications.³ The symptoms and indications that are associated with the existence of bronchiectases are chronic productive cough, recurrent respiratory infections, dyspnea, wheezing, fever, weight loss, chest pain, and hemoptysis.

The cause of bronchiectases in children can be extrinsic or, more rarely, intrinsic. The most frequently encountered etiological factors are infectious ones, which cause irreversible anatomical modifications.⁴ Pathologies such as severe pneumonia, pulmonary tuberculosis, and Bordetella pertussis infections frequently cause the onset of bronchiectases.⁵ The microorganisms involved in infections that favour the occurrence of bronchiectases also include *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Histoplasma*, *H. Influenzae*, flu adenoviruses and viruses. Immune deficiency states are another factor involved therein. Acquired immune deficiencies and congenital agammaglobulinemia are the most frequently cited factors in medical literature. Kartagener Syndrome, Williams-Campbell, and primary ciliary dyskinesia are associated with the existence of cystic and non-cystic bronchiectases.¹ In comparison with adult patients, the etiological factor in paediatric patients can be determined in over 70% of cases.

The clinical symptomatology is determined by a series of factors such as the child's age, extent to which bronchiectases are extended, and other associated pathologies.

¹“Grigore T. Popa” University of Medicine and Pharmacy in Iași, Faculty of General Medicine

²Clinical Hospital of Pneumology, Iași

³“Sfânta Maria” Clinical Paediatrics Hospital, Iași

E-mail: adinagheorghita@yahoo.com, traian@mihaescu.eu

Identifying the location of anatomical modifications is important as it guides the clinician towards a potential etiology. Dry cough is associated with the presence of post-tuberculosis bronchiectases located in the upper lobes. Lobe-level bronchiectases in a child with a previously normal chest X-ray can raise the etiological suspicion of a treated abscessed infection, an endobronchial obstruction

cause by aspiration of foreign bodies or, more rarely, by the existence of a tumour. Generalized bronchiectases can be the cause of an underdiagnosed asthma in young children, of recurrent aspiration of gastric secretions in severe cases of gastric reflux or in case of congenital gastro-oesophageal anatomic anomalies, gas intoxications, and viral or bacterial bronchopneumonia treated either late or incorrectly.

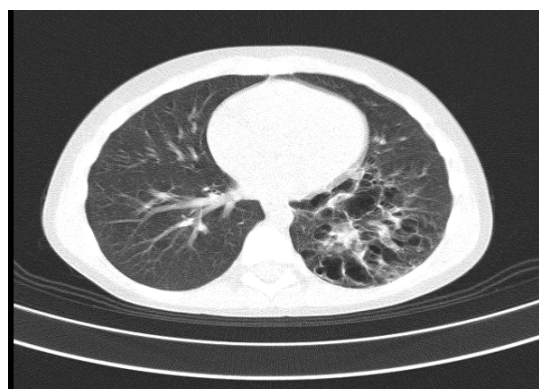
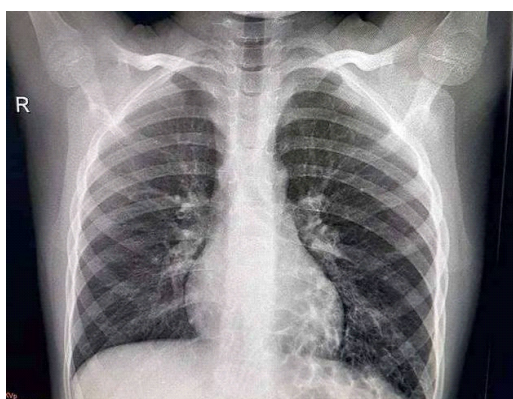


Fig.1 Left basal bronchiectases in a 9 year old child.

In a study published in 2005 and conducted on a sample of 136 patients aged between 3 and 18 years old, *Li AM et al* identify the etiology of bronchiectases confirmed via CT. Thus, they noticed that in 67% of the patients the cause was immune deficiency, foreign body aspiration, and primary ciliary dyskinesia; of the total sample of children, the identification of etiology in 56% of them (77 patients) caused important modifications in terms of medical management of the disease. 26% of the cases were diagnosed with idiopathic bronchiectases. The authors also noticed the existence of an obstructive ventilatory dysfunction in most of the investigated cases, with a mean FEV1 of 71% (15-133% of the forecast). This aspect is relevant because the presence of bronchiectatic modifications on the HRCT was correlated with the decrease in the spirometry parameters. Monitoring these patients is essential for determining a long term bronchodilator treatment.⁵

The results obtained by *Kim HI et al* and published in 2011 are not consistent with Li AM's in terms of frequency of the etiology of bronchiectases cases. Although the study sample was smaller (92 patients), it revealed that obliterative bronchiolitis was the main causal factor for the existence of non-cystic bronchiectases (33%), followed by childhood respiratory infections (tuberculosis, cytomegalovirus), and interstitial pulmonary pathology of various etiologies. Only 14% of the cases were deemed idiopathic. This data is similar with the data in the study described previously in terms of distribution, as bronchiectases are most frequently located in the lower lobes, then in the upper lobes and

bilaterally. The results here also confirm the presence of the obstructive syndrome, with a 63% mean FEV1.⁶

In a study published in *Thorax* in 2004 on a similar patient sample (92 children with an average age of 7.2 years), *Eastham KM et al* identifies the association between bronchiectases and lobar pneumonias as the most frequent etiology (30%), followed by the existence of a congenital or acquired immune deficiency (21%). Idiopathic pathology also describes a significant share of approximately 18% in this study. The data obtained does not support the hypothesis that obliterative bronchiolitis is the main cause of bronchiolitis modifications, as this diagnosis was determined beforehand in just 9% of the children.⁷

In accordance with the results published in 2008 in *Pediatric Lung Disease* by *Bastardo CM et al*, obstructive ventilatory dysfunction in children with bronchiectases is persistent over time, then stabilizes, and does not respond to specific courses of treatment. Mean levels of FEV1 also fluctuated in this study, ranging between 68-71%.⁸ This mandates the careful monitoring of these patients in their adult age in order to identify any potential declines in terms of pulmonary function.

In addition to the evaluation of the pulmonary function via HRCT and X-rays in case of exacerbations, the microbiological testing of sputum for flora and fungi or of bronchial aspirate culture is necessary for sleep quality assessment purposes. Sleep quality is most of the times affected in case of diffuse or localized bronchiectases that cover large pulmonary areas and cause a chronic symptomatology manifested via frequent – and sometimes inefficient – expectoration, at times associated with hypoxia.

Application of the questionnaires known as the Pittsburgh Sleep Quality Index (PSQI) and Paediatric Sleep Questionnaire (PSQ), peripheral oxygen saturation measurement, and sometimes even a polygraph test are necessary for determining an adjuvant treatment.⁹

In accordance with the British Thoracic Society Bronchiectasis (non-CF) Guideline Group (BTS 2010) guidelines, the treatment principles for bronchiectases in both adults and children are based on treating the cause that influences the development of bronchiectases, educating patients and their parents, optimizing the clearance of respiratory tract – physical therapy, exercises, use of mucolytic agents and hyperosmolar solutions, medication for respiratory tropism – anti-inflammatory medicine, bronchodilators, antibiotics, identification of cases with recommended surgical treatment, and optimum complications' management.¹⁰

Targeted antimicrobial therapy is highly recommended. The microorganisms that were most frequently involved in the etiology of bronchiectases and isolated from sputum collected from patients with superinfected bronchiectases are: *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Moraxella catarrhalis*, *Staphylococcus aureus*, and *Klebsiella pneumoniae*.^{8,11,12} The isolation of *Pseudomonas aeruginosa* or the MRSA *staphylococcus* is associated with a chronic colonization and recurrent infectious exacerbations.

Orriols et al studied the effects of long term antibiotic therapy (ceftazidime 1000 mg every 12 h or tobramycin 100 mg every 12 h) in aerosols for children with non-cystic bronchiectases (tested negative for the 31 CF mutation, as well as for AF508, G542X, N1303K) colonized with *Pseudomonas aeruginosa*. The duration and frequency of hospital admissions dropped significantly in comparison with a control group studied. The results thus obtained are encouraging for these patients' outcomes.¹³ The British Thoracic Society Bronchiectasis (non-CF) Guideline Group (BTS 2010) guideline also proposes the use of gentamycin (80 mg every 12 hours), colistin (1-2 million every 12 hours), which was substantiated as having favourable effects. First-line medication recommendations for oral therapy in case of infectious exacerbations differ based on the isolated microorganism, noting that the duration of the treatment is of 14 days irrespective of the case (table 1).¹⁰

Also, the literature cites long term macrolide oral therapy as effective. There were several studies, including that with roxithromycin 4 mg/kg every 12 hours, 12 weeks (*Koh YY et al*), erythromycin 400 mg every 12 hours, 12 months (*Masekela R et al*), azithromycin 30 mg/kg, once a week, 12-24 months (*Valery PC et al*), which highlighted a genuine benefit in reducing the number of hospital admissions and exacerbations.

Table 1. Recommendations for antibiotic therapy in children with superinfected bronchiectases as per the British Thoracic Society Bronchiectasis (non-CF) Guideline Group (BTS 2010) guide.

Pathogen agent	First-line medication	Second-line medication
<i>Streptococcus pneumoniae</i>	amoxicillin	clarithromycin
<i>Haemophilus influenzae</i> (b-lactamase negative)	amoxicillin	clarithromycin or ceftriaxone
<i>Haemophilus influenzae</i> (b-lactamase positive)	co-amoxiclav	clarithromycin or ceftriaxone
<i>Moraxella catarrhalis</i>	co-amoxiclav	ciprofloxacin
<i>Staphylococcus aureus</i> (MSSA)	flucloxacillin	clarithromycin
<i>Pseudomonas aeruginosa</i>	ciprofloxacin	ceftazidime or tazocin or aztreonam or meropenem or combinations
<i>Staphylococcus aureus</i> (MRSA)	rifampicin + trimethoprim (oral)	rifampicin + doxycycline
	vancomycin or teicoplanin (injectable)	linezolid

In the result of the research published in 2010 in the Journal of Pediatrics, *Hare KM et al* focused on identifying the microbial etiology of upper and lower respiratory tract infections in children with bronchiectases in comparison with children without this pathology. *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis* were the main pathogens that caused infectious episodes, sometimes also being identified in association or even all together. The frequency of these germs in children with bronchiectases is not fully known due to the fact that collection of the biologic products is oftentimes impossible, as the patient is too young to be able

to expectorate, while fibrobronchoscopic testing is unavailable in many paediatric medical facilities.¹⁴

Episodes of bacterial or viral superinfection are responsible for increasing morbidity levels, lung function deterioration, and decrease in terms of quality of life. Literature data indicates that almost half of the infectious episodes are viral, thus the use of antibiotics is most often unsuitable. The relevant inflammatory markers such as C-reactive protein, ESR, procalcitonin, IL 6, and SAA should be dosed before establishing a course of treatment. The association of several markers increases the specificity of the diagnosis. In a study published in 2014, *Kapur N et al*

monitored 69 patients with a 7 years old mean age over a period of approximately 13 months. A total of 77 fully investigated exacerbations were identified during the research. Of these, 48% were of viral etiology, most of them being caused by the rhinovirus (26%) and parainfluenzae (8%). These viral exacerbations were associated with the presence of fever, hypoxia, and hospital admission.¹⁵ The results presented by these authors are very important, as they reiterates the importance of accurate and complete investigation of all infections by the specialized departments in paediatric patients with bronchiectases, so as to determine the correct course of treatment and to avoid antibiotic abuse which could subsequently lead to microbial

resistance, secondary candidiasis, and potential food allergies.

Conclusions

Most of the studies confirm that even in children there is a significant percentage of patients for whom it is impossible to determine the etiology of bronchiectases. Owing to access to healthcare, the number of non-cystic bronchiectases cases in developed countries is dropping. The correct use of antibiotics and early management of the disease are essential for the long-term reduction of mortality rates.

References

1. Bogdan M, Mihăescu T, Bumbacea D et al. Pneumologia. Editura Carol Davila.2008.
2. Adina M. Țurcanu, T. Mihăescu : Aspecte fiziopatologice și tratamentul în bronchiectases, Pneumologia. 2011;1:26-29
3. Deirdre Donnelly, Anita Critchlow, Mark L Everard. Outcomes in children treated for persistent bacterial bronchitis. Thorax. 2007;62:80–84
4. Hare KM et al. Respiratory Bacterial Pathogens in the Nasopharynx and Lower Airways of Australian Indigenous Children with Bronchiectasis. J Pediatr. 2010;157:1001-1005
5. Li AM et al. Non-CF bronchiectasis: does knowing the aetiology lead to changes in management?. Eur Respir J. 2005; 26: 8–14
6. Kim HY et al. Bronchiectasis in Children: 10-Year Experience at a Single Institution. Allergy Asthma Immunol Res. 2011 January;3(1):39-45
7. Eastham KM et al. The need to redefine non-cystic fibrosis bronchiectasis in childhood. Thorax. 2004;59:324–327
8. Bastardo CM et al. Non-cystic fibrosis bronchiectasis in childhood: longitudinal growth and lung function. Thorax. 2009;64:246–251
9. Erdem E. et al. Effect of Night Symptoms and Disease Severity on Subjective Sleep Quality in Children With Non-Cystic-Fibrosis Bronchiectasis. Pediatr Pulmonol. 2011;46(9):919-926
10. British Thoracic Society guideline for non-CF Bronchiectasis. Thorax. 2010;65.
11. Banjar HH. Clinical Profile of Saudi Children With Bronchiectasis. Indian J Pediatr 2007;74(2):149-152
12. Munro KA et al. Do New Zealand Children With Non-Cystic Fibrosis Bronchiectasis Show Disease Progression?. Pediatr Pulmonol. 2011; 46:131–138
13. Orriols R et al. Inhaled antibiotic therapy in non-cystic fibrosis patients with bronchiectasis and chronic bronchial infection by Pseudomonas aeruginosa. Respiratory Medicine.1999; 93:476-480
14. Kumar A et al. Non-Cystic Fibrosis Bronchiectasis in Children: Clinical Profile, Etiology and Outcome. Indian J Pediatr. 2015;(52):35-3
15. Kapur N et al. Respiratory viruses in exacerbations of non-cystic fibrosis bronchiectasis in children. Arch Dis Child. 2014;0:1–5.

Correspondence to:

Adina M. Țurcanu
Spitalul Clinic de Pneumologie,
Str. Cihac nr 30,
Iasi,
Tel. 0745099456
E-mail: adinagheorghita@yahoo.com

CYSTIC FIBROSIS MANAGEMENT AT PUBERTY AND THE PROBLEMS OF ADOLESCENT – ADULT TRANSITION PERIOD

Liviu Pop^{1,2}, Ioan Popa^{1,2}, Marilena Lăzărescu^{1,2}

Abstract

Cystic fibrosis is the most frequent monogenic, autosomal recessive disease in Caucasian population. The complexity of this disease involves a special management fitting to every age and to clinical-evolutive moment. In the first part, the paper refers to specific aspects of cystic fibrosis management in teenagers about: the improvement of mucosal-secretion clearance, the control of infection, the maintaining of an optimal nutritional status, the prophylaxis and treatment of other diseases and complications of CF, the psychological support of the patient and his family. In the second part are presented the problems about the teenager-adult transition period, underlining psycho-affective aspects of the moment and care team role.

Keywords: cystic fibrosis, teenager, adolescent, care

Aim importance

Cystic fibrosis (FC) or mucoviscidosis is the most common autosomal recessive monogenic disease in the Caucasian population with chronic, progressive, potentially lethal evolution; a newborn from 2000-2500 is affected and one in 25 individuals is the carrier of the pathological gene^(1,2). In the absence of an early diagnosis, from the newborn period or at the earliest in the first years of life and from the right treatment applied, the chances of survival do not exceed the pre-school age. On the contrary, early diagnosis and correct management of the disease can assure an optimal quality of life for a long time⁽³⁾.

At the moment, the life expectancy and quality of life of the patient with FC have improved significantly first of all due to acquisitions in disease awareness (after the discovery of the gene and defective protein) and, on the other hand, by developing a system complex treatment and care. FC is a complex and expensive disease, especially when we talk about an advanced development, and therefore any measure to prevent the progression of the disease must be applied without any reservation^(3,4).

An important proof of the general interest in CF issues is the development of international programs, like the Cystic Fibrosis Worldwide Association (CFW), for the implementation and development of FC services in developing countries⁽⁴⁾

All these have led in the last decades to substantial changes in the mean survival of patients with FC^(5,6). If until 1970 the average of survival was 16 years, now has reached 32 years. In the same sense, it is estimated that for those born in the early 90's, the average age of survival will be over 40 years.

In this context, there are new problems of care, specific to older ages, also for the adult, many of the complications of the disease being related to the evolution of the disease in time (biliary cirrhosis, multifocal, diabetes, reproductive problems etc.)^(3,4).

Cystic fibrosis management in puberty.

The development of services regarding FC management also in our country led to the improvement of the early diagnosis of the disease, even from the newborn period, toddler and small baby. In the same time, the proper therapy, start at the installation of major complications, has determined, in time, an increasing rate of survival in patients with CF also in our country⁽⁴⁾. This makes the number of pubertal and adolescent patients currently increasing⁽⁷⁾, which leads to new issues related to the management of the disease, including the transition to adulthood. In this context, home care therapy is the decisive component for ensuring a long-lasting quality of life for the patient with FC. Major goals in FC treatment are^(3,8):

1. Improvement of mucosal-secretion clearance
2. Control of infection
3. Maintaining of an optimal nutritional status
4. Prophylaxis and treatment of other diseases and complications of CF
5. Psychological support of the patient and his family

1.Improvement of mucosal-secretion clearance⁽⁹⁾

It is very important in the treatment of FC. The most sophisticated antibiotic treatment will be little or no effective in the absence of consistent and accurate physiotherapy. Physiotherapy has several components:

- airway clearance techniques;
- exercise;

¹Clinic II Pediatrics, University of Medicine and Pharmacy Timisoara

²National Centre of Cystic Fibrosis Timisoara

E-mail: liviupop63@yahoo.com; iioanapopa@yahoo.com; lazaresculinamarinela@yahoo.com

- mucolytic agents (aerosolotherapy): N acetyl cystine, Dornase alpha (breaks the leukocyte cytoplasmic DNA released from the local neutrophil - bacterial conflict, and which significantly accentuates the viscosity of the sputum);
- bronchodilators: since puberty, most CF patients develop bronchial hyperreactivity, bronchodilators (nebulised) become a standard component in the treatment of the disease.

2. Control of infection

When we talk about control of infection in FC is very important to know that there is so-called "point of no return" ⁽¹⁰⁾. The infection once installed, especially with *Pseudomonas aeruginosa*, can no longer be eradicated, pulmonary lesions having a progressive evolution. Practically, infection control is achieved by antibiotherapy and anti-inflammatory therapy.

The principles of antibiotherapy are the following ⁽¹¹⁾:

- doses of drugs administered are higher than in other infections;
- the treatment is guided by the severity of the symptomatology and the causal germ (the germs involved in FC, especially *Pseudomonas ae.*, do not respond to "usual" antibiotics, and it is recommended to use the antibiotics recommended by international working groups)
- the period of treatment will be prolonged, up to 3-4 weeks, including intravenous use.
- The administration of antibiotics nebulised will be done in prolonged months, even permanent ⁽¹²⁾.

Classical anti-inflammatory treatment refers to corticotherapy, reserved for advanced forms of disease, with high levels of circulating immune complexes. Administration is done in aerosols and / or oral, but with questionable benefits. Recent research has revealed a low level of essential fatty acids with an anti-inflammatory role despite good nutritional status, considering this aspect as specific for FC, probably related to the same defective gene ⁽¹³⁾. Consequently, administration of essential fatty acids is regarded as an effective option in the anti-inflammatory treatment of FC.

3. Maintaining of an optimal nutritional status ^(14,15)

Maintaining an optimal nutritional status is aimed once for the compensating for pancreatic insufficiency by administering enzyme supplements exclusively in the form of minimal microspheres and on the other hand providing adequate nutrition according to certain standardized principles. Two aspects are to be taken into account in nutritional management:

- nutrition status monitoring through regular evaluations;
- nutritional intervention, generally reserved for two special situations: psychogenic context and / or exacerbation of pulmonary suffering: it can be achieved by: feeding supplements (Fresenius, Creacon) or by enteral nutrition (oro-nasogastric probe, gastrostomy, jejunostomy)

4. Prophylaxis and treatment of other diseases and complications of CF ⁽¹⁶⁾

4.1. The equivalations of the meconial ileus (distal intestinal obstruction syndrome), a very common situation at older ages, is responsible for mechanical obstruction and emergency surgery. Supplements of pancreatic enzymes and gastrographic enema (under hospital conditions) are beneficial.

4.2. Chronic pancreatitis, for which the risk is very high in patients with a pancreatic phenotype. Monitoring of pancreatic amylases and lipases is mandatory after 10-12 years of age.

4.3. Gastroesophageal reflux, with no greater incidence in puberty and adolescence, should be considered, leading to major discomfort during physiotherapy.

4.4. Hepatobiliary suffering is clearly evident in this age group, translating into different clinical forms, from moderate hepatomegaly with fatty loading to millifocal biliary cirrhosis. Prophylactic treatment involves the administration of ursodeoxycholic acid in prolonged cures for years.

4.5. Decreased glucose tolerance and diabetes mellitus. The end of puberty and the beginning of adolescence represent, statistically, the periods of life when the glucose tolerance decreases and then the onset of diabetes. This evolutionary event has dramatic consequences, being responsible for the marked deterioration of pulmonary function and body mass index ⁽¹⁷⁾. Therefore, OGTT screening is mandatory after 10-12 years of age.

4.6. Associated osteopathy ^(3,21). Recognized as a possible complication in the late '70s is defined by lowering bone density by more than 2 DS of the Z score or by the presence of one or more pathological fractures. Cross-sectional studies have revealed a high rate of fracture in MV patients compared to control groups, particularly in patients on waiting lists for transplantation. Pathogenesis is not fully elucidated. Morphohistometry studies in patients with stabilized disease have revealed a reduction in bone density, by reducing bone remodeling mechanisms and generally by altering the structure of connective tissue in the skeleton. Bone density assessment should be done by dual X-ray absorptiometry (DEXA). This investigation should be considered as part of the evaluation in all CF patients over the age of 6 years.

5 Psychological support of the patient and his family ⁽¹⁸⁾

The complexity of the disease implies an extremely important role of psychological support in the evolution of the disease. This is addressed to the patient, his / her family and caregivers. The ways of psychological "intervention" adapt to the specifics of the disease, the psychology problems specific to the puberty period, adolescence, but also to the clinical-evolutionary moment. Generally, during the puberty period, the issues that occur in the evolution of the disease and which may influence the patient negatively are: *Pseudomonas aeruginosa* suprainfection, complications, increased number of hospitalizations, and decline in pulmonary function. Most frequently we see puberty in non-compliance reactions to treatment, especially physiotherapy ⁽⁹⁾. It is time to apply the newer methods of physiotherapy (flute therapy, PEP mask), which shortens the time allocated

and creates some independence for the sick, may be beneficial.

Problems about the teenager-adult transition period, underlining psycho-affective aspects of the moment and care team role.^(19,20)

Growing up, the teenager faces new medical and social problems. The transition from adolescence to adulthood is more difficult for these chronic patients because:

- must gain its affective and medical independence;
- to find a career path;
- to face the reality of the lack of radical treatment.

It's up to pediatricians and internists to discuss and consider all aspects of this transition. The care team must be complemented by pneumologist, gastroenterologist, surgeon, gynecologist, endocrinologist (diabetologist).

The transfer from the pediatric to the adult network around the age of 18 should be done in an optimal period (maturity, accept, except for periods of exacerbation of lung disease). The transition model depends on multiple factors:

- national and institutional health policy;
- financial possibilities;
- the proximity of pediatric and adult services;

- collaboration between pediatric and adult services.

In this context, the transition can be accomplished directly but with severe affective affects for the patient (not recommended) or progressively by overlapping for a period of time between the two pediatric and adult groups, the pediatrician being the coordinator of the two groups. The interdisciplinary care team must be a supportive professionalism because the quality of life is as important as its prolongation. The goals of adolescents / adults with FC exceed the goal of staying alive. They want independence, social and professional success and want to take responsibility for their lives.

Conclusions

The couple FC disease - is an unwanted marriage and without divorce, with implacable destiny, a life-long and dying battle. That is why, in order to not lose the fight from the start, the disease should not be considered an unbeatable enemy, but an adversary, which unfortunately still requires the rules. If the patient learns and obeys the rules, then his opponent (the disease) will also respect him. And sometimes, your opponent can become a partner, from whose evil one learns patience, dignity, tolerance and tenacity.

References

1. Riordan J.R, Rommens J.M., Tsui L-C et al: Identification of the cystic fibrosis gene: cloning and characterisation of complementary DNA, Science, 1989, 245, 1066-1073
2. Welsh M.J, Tsui L-C, Boat T.F. et al: Cystic Fibrosis, cap in The Metabolic and Molecular Bases of Inherited Disease, 7th Ed, Qoebecor Kingsport, 1995, 3798-3875
3. Kerem E., Conway S., Elborn H., Heijermen H.: Standard of care for patients with cystic fibrosis: a European consensus, Journal of Cystic Fibrosis, 2005, 4, 7-26.
4. Popa I.: Mucoviscidosis, a Public Health Issue (Report - First National Congress of Mucoviscidosis with International Participation, Timișoara, 7-9 May 2003), Vol. Rez within the ARM Bulletin, 2003, 1, 8-95.
5. Cystic Fibrosis Foundation: Patient registry 2000 annual data report. Bethesda MD: Cystic Fibrosis Foundation 2001
6. Elborn J.S et al: Cystic fibrosis current survival and population estimates to the year 2000, Thorax, 1991, 46, 881-885
7. Popa I.: Highlights of CF care in Romania, Report to the Busines Meeting of CFW (28th European cystic Fibrosis Conference, Crete, Greece, 22-25 June, 2005).
8. Maddison J.C: Practical Guidelines for Cystic Fibrosis Care (edd Hill M.C.), Churchill Livingstone, 1998.
9. Zagorca Popa, Pop L (Popa I, sub red.): Fizioterapia în mucoviscidoză (Fibroza chistică), Ed. Mirton, 2004
10. Frederiksen et al: Antibiotic treatment of initial colonisation with Pseudomonas aeruginosa postpones chronic infection and prevents of pulmonary function in cystic fibrosis, pediatric Pulmonology, 1997, 23, 330-335.
11. Cystic Fibrosis Trust: Antibiotic treatment for cystic fibrosis – Report of the UK Cystic Fibrosis Trust Antibiotic Group, 2002.
12. Hoiby N: Microbiology of cystic fibrosis, cap in Cystic Fibrosis, 2nd ed., 2003
13. Van Biervliet et al: Docoheaxenoic acid trials in cystic fibrosis: A review of the rationale behind the clinical trials, Journal of Cystic Fibrosis, 2005, 4, 27-34.
14. Gavin J: Nutritional management, cap. in Practical Guidelines for Cystic Fibrosis Care, Churchill Livingstone, 1998
15. Borowitz et al: Consensus Report on Nutrition for Pediatric Patients with Cystic Fibrosis, Journal of Pediatric Gastroenterology and Nutrition, 2002, 35, 246-259.
16. Popa I., Pop L., Zagorca Popa: Cystic Fibrosis (Mucoviscidosis), Romanian Medical Life, 1998.
17. Moran A et al: Diagnosis, screening and management of cystic fibrosis related diabetes mellitus: a conference raport, Diabetes Res Clin Pract, 1999, 45, 61-73
18. Lask B.: Psihological aspects of cystic fibrosis, cap in Cystic Fibrosis, Chapman and Hall medical, 1995
19. Near S.Z. et al: Transition program from pediatric to adult care for cystic fibrosis patients, J Adolescent Helth, 1992, 13, 682-685)

20. Abadale B. et al: Evaluation of patients with the transition from pediatric hospital to an adult centre, *pediatr. Pulmonol.*, 1994, Supp., 10, 291-292.

21. Elkin S, Haworth C: Cystic fibrosis – related low bone mineral density, in *Cystic Fibrosis*, eds. Hodson M, Geddes D, Bush A, 2007)

Correspondence to:

Pop Liviu Laurentiu
Clinic II Pediatrics,
E Celebi Street no. 1-3,
Timisoara,
E-mail: liviupop63@yahoo.com

NEONATAL CEREBRAL MONITORING IN THE POSTNATAL TRANSITION PERIOD

Nastase Leonard^{1,2}, Stoicescu Silvia Maria^{1,2}

Abstract

The transition to extrauterine life is a complex process. Currently initial assessment at birth is clinical and that is subjective. Current methods of objective assessment of the clinical status of the newborn immediately after birth detect cardiac activity and peripheral oxygen saturation. Although these monitors during the neonatal transition appear to have some benefits, they have not yet been revealed in the long or short term. There remains controversy over which SpO₂ target should be used for resuscitation or oxygen therapy. However, these monitors do not include cerebral monitoring. The brain is the most vulnerable organ especially in the case of a hypoxic-ischemic event during labor or immediately postnatal. Thus, it is necessary to develop some non-invasive, real-time and feasible monitoring technologies in delivery room for the fetal brain status. These can significantly contribute to the optimization of neonatal resuscitation.

Keywords: newborn, cerebral status, cerebral blood flow, electric cerebral activity, cerebral oxygenation

Introduction

Monitoring this process of the Transition to extrauterine life is still a challenge in terms of early detection of disruptions. Initial assessment at birth currently includes clinical evaluation (visual inspection, palpation, auscultation, stimulus reactivity) quantified in the Apgar score including (skin coloration, muscle tone, breathing, heart rate and reflexes) [1]. But clinical evaluation of the newborn has increased variability among observers, causing similar variability of the Apgar score [2]. This variability is amplified in preterm or those requiring neonatal resuscitation [3]. Therefore, the need to monitor vital fetal or neonatal parameters to guide neonatal reanimation has increased. Currently, postnatal cardiac activity (heart rate-HR) and peripheral oxygen saturation (SpO₂) are monitored by pulse oximetry [4]. This is a routine recommendation for preterm newborns by placing the pulse oximeter sensor on the right hand to measure SpO₂ preductal [5]. But there are conflicting observations on heart rate when measured by pulsometry from ECG measurement [6]. These differences are significant in the first few minutes of life [7]. Thus, the current recommendation is to use concurrent pulse oximeter and ECG during neonatal reanimation and / or continuation

of the respiratory support. With regard to oxygenation measured by pulse oximetry, the controversy over which the SpO₂ target is to be used in case of resuscitation or oxygen therapy [8] persists. It is currently recommended to target the 25th reference value in the first 10 minutes of life [9].

Objectives

The brain is the most vulnerable organ especially in the case of a hypoxic-ischemic event during labor or immediately postnatal. Currently, cerebral status is assessed clinically only based on neurological behavior and examination of reflexes and muscle tone [8]. Current routine monitoring (SpO₂ and FC) does not provide information about oxygenation, blood flow or brain activity. Monitoring these parameters can guide the perinatal management of the fetus or neonate with significant effects on the survival or progression of short or long term neurodevelopment. The current study systematically reviews what brain function parameters can be monitored in the newborn with current technologies and assessing their feasibility in the delivery room in the immediate postpartum period.

Material and method

Systematic analysis of randomized or meta-analysis of the studies in which the newborn's cerebral status is assessed. Three different brain neonatal monitoring technologies (transfontal ultrasound, electroencephalogram and near infrared light spectroscopy) assess three different cerebral parameters (cerebral flows, cerebral electrical activity, and cerebral oxygenation). Then, the current studies on the application of these brain monitoring techniques in the delivery room during the transition to extrauterine life were analyzed.

Results

In the last decade, cerebral monitoring was attempted in the human newborn in the delivery room or in the immediate postnatal transition period, that randomly defined as the first 10-15 minutes of life [8]. Cerebral status can be assessed by measuring three main parameters: cerebral blood flow (CBF), cerebral electrical activity, and cerebral regional saturation of oxygen. Each of these brain parameters requires a different technology method.

¹UMF Carol Davila, Bucharest, Romania

²National Institute for the Mother and Child Health "Alessandrescu Rusescu", Polizu Maternity, Bucharest, Romania
E-mail: nastaseleonard@gmail.com; stoicescusiulia@yahoo.com

Thus cerebral blood flow can be assessed by Doppler ultrasound, electrical brain by electroencephalography and cerebral oxygen saturation by measuring the oxygen and non-oxygenated hemoglobin proportions by in vivo spectroscopy with near infrared light (NIRS).

1. Doppler ultrasound.

Cerebral perfusion defined cerebral blood flow (CBF) was evaluated with transfontanelar Doppler ultrasound. It has the advantage of being non-invasive and can explore brain flow in multiple brain areas. The first studies in term newborns [10-11] show a decrease of approximately 20% in systolic, diastolic and medial cerebral blood flow in the first few minutes but without changes in blood pressure or heart rate. The pulsatility index (PI) in the fetal brain flow is constant during and between contractions (1.39 ± 0.36 and 1.4 ± 0.39 respectively) [11], decreases significantly to 4 minutes postnatally (1.06 ± 0.3), increases significantly in 1 hour of life (1.5 ± 0.25) and decreases on the first day to 0.95 ± 0.25 [12]. The mode of delivery influences transient fetal brain flow, observing initial increases in the first few minutes of life, but with the equalization of the CBF and PI velocity in neonates appropriate for gestational age by caesarean versus vaginal birth [13]. Recent studies on a lot of term vaginal newborns show that the mean cerebral artery velocity decreases from 34 cm / s to 7 minutes at 25 cm / s at 14 minutes and has a dynamic evolution inversely proportional to that of shunt by patent arterial duct (PDA) [14]. Reduction of postnatal CBF may be due to increased arterial O₂ pressure and / or shunt reduction through PDA. However, the clinical implications of this postpartum decline of CBF remain questionable because comparative studies are difficult to achieve. Measurements are different due to differences in diameters of the measured arteries, insensitivity angle, or different time of measurement. Other limitations of the ultrasound method in the postpartum period are determined by the artifacts produced by the newborn movement, the assessment can not be carried out continuously, the velocity of CBF is measured, but not the CBF, and the technical difficulty in the delivery room, especially during reanimation [8].

2. Integrated Amplitude Electroencephalography (aEEG.)

May record neonatal brain electrical activity. This technique has the advantage of being a non-invasive method of continuous monitoring. aEEG trace of early life-time correlated with clinical status have prognostic value in neonates with perinatal asphyxia [15]. Recent studies of neonates have been post-partum monitored brain electrical activity with aEEG combined with monitoring regional cerebral saturation through the NIRS method. These studies have shown feasibility in this type of post-natal monitoring and increased brain activity in parallel with increased cerebral oxygenation in term newborns. The baseline aspect of the EEG is different in neonates requiring neonatal resuscitation [16]. The limitations of this method of

monitoring electrical activity are the technical difficulties of application of neonatal scalp sensors and interpretation problems due to increased artifacts incidence.

3. Near-Infrared Spectroscopy (NIRS).

In the last years, the interest for brain monitoring through NIRS in the postpartum period, has increased greatly. The first study was conducted by Peeble in 1992, a case study of a term newborn, observing the gradual increase of oxygenated hemoglobin after birth. Cerebral oxygen saturation in the immediate postnatal neonate is first reported by Isobe et al (2002) [17]. Recent studies highlight normal values in the first 10-15 minutes of term newborns born by vaginal or caesarean section and which do not require neonatal resuscitation [16]. An increase in rcSO₂ is observed parallel to the SpO₂ increase with the difference that rcSO₂ reaches a plateau at 7-8 minutes of life versus SpO₂ which achieves a maximum of 10 minutes of life [18]. rcSO₂ is significantly higher in the first 4 minutes of life in vaginal birth versus extraction through C-section (Urlesberger et al 2010). Cerebral Fractional Tissue Oxygen Extraction (Cerebral FTOE) fraction defined as the ratio of difference SpO₂-rcSO₂ to SpO₂ has an inverse dynamic, downward, versus saturation. FTOE increases after 8 minutes of life with a slight decrease in rcSO₂ in vaginal births [19]. This may be due to the decrease in cerebral flow after 8 minutes by increasing the oxygen arterial concentration and the reduction of the flow through the PCA [14]. rcSO₂ is with 7% higher in term newborns at 15 minutes of life with shunt through the PDA left-right visibly to those without a detectable shunt [20]. Cerebral FTOE compared to the somatic peripheral have a faster postnatal plateau immediately showing the favored oxygen supply of the brain [21] confirmed by the increase of CBF in this transition period confirmed by ultrasonography [11].

NIRS is a viable method during the postnatal transition period. NIRS limits are due to the differences between current devices that use different technologies and algorithms. Out of the transition period, brain oxygenation values in the newborn show approximately 10% differences between the different devices. In the case of postpartum measurements, there were differences between devices of lower rcSO₂ values of 2-3% [22]. However, this method allows the optimization of oxygen therapy in the immediate postnatal period by preventing the complications of hypoxemia or hepiroxiemia.

Discussions

The assessment of these three brain parameters and their combination can provide extremely useful information about intrapartum and postnatal fetal status during the transition period. There are some issues that may affect the measurements. As for NIRS sensors that are applied in the frontal cerebral area, excluding important brain areas that are more vulnerable to ischemic hypoxic fluctuations, and should be taken into account large brain fissures (eg. Sylvius sulcus), if sensors are applied in other areas. Maternal medication, especially analgesic or anesthetic, can

significantly affect brain parameters. We noticed a significant decrease in FTOE in neonates from mothers who received nitrous oxide analgesia (data currently under publication). aEEG is currently performed with 2 or 4 channels / sensors that may be insufficient in many cases. The optimal minimum number of aEEG sensors is 8-12 channels, but the difficulty of their application in the delivery room increases.

Conclusions

The assessment of brain status is extremely important from the delivery room. Currently, cerebral status is evaluated only by subjective clinical mode. Objective and noninvasive cerebral monitoring with appropriate devices is feasible in the delivery room. The development of these devices to assess cerebral blood flow, cerebral electrical activity, and brain oxygenation of newborn in early postpartum period provide vital information about intrapartum fetal and transitional neonatal evolution and optimize neonatal reanimation management.

References

1. Apgar V. A proposal for a new method of evaluation of the newborn infant. *Curr Res Anesth Analg* 1953;32:260–267.
2. O'Donnell CP, Kamlin CO, Davis PG, Carlin JB, Morley CJ: Interobserver variability of the 5-minute Apgar score. *J Pediatr* 2006;149:486-489.
3. Bashambu MT, Whitehead H, Hibbs AM, Martin RJ, Bhola M: Evaluation of interobserver agreement of Apgar scoring in preterm infants. *Pediatrics* 2012;130:e982-e987
4. Dawson JA, Kamlin CO, Vento M, Wong C, Cole TJ, Donath SM, Davis PG, Morley CJ: Defining the reference range for oxygen saturation for infants after birth. *Pediatrics* 2010;125:e1340-e1347.
5. Wyckoff Care Myra H., Chair; Khalid Aziz; Marilyn B. Escobedo; Vishal S. Kapadia; John Kattwinkel; Jeffrey M. Perlman; Wendy M. Simon; Gary M. Weiner; Jeanette G. Zaichkin. Part 13: Neonatal Resuscitation 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular. *Circulation*. 2015;132[suppl 2]:S543–S560
6. Katheria A, Rich W, Finer N. Electrocardiogram provides a continuous heart rate faster than oximetry during neonatal resuscitation. *Pediatrics*.2012;130:e1177–e1181.
7. van Vonderen JJ, Hooper SB, Kroese JK, Roest AA, Narayan IC, van Zwet EW, te Pas AB: Pulse oximetry measures a lower heart rate at birth compared with electrocardiography. *J Pediatr*. 2015 Jan;166(1):49-53.
8. Pichler G., Cheung P.-Y. Aziz K · Urlesberger B. Schmölzer G.M. How to Monitor the Brain during Immediate Neonatal Transition and Resuscitation: A Systematic Qualitative Review of the Literature. *Neonatology* 2014;105:205–210
9. Wyllie Jonathan, Jos Bruinenberg, Charles Christoph Roehr, Mario Rüdiger, Daniele Trevisanuto and Berndt Urlesberger. European Resuscitation Council Guidelines for Resuscitation 2015: Section 7. Resuscitation and support of transition of babies at birth. *Resuscitation*, October 2015, Pages 249 - 263
10. Sonesson SE, Winberg P, Lundell BP: Early postnatal changes in intracranial arterial blood flow velocities in term infants. *Pediatr Res* 1987;22:461-464.
11. Maesel A, Sladkevicius P, Valentin L, Marsál K: Fetal cerebral blood flow velocity during labor and the early neonatal period. *Ultrasound Obstet Gynecol* 1994;4:372-376
12. Ipsiroglu OS, Stöckler S, Häusler MC, Kainer F, Rosegger H, Weiss PA, Winter R: Cerebral blood flow velocities in the first minutes of life. *Eur J Pediatr* 1993;152:269-270
13. Maesel A, Sladkevicius P, Gudmundsson S, Marsal K: Mode of delivery and perinatal cerebral blood flow. *Early Hum Dev* 1996;44:179-185.
14. Noori S, Wlodaver A, Gottipati V, McCoy M, Schultz D, Escobedo M: Transitional changes in cardiac and cerebral hemodynamics in term neonates at birth. *J Pediatr* 2012;160:943-948.
15. de Vries LS, Hellström-Westas L. Role of cerebral function monitoring in the newborn. *Archives of Disease in Childhood - Fetal and Neonatal* Edition 2005;90:F201-FF207.
16. Pichler G, Avian A, Binder C, Zotter H, Schmölzer GM, Morris N, Müller W, Urlesberger B: aEEG and NIRS during transition and resuscitation after birth: promising additional tools; an observational study. *Resuscitation* 2013;84:974-978.
17. Isobe K, Kusaka T, Fujikawa Y, Okubo K, Nagano K, Yasuda S, Kondo M, Itoh S, Hirao K, Onishi S: Measurement of cerebral oxygenation in neonates after vaginal delivery and cesarean section using full-spectrum near-infrared spectroscopy. *Comp Biochem Physiol A Mol Integr Physiol* 2002;132:133-138
18. Fauchère JC, Schulz G, Haensse D, Keller E, Ersch J, Bucher HU, Wolf M: Near-infrared spectroscopy measurements of cerebral oxygenation in newborns during immediate postnatal adaptation. *J Pediatr* 2010;156:372-376.
19. Kratky E, Pichler G, Rehak T, Avian A, Pocivalnik M, Müller W, Urlesberger B: Regional cerebral oxygen saturation in newborn infants in the first 15 min of life after vaginal delivery. *Physiol Meas* 2012;33:95-102.

- | | |
|--|---|
| <p>20. Urlesberger B, Brandner A, Pocivalnik M, Koestenberger M, Morris N, Pichler G: A left-to-right shunt via the ductus arteriosus is associated with increased regional cerebral oxygen saturation during neonatal transition. <i>Neonatology</i> 2013;103:259-263.</p> <p>21. Urlesberger B, Grossauer K, Pocivalnik M, Avian A, Müller W, Pichler G: Regional oxygen saturation of the</p> | <p>brain and peripheral tissue during birth transition of term infants. <i>J Pediatr</i> 2010;157:740-744.</p> <p>22. Almaazmi M, Schmid MB, Havers S, Reister F, Lindner W, Mayer B, Hummler HD, Fuchs H: Cerebral near-infrared spectroscopy during transition of healthy term newborns. <i>Neonatology</i> 2013;103:246-251.</p> |
|--|---|

Correspondence to:

Leonard Nastase
National Institute for the Mother and Child Health
“Alessandrescu Rusescu”, Polizu Maternity
Gheorghe Polizu Street no. 38-52, Sector 1,
Bucharest
E-mail: nastaseleonard@gmail.com

RASPBERRY PI AS A FRAMEWORK FOR A PAIN SIGNALING SYSTEM IN THE NEONATE

Alexandra Nyiredi^{1*}, Daniela Iacob², Emil-Radu Iacob¹, Andrei Lihu³, Constantin Ilie²

Abstract

In the Neonatal Intensive Care Unit (NICU) patient monitoring is continuous and the most frequent parameters followed are the heart rate (HR) and peripheral oxygen tissue saturation (SpO₂). These parameters are also used in neonatal pain assessment when applying various pain scales. Thus, using the Raspberry Pi, a tool of Internet of Things (IoT), we created a script of data collection during NICU patient monitoring by pulse oximetry and we proposed a framework for a pain signaling system in the newborn. Data was collected by monitoring neonates undergoing painful procedures (heel stick for hypothyroidism and phenylketonuria screening and during Bacillus Calmette–Guérin (BCG) vaccination. Data plotting using the Jupyter Notebook revealed similarities in between the increase of heart rate in the presence of the painful stimulus that may lead to creating a pain signaling system in the neonate using artificial intelligence tools.

Keywords: pain, procedural pain, neonate, Internet of Things, Raspberry Pi

Introduction

Pain is considered to be the fifth vital sign that needs to be recognized and monitored in any medical ward (1). According to several studies the neonate experiences pain just like any other older child or person, however due to their impossibility to state their discomfort or degree of pain, assessment and signaling pain in the newborn is difficult (2).

Over time multiple validated pain scoring systems have been created, but there is no standardized means of assessing neonatal pain (3), and during their stay in the NICU the newborns are subjected to a multitude of painful procedures needed for both diagnosis and treatment (4-6).

What is more, the lack of diagnosis and medical intervention to neonatal pain results in physiological and behavioral impairments, together with injury to the nervous system that lead to an altered development of the future person (7).

On the other hand, impressive technological advancements have been made in most medical fields. Neonatology registered a real "boom" in this regard over the

past few decades. However great costs are involved when acquiring new technology.

The Internet of Things (IoT) defined as a interconnection among people, animal or object that is often equipped with intelligence able to exchange data over a network without involving human beings or other devices (8). And, it should allow new applications to be added, thus promoting innovation and cross-domain systems and applications to be developed (9, 10).

Within the IoT, a special object is the Raspberry Pi (RPI) a low cost, small and portable computer board that can be used as a standard PC, with a keyboard for command entry, a display unit and a power supply (11). It has a built in software that permits program or script developing and design of animation, game or videos (8).

Thus the aim of this paper is to propose a framework for a system that signals pain in the neonate using a data acquisition script created with Python and runs on a RPi.

Material and method

The project was conducted in between September - November 2017 in the Neonatology Department of the Bega University Clinic from the Timisoara County Emergency Clinical Hospital.

For this project we used: Raspberry Pi 3 B Model, Massimo Radical 7 pulse oximeter, FTDI RS232-USB convertor, network cable and a notebook. We developed a script for data collection using Python v. 2.7 that records HR and SpO₂ values of the patient during pulse oximetry monitoring. We performed data collection on 10 patients during procedural induced pain in the healthy newborn, undergoing standard heel stick procedure for hypothyroidism and phenylketonuria screening and during Bacillus Calmette–Guérin (BCG) vaccination. Data was analyzed using Jupyter Notebook.

Results

Using Jupyter Notebook, an open-source software that interactively allows use of code execution, rich text, mathematics, graphical representation and a variety of materials, we found a series of similarities in the charts created, based upon data collection from newborns undergoing procedural pain.

¹Victor Babes University of Medicine and Pharmacy Timisoara - Department of Pediatric Surgery

²Victor Babes University of Medicine and Pharmacy Timisoara - Department of Neonatology

³Polytechnic University of Timisoara – Department of Computer and Information Technology

*PhD Student

E-mail: alexnyiredi@gmail.com, danielariacob@yahoo.com, radueiacob@umft.ro, andrei.lihu@gmail.com, constantinilie@umft.ro

Below is the data plotting with two data parameters: HR and SpO2. In Figure 1, is data collected from five neonates during heel prick test and the arrow indicates the moment of procedural pain induction. Figure 2 contains the

representation of data collected during BCG vaccination in neonates. The first arrow in each picture represents the moment of pricking whereas the second arrow represents the moment of substance injection.

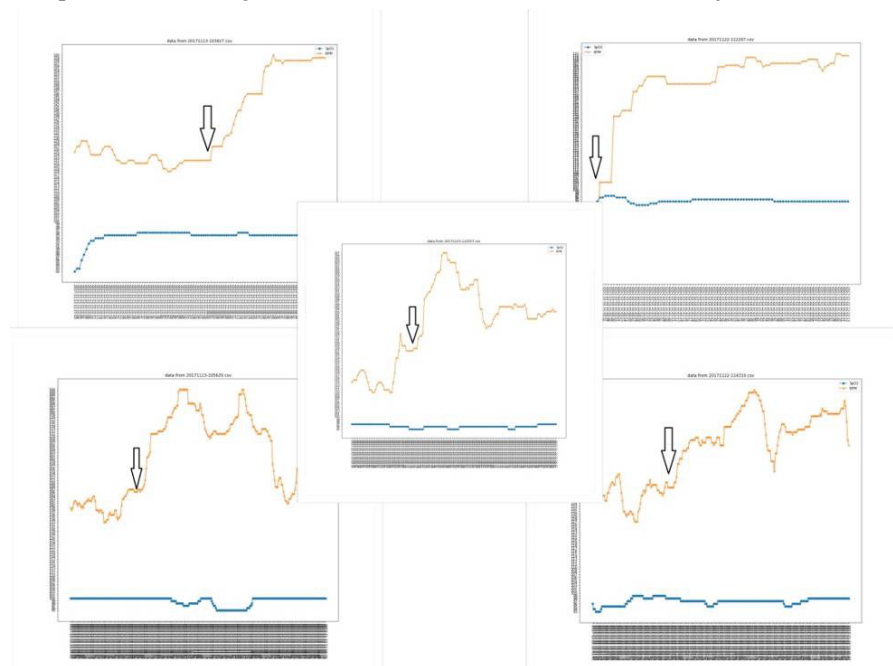


Figure 1. Heel prick test in five neonates.

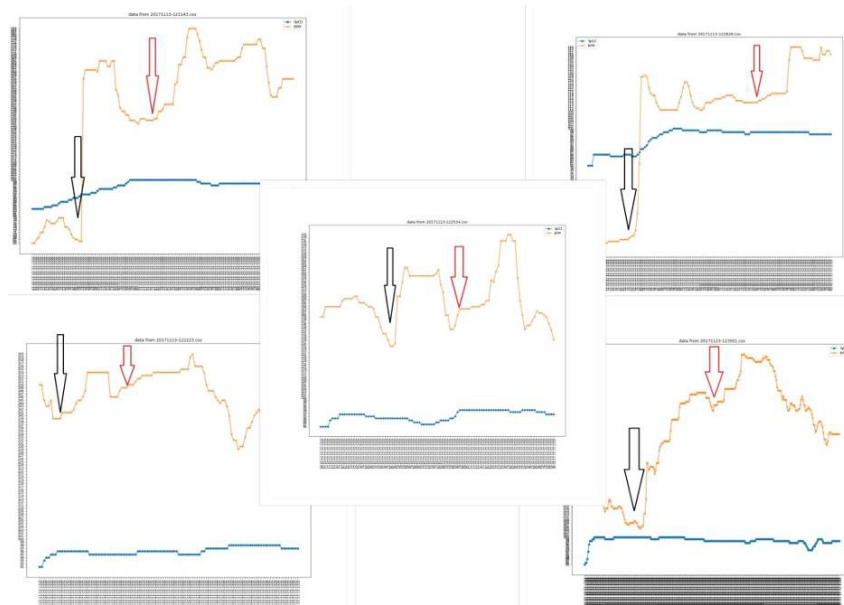


Figure 2. BCG vaccination in five neonates.

Discussions

Impressive pieces of evidence show that the newborn detects, perceives and responds to painful stimuli. They respond by three means that are: behavioral (facial expression, crying, motor response); physiologic and autonomic (HR, respiratory rate, blood pressure, intracranial

pressure, sweating, decrease in SpO2, skin color, nausea, vomiting, hiccupping, etc.) and biochemical (increased secretion of catecholamines, epinephrine, glucagon, corticosteroids/cortisol and decreased secretion of prolactin, insulin and immune responses) (1).

What is more, several pain scales are used to evaluate pain in the neonate: the neonatal infant pain scale (NIPS); neonatal facial coding system (NFCS); neonatal pain, agitation, and sedation scale (N-PASS); cry, required oxygen, increased vital signs, expression, sleeplessness scale (CRIES); COMFORT Scale; Douleur Aigue Nouveau-ne (DAN) scoring system, the premature infant pain profile (PIPP) is a validated pain scoring system for preterm neonates (2, 12). All of these scales are either unidimensional or multidimensional in connection with the number of parameters used.

In the past few years great research was oriented on a more objective means of pain assessment such as heart rate variability (HRV) - ANI/NIFE monitor -, skin conductance, near-infrared spectroscopy (NIRS), electroencephalography (EEG), and magnetic resonance imaging (MRI) (1.;13)

In creating the data collection system and framework for neonatal pain signaling we used a RPi board due to its low costs, size and most of all for its software support that is complex and user friendly. The need for a neonatal pain

signaling system is raised by the serious impairment that arises from long exposure to pain in the neonatal period, the absence of an universal pain assessment tool, and last due to the fact that there are differences between the provider's level of training and experience in the recognition of pain (14-16).

Moreover, a cheap, feasible and objective tool is needed, reasoning by which the HR and SpO2 are sole parameters used in the created software. These parameters are also returned by each pulse oximeter and regardless the level of equipment of NICU in question, there is no need for new products to be acquired.

Conclusions

Pain as a fifth vital sign needs to be signaled, monitored and treated. The proposed framework for a neonatal pain signaling system needs future work like: a large sample of data and the use of an artificial intelligence means for pattern detection would bring a solution to "painful" NICU issue.

References

1. Cong, X., et al. Pain assessment and measurement in neonates: an updated review. *Advances in Neonatal Care*, 2013, 13.6: 379-395
2. Bellieni, C.V., et al. Inter-observer reliability of two pain scales for newborns. *Early human development*, 2007, 83.8: 549-552.
3. Anand KJ, Aranda JV, Berde CB, et al. Summary proceedings from the neonatal pain-control group. *Pediatrics*. 2006;117(3 Pt 2):S9–22.
4. Cruz MD, Fernandes AM, Oliveira CR. Epidemiology of painful procedures performed in neonates: a systematic review of observational studies. *Eur J Pain*. 2016;20(4):489-98. doi: 10.1002/ejp.757. ;
5. Kyololo OM, Stevens B, Gastaldo D, Gisore P. Procedural pain in neonatal units in Kenya. *Arch Dis Child Fetal Neonatal*. 2014;99(6):F464-7. doi: 10.1136/archdischild-2014-306003;
6. Roofhooft DWE, Simons SH, Anand KJ, Tibboel D, van Dijk M. Eight years later, are we still hurting newborn infant? *Neonatology*. 2014;105(3):218-26. doi: 10.1159/000357207
7. Witt, N., et al. A guide to pain assessment and management in the neonate. *Current emergency and hospital medicine reports*, 2016, 4.1: 1-10
8. Zhao, C.W.; Jegatheesan, J.; Loon, S. C.. Exploring IOT Application Using Raspberry Pi. *International Journal of Computer Networks and Applications*, 2015, 2.1: 27-34.
9. Uckelmann D., Harrison M., Michahelles F. *Architecting the Internet of Things*. Springer 2011.
10. Maksimovic M.; Vujovic V.; Davidović N.; et. al. Raspberry Pi as Internet of Things hardware: Performances and Constraints. *Proceedings of 1st International Conference on Electrical, Electronic and Computing Engineering, IcETRAN 2014, Vrnjačka Banja, Serbia, June 2 – 5, 2014*, p. ELI1.6.1-6
11. Schmidt M. *Raspberry Pi – A Quick Start Guide*, The Pragmatic Bookshelf, 2013
12. Scott J, Huskisson EC. Graphic representation of pain. *Pain*. 1976;2(2):175–84.
13. Issa, R., et al. Evaluation of the analgesia nociception index (ANI) in healthy awake volunteers. *Canadian Journal of Anesthesia/Journal canadien d'anesthésie*, 2017, 1-8.
14. Stevens BJ, Abbott LK, Yamada J, et. al. CIHR team in children's pain. epidemiology and management of painful procedures in children in canadian hospitals. *CMAJ*. 2011;183(7):E403–10.
15. Karling M, Renström M, Ljungman G. Acute and postoperative pain in children: a Swedish nationwide survey. *Acta Paediatr*. 2002;91(6):660–6.
16. Carbajal R, Rousset A, Danan C, et. al. Epidemiology and treatment of painful procedures in neonates in intensive care units. *JAMA*. 2008;300(1):60–70.

Correspondence to:

Daniela Iacob
Victor Babes University of Medicine and Pharmacy Timisoara
- Department of Neonatology
Eftimie Murgu Square, no. 2,
Timisoara
E-mail: danielariacob@yahoo.com

NEONATAL NEUROLOGICAL OUTCOME OF SMALL FOR GESTATIONAL AGE VERSUS PREMATURE INFANTS

Teofana Bizerea^{1,2}, Ramona Stroescu^{1,2}, Constantin Ilie^{1,3}, Claudiu Angelescu^{1,3},
Stefana-Gheorghina Dezs^{4,5}, Otilia Mărginean^{1,2}

Abstract

Introduction Neonates born prematurely or small for gestational age (SGA) as a consequence of intrauterine growth restriction (IUGR) have a higher risk of neurological injury due to fetal hypoxia. Hypoxic ischemic encephalopathy (HIE) and intraventricular hemorrhage (IVH) are the main clinical forms of brain injury. The patterns and underlying mechanisms of neurological injury are interrelated. **Aim of the study** The purpose of the study was to evaluate the neurological outcome of SGA newborns versus neonates born preterm. **Materials and methods** A 3 year randomized case – control study was conducted between the 1st of January 2014 and the 31th of December 2016, at the Emergency County Hospital, Timisoara. 170 SGA newborns and 170 AGA newborns matched 1:1 for gestational age and birth month were included in the study. Patients were divided in 4 subgroups according to gestational age: 101 SGA newborns born at term (SGA-Term) and 69 SGA newborns born preterm (SGA-Preterm), 101 AGA neonates born at term (AGA-Term) and 69 AGA neonates born preterm (AGA-Preterm). **Results and discussions** Preterm neonates had difficulties of early neonatal adaptation, as indicated by a low APGAR score. Preterm neonates irrespective of birth weight, had a higher incidence of both HIE (26.1% SGA Preterm versus 11.8% SGA Term and 11.5% AGA Preterm compared to 0.0% AGA Term) and IVH (20.3% SGA Preterm versus 7.9% SGA Term and 15.9% AGA Preterm compared to 0.0% AGA Term). **Conclusions** Neonates born preterm have a poorer neurological outcome compared to term newborns, regardless of birth weight. SGA is an additional, aggravating factor for neurological injury. More extensive studies on the different subgroups of SGA newborns are required in order to understand the underlying mechanisms.

Keywords: newborn, neurological injury, fetal hypoxia

Introduction

Preterm and small for gestational age (SGA) births with associated intrauterine growth restriction (IUGR) have been

linked to neonatal neurological morbidity [1-5]. These disturbances of intrauterine growth and development are caused by an impaired placental blood flow with subsequent chronic fetal hypoxia [6-9]. Fetal and neonatal brain development is vulnerable to oxidative stress from hypoxic-ischemic injury. Although, disturbances in vascular autoregulation and their effect on the immature vascular supply of the brain represent a common pathway to neurological damage, establishing a causal relationship between type and onset of the neurological insult and specific forms of brain injury is difficult due to the fact that the underlying mechanisms are multifactorial and overlapping. Hypoxic ischemic encephalopathy (HIE) and intraventricular hemorrhage (IVH) represent the main clinical forms of brain injury that occur as a result of repeated episodes of ischemia-reperfusion during the prenatal, intrapartum or postnatal period [3, 10-12].

Aim of the study

The purpose of the study was to evaluate the neurological outcome of SGA newborns versus neonates born preterm by evaluating the incidence, risk factors and underlying mechanisms of HIE and IVH in these newborns.

Material and method

A 3 year randomized case – control study was conducted between the 1st of January 2014 and the 31th of December 2016, at the Neonatology Department of the Clinic of Obstetrics, Gynecology and Neonatology, Emergency County Hospital, Timisoara.

According to the literature, newborns are framed as being SGA if their length and/or height is less than two standard deviations (< -2SD) below the mean for gestational age or less than the 10th percentile (< Perc 10%) of a population-specific birth weight [13, 14]. Likewise, preterm birth is defined as a live birth that occurs prior to 37 weeks of gestation [15, 16].

¹“Victor Babes” University of Medicine and Pharmacy, Timisoara, Romania

²1st Pediatric Clinic “Louis Turcanu” Children’s Clinical and Emergency Hospital, Timisoara, Romania

³Clinic of Obstetrics, Gynecology and Neonatology, “Pius Brânzeu” Emergency County Hospital, Timisoara, Romania

⁴West University of Timisoara, Department of Biology-Chemistry, Timisoara, România

⁵Laboratory of Advanced Researches in Environmental Protection, Timisoara, România

E-mail: teofanabizerea@yahoo.com, ramona.giurascu@gmail.com, constantinilie@umft.ro, angelescu.claudiu@ymail.com, omarginean@ymail.com, stefana.dezsi@yahoo.com

Patient data collected from medical records was anonymized and organized into an electronic directory. Medical records of all inborn patients aged between 0-28 days were reviewed. Patient selection was made according to the following exclusion criteria: syndromal, chromosomal or infectious etiology of low birth weight and chronic maternal disease.

The study group consisted of 170 SGA newborns and the control group of AGA neonates was matched 1:1 for gestational age and birth month. Patients were divided in 4 subgroups according to gestational age: 101 SGA newborns born at term (SGA-Term) and 69 SGA newborns born

preterm (SGA-Preterm), 101 AGA neonates born at term (AGA-Term) and 69 AGA neonates born preterm (AGA-Preterm).

Cerebral ultrasound was performed in the first day postpartum in all newborns included in the study. Changes of the cerebral structure consistent with HIE or IVH were noted.

HIE was diagnosed using an ultrasound classification adapted from Ilves (Table 1) [17].

IVH was evaluated by ultrasound and classified according to the grading systems of Papile et al. and Volpe, shown in Table 2 [5, 18].

Table 1. Ultrasound findings in Hypoxic-Ischaemic Encephalopathy adapted from Ilves.

Form Method	Mild	Moderate	Severe
Grey-Scale Sonography	moderate increase of parenchymal echogenicity; age: 48 -72 h		moderate/severe increase of parenchymal echogenicity; age: 12 ± 2 h
	reversed appearance of hypoechoic grey matter and hyperechoic white matter		increased echogenicity with central pattern of injury
	spared regions: brainstem, cerebellum, deep grey matter structures		affected regions: deep grey matter structures
Doppler Sonography	increased mean cerebral blood flow velocity (BFV) in all the cerebral arteries		severe increase in cerebral BFV
	diminished resistive indexes (RI) in the cerebral arteries		decrease in RI hypovascularity and/or hyperemia in the basal ganglia

Table 2. Ultrasound grading of Intraventricular Hemorrhage.

Grade	Papile Criteria	Volpe Criteria
I	unilateral/bilateral germinal matrix hemorrhage	germinal matrix hemorrhage with no IVH or IVH occupying < 10% of the ventricular area on parasagittal view
II	IVH without ventricular dilatation	IVH occupying 10- 50% of the ventricular area on parasagittal view
III	IVH with ventricular dilatation	IVH occupying 50% of the ventricular area on parasagittal view ± periventricular echodensities
IV	IVH extending into adjacent brain parenchyma	periventricular venous hemorrhagic infarction (PVHI); cystic periventricular leukomalacia

Results

Anthropometric characteristics and neonatal adaptation score of the studied groups are shown in Table 3. Difficulties of early neonatal adaptation, as indicated by a

low APGAR score, are noticed in preterm neonates in both SGA study group and AGA control group.

Table 3. Anthropometric data and neonatal adaptation score of the studied neonates.

Group		n	Gestational Age	Birth Weight	Birth Length	APGAR score
SGA Study Group	Term	101	39.48 ± 1.18	2296.46 ± 163.14	46.67 ± 1.67	8.81 ± 0.70
	Preterm	69	34.49 ± 1.94	1706.60 ± 374.56	43.00 ± 2.87	8.05 ± 1.25
AGA Control Group	Term	101	40.00 ± 1.15	3427.17 ± 467.18	50.90 ± 0.35	9.00 ± 0.56
	Preterm	69	33.44 ± 2.04	2282.08 ± 147.12	46.34 ± 1.01	8.49 ± 0.90

AGA – appropriate for gestational age; SGA-small for gestational age.

Figures 1 and 2 show the percentage distribution of HIE and IVH respectively, among newborns included in the study.

Preterm neonates irrespective of birth weight, have a higher incidence of HIE, namely 26.1% SGA Preterm versus 11.8% SGA Term and 11.5% AGA Preterm compared to 0.0% AGA Term. A higher incidence of IVH in both SGA and AGA preterm neonates was also noticed: 20.3% SGA Preterm versus 7.9% SGA Term and 15.9% AGA Preterm compared to 0.0% AGA Term newborns.

HIE and IVH classification according to severity are illustrated in Figures 3 and 4. As shown in Figures 3 and 4, SGA-Preterm neonates have the most severe degree of impairment of both HIE and IVH: 22.2% severe HIE and 6.6% grade IV IVH respectively.

Figure 5 displays a significant correlation between metabolic acidosis and HIE. It can be mentioned that there was no such correlation noted between metabolic acidosis and IVH.

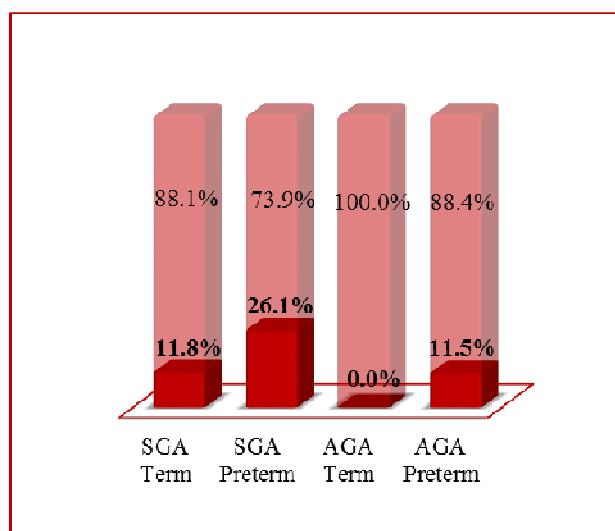


Fig.1: Incidence of HIE among studied neonates.

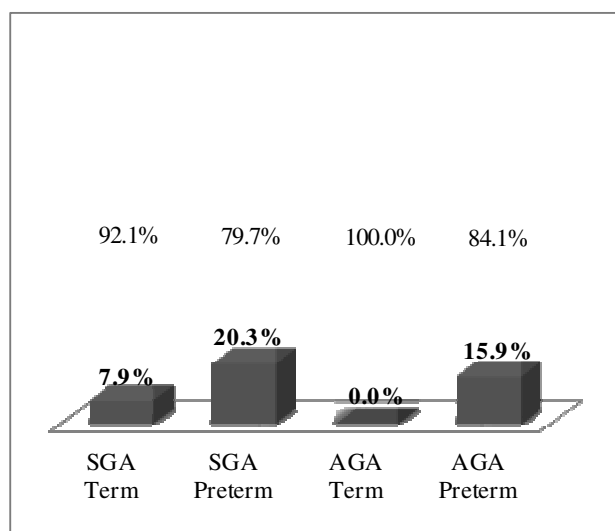


Fig.2: Incidence of IVH among studied newborns.

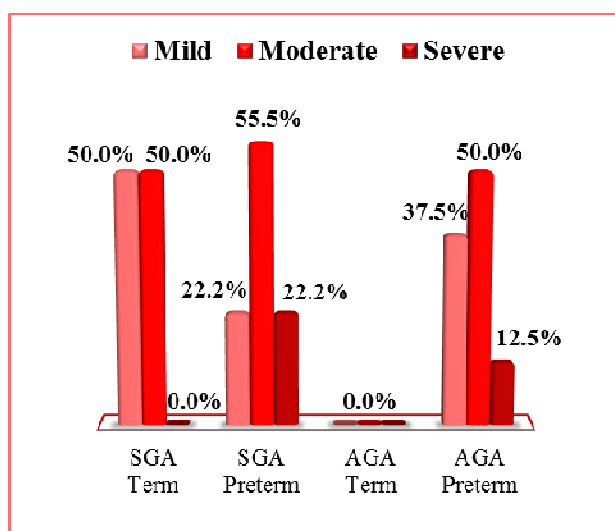


Fig.3: HIE severity classification in the studied groups.

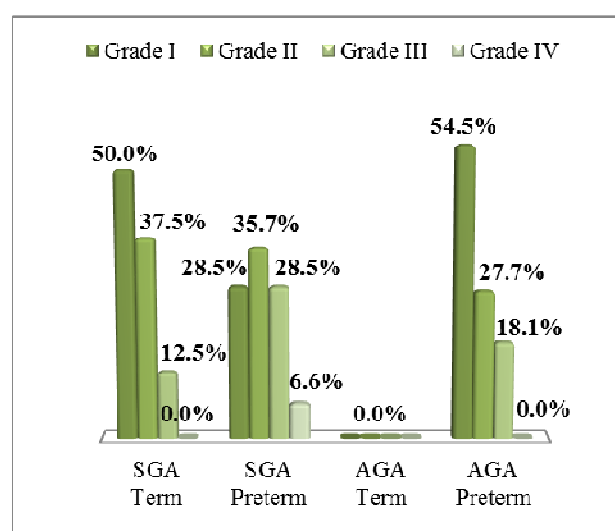


Fig.4: IVH severity distribution in the studied groups.

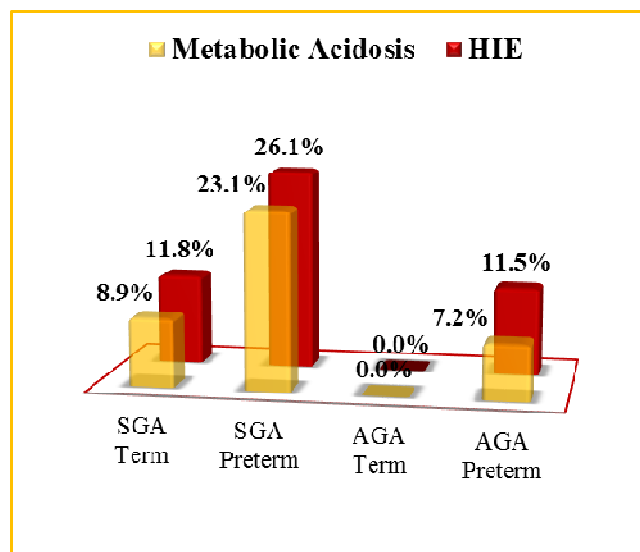


Fig.5: Metabolic acidosis and HIE overlap in the study groups.

Discussions

HIE and IVH are believed to be pathologically interrelated [19-21]. This is also supported by results of the current study which underline similar patterns regarding percentage distribution of both HIE and IVH.

While data from literature support a strong correlation between preterm birth and HIE [4, 22, 23] the link between prematurity and IVH continues to be debated [5, 18, 24]. In this study both HIE and IVH had a higher incidence among premature neonates regardless of birth weight, suggesting that the potential underlying mechanism might be explained as a hypoxic injury affecting immature cerebral structures.

Impaired cerebral blood flow and oxygen delivery to the immature brain are possible processes linking premature birth and hypoxic-ischemic neurological injury [10, 25]. This could explain why prematurity and superimposed SGA are stronger correlated to HIE and IVH compared to SGA alone.

Conclusions

Premature birth appears to be directly linked to neurological morbidity in neonates irrespective of birth weight.

The incidence of HIE and IVH was higher in SGA Preterm neonates, which leads to the conclusion that SGA is an additional, aggravating factor for neurological injury.

Further studies comparing the effect of preterm birth versus SGA as a consequence of IUGR on neonatal neurological outcome are needed in order to fully understand the underlying mechanisms.

Acknowledgement:

The first author acknowledges that this paper was published under the frame of European Social Found, Human Resources Development Operational Programme 2007-2013, Project: Parteneriat strategic pentru creșterea calității cercetării științifice din universitățile medicale prin acordarea de burse doctorale și postdoctorale – DocMed.Net_2.0, POSDRU/159/1.5/S/136893.

References

1. Roelants-van Rijn, A.M., et al., Cerebral structure and metabolism and long-term outcome in small-for-gestational-age preterm neonates. *Pediatr Res*, 2004. 56(2): p. 285-90.
2. Futrakul, S., P. Praisuwanna, and P. Thaitumyanon, Risk factors for hypoxic-ischemic encephalopathy in asphyxiated newborn infants. *J Med Assoc Thai*, 2006. 89(3): p. 322-8.
3. Vesoulis, Z.A. and A.M. Mathur, Cerebral Autoregulation, Brain Injury, and the Transitioning Premature Infant. *Frontiers in Pediatrics*, 2017. 5(64).
4. Vladareanu, S., et al., Correlation between maternal risk factors and hypoxic ischemic encephalopathy in preterm neonates. *Proceedings of the 49th Annual Scientific Meeting of the European Society for Clinical Investigation*, 2015: p. 343-347.
5. Volpe, J.J., Intraventricular hemorrhage in the premature infant—current concepts. Part I. *Annals of Neurology*, 1989. 25(1): p. 3-11.
6. Hampl, V. and V. Jakoubek, Regulation of fetoplacental vascular bed by hypoxia. *Physiol Res*, 2009. 58 Suppl 2: p. S87-93.
7. Hutter, D., J. Kingdom, and E. Jaeggi, Causes and mechanisms of intrauterine hypoxia and its impact on the fetal cardiovascular system: a review. *Int J Pediatr*, 2010. 2010: p. 401323.

8. Kadyrov, M., et al., Maternal-Placental Interactions and Fetal Programming. *Zeitschrift Fur Geburtshilfe Und Neonatologie*, 2013. 217(3): p. 88-94.
9. Irwinda, R., R. Surya, and L.F. Nembo, Impact of pregnancy-induced hypertension on fetal growth. *Medical Journal of Indonesia*, 2016. 25(2): p. 104.
10. Allen, K.A. and D.H. Brandon, Hypoxic Ischemic Encephalopathy: Pathophysiology and Experimental Treatments. *Newborn Infant Nurs Rev*, 2011. 11(3): p. 125-133.
11. Baburamani, A.A., et al., Vulnerability of the developing brain to hypoxic-ischemic damage: contribution of the cerebral vasculature to injury and repair? *Front Physiol*, 2012. 3.
12. Malhotra, A., et al., Detection and assessment of brain injury in the growth restricted fetus and neonate. *Pediatr Res*, 2017.
13. Sharma, D., S. Shastri, and P. Sharma, Intrauterine Growth Restriction: Antenatal and Postnatal Aspects. *Clinical Medicine Insights. Pediatrics*, 2016. 10: p. 67-83.
14. Niklasson, A., et al., An update of the Swedish reference standards for weight, length and head circumference at birth for given gestational age (1977-1981). *Acta Paediatr Scand*, 1991. 80(8-9): p. 756-62.
15. Institute of Medicine Committee on Understanding Premature, B. and O. Assuring Healthy, The National Academies Collection: Reports funded by National Institutes of Health, in *Preterm Birth: Causes, Consequences, and Prevention*, R.E. Behrman and A.S. Butler, Editors. 2007, National Academies Press (US) National Academy of Sciences.: Washington (DC).
16. Howson, C.P., et al., Born Too Soon: Preterm birth matters. *Reproductive Health*, 2013. 10(Suppl 1): p. S1-S1.
17. Pilvi Ilves, Sonographic Changes in Hypoxic-Ischaemic Encephalopathy, *Miscellanea on Encephalopathies - A Second Look*, Dr. Radu Tanasescu (Ed.), InTech, 2012; DOI: 10.5772/47907.
18. Papile, L.-A., et al., Incidence and evolution of subependymal and intraventricular hemorrhage: A study of infants with birth weights less than 1,500 gm. *The Journal of Pediatrics*, 1978. 92(4): p. 529-534.
19. Hill, A. and J.J. Volpe, Seizures, hypoxic-ischemic brain injury, and intraventricular hemorrhage in the newborn. *Annals of Neurology*, 1981. 10(2): p. 109-121.
20. Douglas-Escobar, M. and M. Weiss, Biomarkers of Brain Injury in the Premature Infant. *Frontiers in Neurology*, 2013. 3(185).
21. Barnes, P.D., Neuroimaging and the timing of fetal and neonatal brain injury. *J Perinatol*, 2001. 21(1): p. 44-60.
22. Gopagondanahalli, K.R., et al., Preterm Hypoxic–Ischemic Encephalopathy. *Frontiers in Pediatrics*, 2016. 4: p. 114.
23. Logitharajah, P., M.A. Rutherford, and F.M. Cowan, Hypoxic-ischemic encephalopathy in preterm infants: antecedent factors, brain imaging, and outcome. *Pediatr Res*, 2009. 66(2): p. 222-9.
24. Kratzer, I., S. Chip, and Z.S. Vexler, Barrier mechanisms in neonatal stroke. *Frontiers in Neuroscience*, 2014. 8(359).
25. de Vries, L.S. and F. Groenendaal, Patterns of neonatal hypoxic–ischaemic brain injury. *Neuroradiology*, 2010. 52(6): p. 555-66.

Correspondence to:

Teofana Otilia Bizerea
I. Nemoianu Street, no.2,
Timisoara,
Romania,
E-mail: teofanabizerea@yahoo.com

NEUROFIBROMA OF THE THIGH WITH COMPRESSION OF THE SCIATIC NERVE IN A CHILD

Narcis Flavius Tepeneu^{1,2}

Abstract

Peripheral nerve sheath tumors account for nearly 12% of the benign and 7-8% of the malignant soft tissue neoplasms. Neurofibromas and schwannomas constitute the benign category, while the malignant peripheral nerve sheath tumor (MPNST) comes under the malignant category.

A 5 year old male patient was admitted to the hospital having a painful tumor of approximately 10 cm diameter on the posterior left thigh with sciatic neuropathy and flexion contracture of the knee.

The patient was living in the rural area under poor social conditions. A neurofibromatosis type I was diagnosed and the child underwent successful surgical removal of the tumor which was compressing the sciatic nerve without relapse at follow-up 18 month after surgery. The histology confirmed the suspicion of a neurofibroma. After postoperative physiotherapy he could resume walking.

Keywords: neurofibromatosis type I (NF I), sciatic nerve, neurofibroma, sciatic neuropathy, child

Introduction

Peripheral nerve sheath tumors account for nearly 12% of the benign and 7-8% of the malignant soft tissue neoplasms. Neurofibromas and schwannomas constitute the benign category, while the malignant peripheral nerve sheath tumor (MPNST) comes under the malignant category.

Neurofibromatosis, also named von Recklinghausen disease for the man who described the disease in 1882, was formerly considered a single disease but is now known to be at least two clinically and genetically distinct diseases. The more common disease, formerly known as the peripheral form of neurofibromatosis, is designated neurofibromatosis 1 (NF1), whereas the less common disease, formerly known as the central form, is designated neurofibromatosis 2 (NF2) (bilateral vestibular schwannoma). A common genetic disease, NF1 affects 1 in every 3500 individuals. It is inherited as an autosomal dominant trait with a high rate of penetrance. Because only half of the patients with this disease have affected family members, the disease in the remaining patients represents new mutations. In the typical patient, NF1 becomes evident within the first few years of life when café au lait spots develop. These pigmented macular lesions resemble freckles, especially during the early stage when they are small. Typically, they become

much larger and darker with age and occur mainly on unexposed surfaces of the body.

Neurofibromas, the hallmark of the disease, make their appearance during childhood or adolescence after the café au lait spots. The time course varies greatly: some tumors emerge at birth, and others appear during late adult life.

They may be found in virtually any location and, in rare instances, may be restricted to one area of the body (segmental neurofibromatosis). Unusual symptoms have been related to the presence of these tumors in various organs such as the gastrointestinal tract. The tumors are usually slowly growing lesions. Acceleration of their growth rate has been noted during pregnancy and at puberty. A sudden increase in the size of one lesion should always raise the question of malignant change.

Case presentation

A 5 year old male patient was admitted to the hospital having a painful tumor of approximately 10 cm diameter on the posterior left thigh with signs of sciatic neuropathy and flexion contracture of the knee (Figure 1). The patient was living in the rural area under poor social conditions.

On clinical exam multiple café au lait spots were present. After a careful anamnesis a neurofibromatosis type I was suspected. The father of the patient turned out to have also multiple criteria for neurofibromatosis I.

The patient was then investigated and a neurofibromatosis I was confirmed. The patient had a optic glioma and 3 Lisch nodules. He also had palpable neurofibromas on the left arm, but without an obvious symptomatology.

X-rays of the left thigh showed no abnormalities. Ultrasound of the tumefaction revealed a non-compressive, anechoic mass with a marginal Doppler signal. Magnetic resonance imaging (MRI) showed a tumor of the thigh with dimensions of 10,4x8,9x6,8 cm with compression of the sciatic nerve with low signal intensity on T1 images, high signal intensity on T2 images, and a heterogeneous pattern.

Foot weakness with primarily tibialis anterior weakness (foot drop) was seen in the patient. Intensity of pain as a symptom of sciatic neuropathy was difficult to evaluate in the young patient, but the parents were able to report that in the last 2 weeks before presenting to the hospital ambulation was not possible at all. Muscular knee contraction was present at clinical examination. A surgical excision of the neurofibroma was performed under general anesthesia (Figure 2, Figure 3).

¹Department of Pediatric and Adolescent Surgery, General Hospital Klagenfurt, Austria

²“Victor Babes” University of Medicine and Pharmacy Timisoara, Romania

E-mail: nftepeneu@yahoo.com



Figure 1 – Clinical aspect of the neurofibroma.

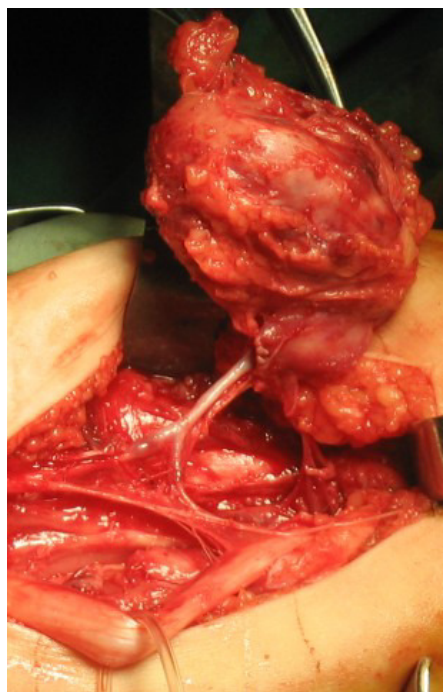


Figure 2 – Intraoperative aspect.

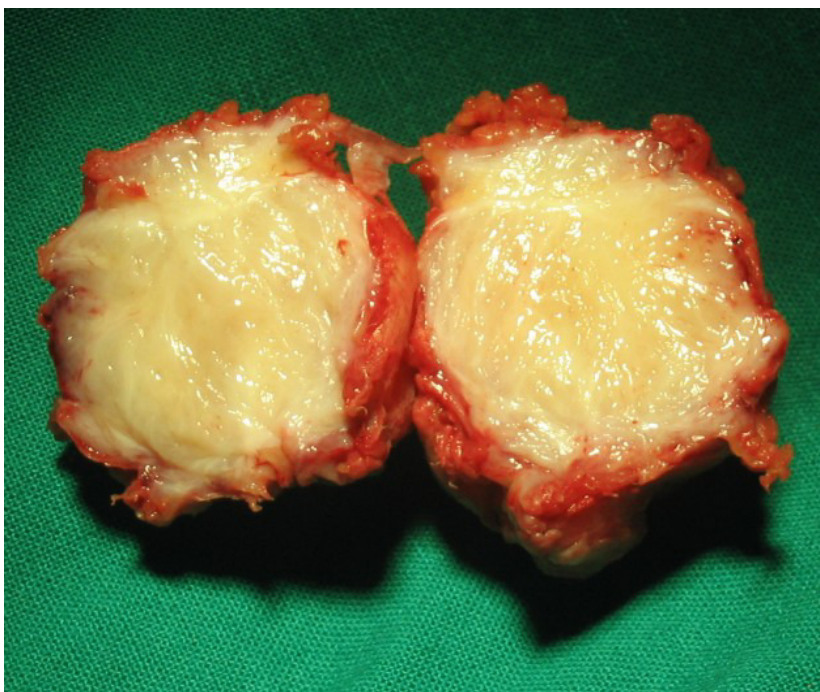


Figure 3 – Removed neurofibroma.

Histological examination confirmed the diagnosis (Figure 4).

There were no complications in the postoperative period. The patient was released from the hospital on the 6th postoperative day. After postoperative physiotherapy he was able to resume walking.

No local relapse of the tumor at follow-up 18 month after surgery was noticed clinically and on control MRI.

Unfortunately the patient was lost from our evidence because the family emigrated to a foreign country.

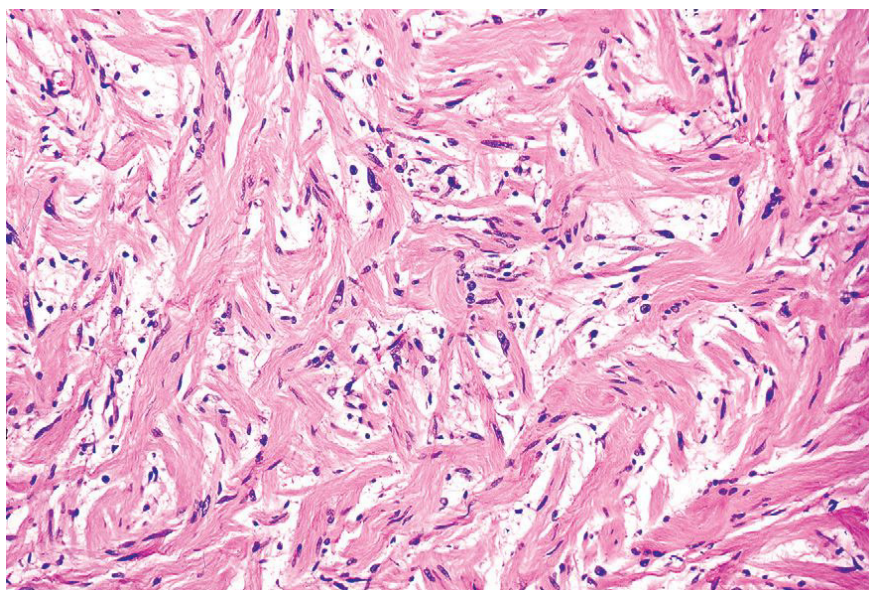


Figure 4 – Histological aspect.

Discussions

A neurofibroma is a benign tumor of the connective tissue, specifically the endoneurium, of peripheral nerves [1]. It is generally associated with neurofibromatosis type I; however, it can occur in isolation, in which case it is called a solitary neurofibroma. This tumor is rare, unlike

a schwannoma, which is the most frequent tumor of the peripheral nerves; the prevalence of schwannomas reached 55 % of all tumors in some series [2]. Both tumors result from the nerve sheath, which in turn originates from the neuroectoderm and neural crest. The distinction between a schwannoma and neurofibroma is important. Neurofibromas deeply invade the nerve, and total resection often has functional consequences; in contrast, schwannomas arise from Schwann cells and form a macroscopically smooth, rounded, yellowish, encapsulated proliferation, the enucleation of which is easy and without loss of continuity [1].

In addition to peripheral neurofibromas, patients with NF1 also develop central nervous system tumors, including optic nerve glioma, astrocytoma, and a variety of heterotopias. Vestibular

schwannoma, the hallmark of NF2, is virtually never encountered in NF1.

Ultrasound can help in detecting and diagnosing nerve tumors. In their classic forms, peripheral nerve tumors are well-defined, round, oval or spindle hypoechoic masses [3] as eccentric masses with a homogeneous structure, acoustic posterior enhancement, intratumoral cystic modifications, and intratumoral vascularity on color Doppler examination. In contrast, neurofibromas appear echogenic and hypovascular on Doppler examination [3,4,5]. MRI is a gold standard for evaluating nerve tumors.

The signal intensity of a normal nerve on MRI is of intermediate to low on T1-weighted sequences becoming

slightly higher on T2-weighted and other fluid-sensitive sequences.

In entrapment syndromes of peripheral nerves hyperintense signal of the denervated muscle

is usually identified when entrapment is acute, and fatty infiltration and muscle atrophy are the signs of chronic neuropathy in longstanding cases [6,7].

In most cases, MRI permits differentiation between neurofibromas and schwannomas. A rounded appearance, peripheral location, and more or less homogeneous, central low signal intensity on T2-weighted images are the characteristics of schwannomas; neurofibromas are usually heterogeneous on both T1 and T2 images [8,9].

Plexiform neurofibromas as well as neurofibromas of larger nerves have a significantly higher risk of malignancy than solitary neurofibromas of smaller nerves [10,11]. This is why it is important to have an exact diagnosis, which sometimes ultimately requires surgery and histopathological examination as in the case of our patient.

MRI following the administration of intravenous contrast materials improves contrast resolution in evaluation of soft-tissue tumors [10]. Imaging following contrast is particularly important with masses that have high water content or are composed of prominent necrotic/hemorrhagic foci allowing identification and differentiation of these regions from enhancing solid cellular tissue [12].

Surgical treatment for the nerve sheath tumors such as schwannoma or neurofibroma is primarily reserved for the symptomatic tumors.

McMillan et al. have reported 7 cases of sciatic neuropathy due to tumor [13]. In 3 children, this was due to infiltration of the nerve by sarcomas external to the nerve, an osteosarcoma of the femur in 2 patients and a rhabdomyosarcoma of the pelvis in one child.

Venna et al. reported a case of a child with unilateral chronic progressive sciatic nerve dysfunction found to be due to nerve entrapment in the thigh by a fibrovascular band. Sectioning of the band was followed by marked improvement in the nerve function. They concluded that compression by a band is a rare but treatable cause of sciatic neuropathy [14].

Conclusions

Sciatic neuropathy is an uncommon mononeuropathy in children and the causes of sciatic neuropathy are varied and

unique. Peripheral nerve tumors of the sciatic nerve is a rare condition. Especially, primary tumors of the sciatic nerve are rare. A palpable mass is usually the only presenting symptom of peripheral nerve tumors. Other clinical symptoms include radicular pain, paresthesia, hypoesthesia and motor deficiencies. Sciatic neuropathy due to neurofibroma of the thigh in a child 5 years of age is also a very rare condition, which to the best of our knowledge has never been described in the medical literature.

References

1. Le Guellec S. Nerve sheath tumors. *Ann Pathol.* 2015;35:54–70.
2. Tiel R, Kline D. Peripheral nerve tumors: surgical principles, approaches, and techniques. *Neurosurgery Clinics of North America*, 2004, 15 (2): 167–75– vi.
3. Bianchi S, Montet X, Martinoli C, Demondion X, Bard H. Échographie des nerfs des membres inférieurs. *Rev Rhum.* 2007;74:415–23.
4. Martinoli C, Bianchi S, Gandolfo N, Valle M, Simonetti S, Derchi LE. US of nerve entrapments in osteofibrous tunnels of the upper and lower limbs. *Radiographics.* 2000;20:199–213.
5. Hoddick WK, Callen PW, Filly RA, Mahony BS, Edwards MB. Ultrasound evaluation of benign sciatic nerve sheath tumors. *J Ultrasound Med.* 1984;3:505–7.
6. Kim S. J., Hong S. H., Jun W. S. et al., MR imaging mapping of skeletal muscle denervation in entrapment and compressive neuropathies, *Radiographics*, vol. 31, no. 2, pp. 319–332, 2011.
7. Petchprapa C. N., Rosenberg Z. S., Sconfienza L. M., Cavalcanti C. F. A., Vieira R. L., and Zember J. S., MR imaging of entrapment neuropathies of the lower extremity: part 1. The pelvis and hip, *Radiographics*, vol. 30, no. 4, pp. 983–1000, 2010.
8. Kralick F, Koenigsberg R. Sciatica in a patient with unusual peripheral nerve sheath tumors. *Surg Neurol.* 2006;66:634–7.
9. Huang J, Mobbs R, Teo C. Multiple schwannoma of the sciatic nerve, *J Clin Neurosci.* 2003;10:391–3.
10. Artico M, Cervoni L, Wierzbiński V, D'Andrea V, Nucci F. Benign neural sheath tumours of major nerves: characteristics in 119 surgical cases. *Acta Neurochirurgica*, 1997, 139 (12): 1108–1116.
11. Baehring JM, Betensky RA, Batchelor TT. Malignant peripheral nerve sheath tumor: the clinical spectrum and outcome of treatment. *Neurology*, 2003 61 (5): 696–698.
12. Benedikt RA, Jelinek JS, Kransdorf MJ, Moser RP, Berrey BH. MR imaging of soft-tissue masses: role of gadopentetate dimeglumine. *J Magn Reson Imaging*, 1998, 4:485–490., 1994, 11–828.
13. McMillan HJ, Srinivasan J, Darras BT, et al. Pediatric sciatic neuropathy associated with neoplasms. *Muscle Nerve* 2011;43:183–188.
14. Venna N, Bielawski M, Spatz EM. Sciatic nerve entrapment in a child: case report. *J Neurosurg* 1991;75:652–654.

Correspondence to:

Tepeneu Narcis Flavius
Department of Pediatric and Adolescent Surgery,
General Hospital Klagenfurt,
Feschnigstraße 11
9020 Klagenfurt,
Austria,
T +43 463 538-39303
F +43 463 538-39306
E-mail: nftepeneu@yahoo.com

OTITIS MEDIA IN CHILDREN-RISK FACTORS AND COMPLICATIONS

Ana-Simona Drochio¹, Magdalena Iorga², Mihaela Corlade-Andrei³,
Elena-Madalina Pitorac⁴, Dana-Teodora Anton-Păduraru¹

Abstract

Introduction: Acute otitis media (AOM) is the most frequent diagnosis of the sick children visiting clinicians' offices and the most common reason for administration of antibiotics.

Method: The study included 104 patients discharged from Pediatric Clinic III - "Saint Mary's" Children's Clinical Emergency Hospital of Iasi from January 2015 to January 2017, diagnosed with "Acute otitis media".

Objective: On this batch we performed a retrospective study based on the data found in the children's medical charts, by observing the risk factors to which they were exposed and that favor the illness, and also the connection between the risk factors and the occurrence of complications.

Results: The risk factors for acute otitis media that we identified in this group were the cold season, male gender, premature birth, low birth weight, artificial alimentation in the first year of life, incorrect dietary diversification, child's becoming a community member, higher number of siblings, association of respiratory tract infections, of chronic diseases or immune deficiencies, allergic status, exposure to pollutants. To prevent premature and late complications, it is important to accurately specify the diagnosis and establish individualized therapy according to guidelines. It is also essential to follow up and ensure directly observed therapy for children through the collaboration of a pediatrician with the family doctor and the ENT specialist.

Keywords: acute otitis media, prevalence, risk factors, children

Introduction

Upper respiratory tract infections represent the most frequent cause for doctor consults, but also for mortality in patients under 5 years old, regardless of whether they come from developed or developing countries. A significant proportion of upper respiratory tract infections (approximately 30%) is represented by acute otitis media,

often a complication of other respiratory pathologies. It is estimated that 20,000 people die annually due to complications of otitis media and the majority are children under 5 years old (1).

RISK FACTORS

Over the years, several hypotheses have been launched to justify the increased prevalence of acute otitis media in pediatric patients compared to adults.

It was found that the age between 6 months and 3 years, followed by the age of 4-5 years - associated with the moment of becoming a community member is the main risk factor in the occurrence of this infection, besides the anatomical features of the child (shorter and horizontalized Eustachian tube) (5,7). Also, about one third of children with otitis media have a genetic dysfunction of the Eustachian tube or other syndromes with anatomic anomalies (palatoschisis) or changes in the airways' function that could favor neighboring infections (Kartagener's syndrome) (5). Acute adenoiditis characteristic of children leads to decreased nasal pH, with persistence of bacterial outbreak. These factors result in varying degrees of tubal obstruction, with pressure drop in the middle ear, resorption of air and fluid accumulation in the middle ear, initially of the transudate type, characteristic to serous otitis media, often asymptomatic. The superinfection of this fluid leads to suppurative otitis media (8,11).

There are also other endogenous risk factors such as male gender, race (Amerindians, Eskimos), immune deficiencies, atopic tendency, low birth weight, premature birth, protein-calorie malnutrition, recurrent upper airway infections, nasotracheal intubation (5,6).

Natural alimentation plays an important protective role. It has been demonstrated that the incidence of otitis media decreases by 13% during the first 3 months, probably through the transfer of immunoglobulins, cellular elements and non-specific components of breast milk with antibacterial, antiviral and antiparasitic properties.

¹"Grigore T. Popa" University of Medicine and Pharmacy of Iasi Faculty of Medicine, Department of Mother and Child Medicine

²"Grigore T. Popa" University of Medicine and Pharmacy of Iasi Faculty of Medicine, Department of Preventive Medicine and Interdisciplinarity

³"Grigore T. Popa" University of Medicine and Pharmacy of Iasi Faculty of Medicine, Department of Surgery (II)

⁴"Grigore T. Popa" University of Medicine and Pharmacy of Iasi Faculty of Medicine, Student

E-mail: simonadrochio¹@yahoo.com, magdaiorga²@yahoo.com, corladeandrei.mihaela³@yahoo.com, elena_m_pitorac⁴@yahoo.com, antondana66⁴@yahoo.com

The α -lactalbumin from the breast milk has a bactericidal effect on pneumococcus, while oligosaccharides bind to pneumococcal adhesins, preventing the adhesion of bacteria to the epithelium (5,12).

One of the most important exogenous risk factors is the attendance of a community, such as nurseries, from a small age.

The living environment, precarious hygiene, families with numerous siblings who may have a history of otic infections double the risk of developing otitis media (4,13).

Passive smoking, especially in the first year of life is incriminated for approximately 2 million episodes of otitis media and over 150,000 tympanostomies. The pathophysiological mechanism is probably hypersecretion of mucus in the respiratory tract and damage of the mucociliary transport (3,10).

The use of the pacifier increases the risk of otitis media in children over 1 year by 24% as continuous suction causes dysfunction of the Eustachian tube and leads to the inoculation of the middle ear with pathogenic bacteria (7,9).

According to the etiology of acute otitis media, its main cause is bacteria (70-90% of cases), in the following order: *Streptococcus pneumoniae* - 27-52%, *Haemophilus influenzae* - 16-52%, *Moraxella catarrhalis* 2-15 % producing beta-lactamases. Much less rarely were isolated *Staphylococcus aureus*, *Streptococcus pyogenes*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Escherichia coli*, *Alloicoccus otitidis*, mycobacteria. Infections with these germs were found more frequently in immunosuppressed patients (2,7,12,14).

Material and method

The study included 104 patients discharged from Pediatric Clinic III - "Saint Mary's" Children's Clinical Emergency Hospital of Iasi from January 2015 to January 2017, diagnosed with "Acute otitis media". These patients were selected from the total number of patients admitted to this clinic during those two years.

On this batch we performed a retrospective study based on the data found in the children's medical charts, by observing the risk factors to which they were exposed and that favor the illness, and also the connection between the risk factors and the occurrence of complications.

The diagnosis of acute otitis media was established in accordance to the guidelines. Thus, according to the American Academy of Pediatrics, the diagnosis of acute otitis media is required when the onset is sudden, with pain, fever, inflammatory otitis signs, accompanied by exudate found in the middle ear during an otoscopic examination. In the case of babies, marked agitation, the tendency to lean their heads on the affected side, refusal to eat, lack of sleep, crying or screaming apparently without reason are signs that draw attention to the otic affection.

Results

41.8% of the 104 children included in the study came from rural areas and 58.2% from urban areas, having varying socio-economic conditions (good and very good, and only sporadically children coming from extremely poor environments and exclusively supported by the State) (Figure 1).

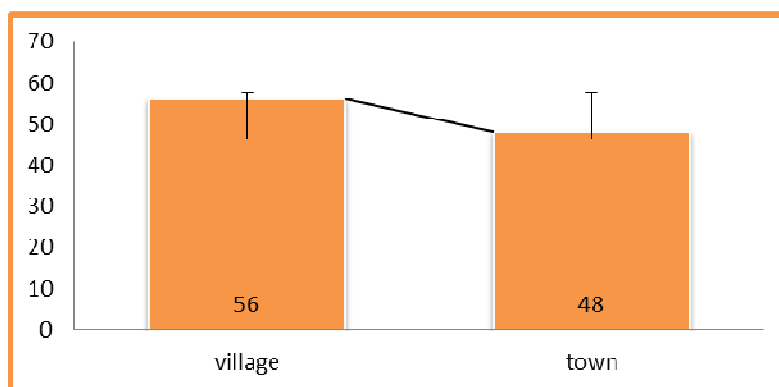


Fig. 1. Distribution according to the home environment.

The distribution by gender observes the pattern of incidence of the studied pathology, with predominance of the male gender (66 boys and 38 girls).

Also, patient ages correspond to the peak incidence of otitis media in the pediatric population, noting that:

- over 80% of cases occur under 6 years, of which over 50% are under the age of 2 years
- two maximum frequencies have been reported: at the age of 1 (25% of cases) and at the age of 4-5, when children usually become members of specific communities (Fig. 2)

Regarding the attendance of communities, more than half of the patients who came to the doctor were under the age of 2. The high number of illnesses can be influenced by the attendance of a community by older siblings; 68% of cases attend communities and 32% do not.

Out of the 104 children included in the study, 87.5% were born on term (37-42 weeks) and 12.5% were born premature (between 32-36 weeks). In the case of girls, the incidence of prematurity was 14%, higher than the incidence in boys (10.7%).

Of all the births, 67.3% were natural births and 22.7% caesarean sections. 14.42% were laborious births, complicated mainly by nuchal cord, haemorrhages that required transfusions and fetus-pelvis disproportions with perineal ruptures.

Given that exposure of the child to aeroallergens or pollutants, especially passive smoking, is an important risk

factor in the occurrence and recurrence of acute otitis media and respiratory tract infections, we considered relevant to assess its presence:

- 60.5% were not exposed to pollutants;
- 23% were exposed to cigarette smoke;
- 16.5% were exposed to other pollutants, such as toxic gases (Fig. 2).

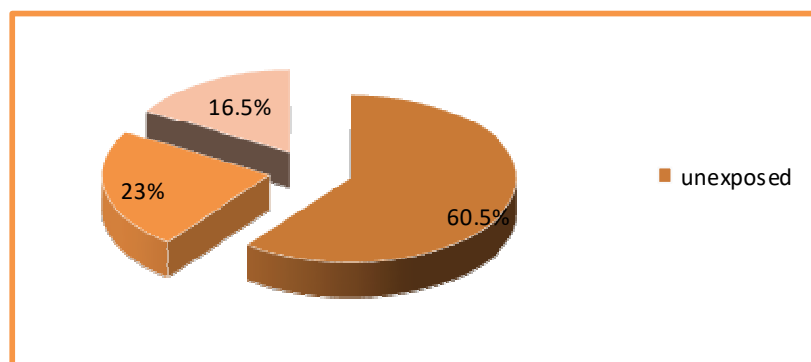


Fig. 2 Exposure of the patients in the studied group to pollutants.

Only 48.2% of the children were breastfed after birth, and the remaining 52.8% were artificially fed cow milk either immediately after birth or after 2-3 months of breastfeeding.

As far as the environment of origin is concerned, urban children were more frequently breastfed (48.21% compared to 42.71% from rural areas), which can be explained by the higher level of education and degree of information on the importance of breastfeeding.

At the time of admission, some deficiency-related conditions were identified: 35 of the children (32%) –

deficiency anemia, 17 cases (15%) – protein-calorie malnutrition, 8 cases (7%) – deficiency rickets and 7 cases (%) associated multiple deficiencies.

Selected cases have frequently reported association of pathologies that have been shown to influence or even cause acute otitis media: repeated upper respiratory tract infections, recurrent wheezing, pneumonia, acute or chronic adenoiditis, chronic background diseases, atopic tendency or congenital immune deficiency (Fig. 3).

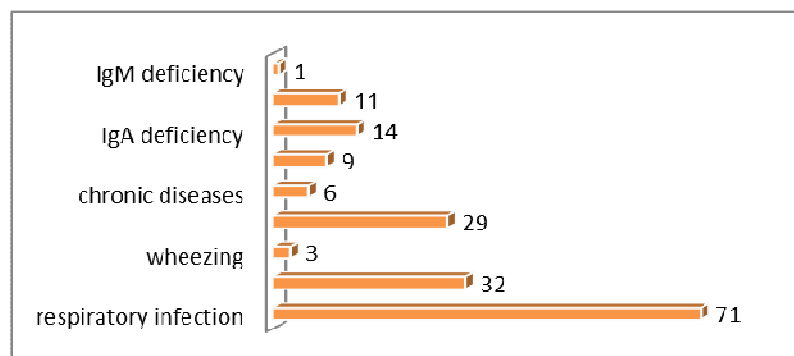


Fig.3 Related diseases present in the studied group.

The association with other upper respiratory tract infections was highlighted in 68.26% of the patients, which proves that they are a fundamental risk factor in the occurrence of acute otitis media. The association to a higher

degree of adenoiditis with maximum frequency between 2 to 3 years of age (37.5% of the total cases), followed by the age group of 4-5 years (28.13%), and then of 0-2 years (21.88%) and children over 5 years (12.49%) was noted.

Also, a significant percentage (30.76%) was represented by the coexistence of chronic adenoiditis followed by pneumonia (27.88%), immune deficiency (25%), atopy (8.65%), chronic diseases (7%) and recurrent wheezing (2.88%). Among the atopic patients, one was allergic to latex, one to mold, and 7 to antibiotic allergens (ceftriaxone, amoxicillin and penicillin).

Among children with respiratory tract infections, 38% were simultaneously diagnosed with deficiency anemia, 21.13% with protein-calorie malnutrition, 14% with IgA and / or IgG immune deficiencies, and 64.79% were artificially fed.

Another risk factor that we have pursued in this study was the vaccine situation of the patients, regarding the observance of both the National Vaccination Scheme and the pneumococcal vaccination (optional vaccination). We found that 67.3% of the children were vaccinated according to the national scheme in force, with only 17.14% receiving the pneumococcal vaccine. The incidence of unvaccinated children in the study group according to age was the following: 26.92% in infants, 10.77% in patients between 1-2 years of age, 17.27% for patients between 2-3 years of age, 27.5% in patients between 4-5 years of age and 17.54% in patients over 5 years.

The season in which the disease occurred is also part of the cumulative factor favoring otitis. 62% of children got sick in the hot season, and in 38% of the cases the sickening occurred in autumn and winter.

The number of episodes of otitis occurring in each patient is a parameter that allows the assessment of recurrent otitis. 63.4% of the children were at their first episode, 27.04% at their second, while 17.6% experienced more than 3 illnesses. The highest number of doctor consults with the diagnosis of acute otitis media was that of a 2-year old child (7 episodes).

The youngest patients admitted were 2 newborns of 18 days, and 27 days respectively, the latter with two episodes of otitis. At the other extreme was a 17-year-old patient in their first episode. In the category of children under 1 year, 69.2% were at their first illness, 19.2% in the second and

11.6% had at least 3 bouts. From the age group of 1-2 years, 47.3% were at their first episode, and 19.5% were at their second episode of otitis.

Symptomatology at the time of admission was represented by:

- Fever - 95 cases (91.3%)
- otalgia - 45 cases (43.27%)
- otorrhea - 12 cases (12.5%)
- hypoacusis - 16 cases (15.38%)
- psychomotor agitation and nonspecific symptoms - 19 patients (18.27%) and 73% of infants respectively.

Thus, the established diagnosis is:

- acute suppurative otitis media - 38.46% of children
- acute serous otitis media - 36.54%
- acute congestive otitis media - 25%

In order to support the diagnosis of acute otitis media, laboratory tests were performed: haemoleucogram, inflammatory syndrome (ESR, fibrinogen, reactive C protein).

In 27.88% of the patients, the haemogram revealed the existence of anemia.

36.54% had leukocytosis at the time of admission. In 49% of the cases included in the study, neutrophilia was detected, in 60.57% lymphocytosis and in 61.54% monocytosis.

Elevated ESR rates were reported in 66.35% of patients, increased fibrinogen rates in 39.42%, and C-reactive protein had elevated rates in 31.73% of cases.

In 13 (32.5%) of the 40 patients with acute suppurative otitis media, otic secretion cultures were performed with antibiogram. In two of them *Staphylococcus aureus* was isolated, sensitive to oxacillin, as well as a coagulase-negative *Staphylococcus* strain, four cultures were positive for pneumococcus sensitive to Levofloxacin and Clindamycin, in two media diphtheria bacilli developed, in one medium *Enterobacter cloacae* developed, on one medium *Escherichia coli* developed, and the exudate of one patient was polymicrobial, with the isolation of *Staphylococcus aureus* and *Escherichia coli* (Fig. 4).

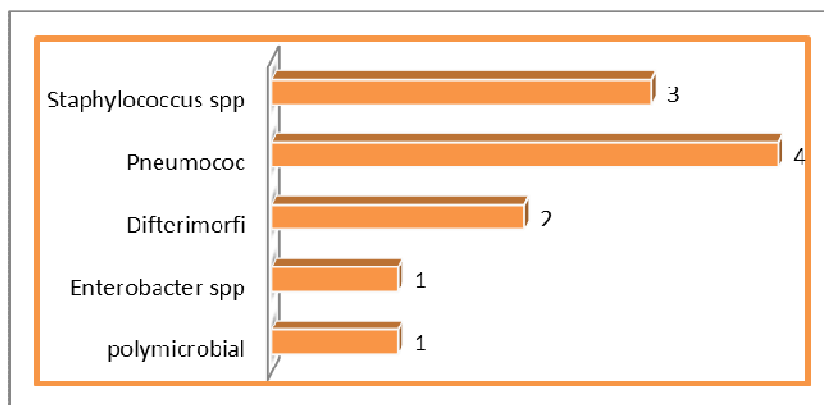


Fig. 4 Results of cultures from otic secretion in suppurative otitis.

Out of the 104 cases constituting the studied group, 32% developed complications:

- hypoacusis: 11 cases (11.53%)
- mastoiditis: 9 cases (9.63%)
- ethmoiditis: 2 cases (1.92%)
- cerebral venous thrombosis: 2 cases (1.92%)
- cerebral abscess: 2 cases (1.92%)
- septicemia: 3 cases (3.85%).

The treatment of acute otitis media included symptomatic therapy with the use of antipyretics, nonsteroidal anti-inflammatory drugs, mucolytics, and etiologic therapy (antibiotic therapy).

In complicated cases, surgical interventions were performed to excise abscesses, as well as mastoid debridement, and transtympanic aerators were inserted.

In terms of etiologic treatment, the main therapeutic classes used as a first choice were third-generation cephalosporins in 60 children, natural penicillins in 22 children, second-generation cephalosporins in 6 children, aminopenicillins in 6 patients, fluoroquinolones in 5 patients, followed by lincosamide, aminoglycosides, macrolides, sulfonamides, with lower use.

Discussions

Concerning the 104 patients included in the study group, their socio-economic conditions were predominantly good and very good, sporadically precarious, and gender distribution complied with the incidence pattern of the studied pathology (male gender: female = 1.74: 1).

The percentage of infants included in the batch was 25%, as was the case of children aged 1-2 years, consistent with the data in the literature, which claim that the peak of incidence is around 1 year of age (with a limit between 6 and 18 months). This is explained by the anatomy of age, when the Eustachian tube is shorter and horizontalized, but also by increased susceptibility to infections due to the immaturity of the immune system.

In terms of nutrition, only 47 of the children were breastfed after birth, the remaining 57 being artificially fed. It is known that the initiation and support of lactation is related to genetic, constitutional and anatomical factors, as well as to socio-economic factors, such as stress, professional insertion and mother's nutrition.

Paradoxically, we noticed that the proportion of unvaccinated individuals is higher among those from urban areas and whose parents attended higher education. This can probably be explained by easier access to information sources that promote the refusal to vaccinate for reasons lacking a medical base.

Among the exogenous risk factors, we found a higher exposure to pollutants, mainly passive smoking in infants, in a proportion of 32% of the total number of exposed patients.

At the age of 2-3 years, there is an increased incidence of acute adenoiditis, favoring tubal dysfunction and recurrence of otitis. The age group of 4-5 years associates a large number of artificially fed and unvaccinated children with adenoiditis in the first year of life. A large proportion of them were born by caesarean section, with an Apgar score of less than 8 and had a low birth weight.

Among children over 5 years old, we have identified the highest proportion of unvaccinated patients with allergies and incorrectly diversified diet. They were also exposed to pollutants and came from families with several children.

A risk factor regardless of age quoted in the specialized literature is the cold season, which is also confirmed in the studied group.

Conclusions

Acute otitis media is an important part of the pathology of pediatric patients, leading to increased addressability to the doctor, especially during the cold season.

The incidence peak of acute otitis media in infants, equal to that of children aged 1 to 2 years, is due to the cumulative number of risk factors in this age group, namely: the more frequent association of other upper respiratory tract infections, pneumonia, anemia, protein-calorie malnutrition, rickets and incorrect dietary diversification. In addition, increased exposure to pollutants, especially cigarette smoke, is added in case of infants.

The rate of complicated otitis was 19.23%, and 6.73% of the children developed simultaneous multiple complications, including: hearing hypoacusis, acute ethmoiditis, acute otomastoiditis, cerebral thrombophlebitis, cerebral abscesses, septicemia.

Nonspecific symptomatology was common in infants (19 patients under 1 year, and 73% of infants manifested psychomotor agitation and nonspecific symptoms) and the routine otoscopic examination of all children with respiratory infections is an essential condition for the diagnosis of otitis media.

The risk factors for acute otitis media that we identified in this group were the cold season, male gender, premature birth, low birth weight, artificial alimentation in the first year of life, incorrect dietary diversification, becoming a the community member, higher number of siblings, association of respiratory tract infections, of chronic diseases or immune deficiencies, allergic status, exposure to pollutants.

To prevent premature and late complications, it is important to accurately specify the diagnosis and establish individualized therapy according to guidelines. It is also essential to follow up and ensure directly observed therapy for children through the collaboration of a pediatrician with the family doctor and the ENT specialist.

References

1. Anne Vergison, Ron Dagan, Adriano Arguedas, Jan Bonhoeffer, Robert Cohen, Ingeborg D. Hooze, Alejandro Hoberman, Johannes Liese, Paola Marchisio, Arto A Palmu, G Thomas Ray, Elisabeth A M Sanders, Eric A F Simões, Matti Uhari, Johan van Eldere, Stephen I Pelton. Otitis media and its consequences:

- beyond the earache. *Lancet Infect Dis* 2010; 10: 195–203.
2. Goția S., Moraru E., Ailioaie C., Rugină A., Murgu A. - *Pediatrie, Boli respiratorii, boli cu mecanism imun, hepatologie*, Iași, Editura Vasiliana '98, 2008, 20-23
 3. Hwang SH, Hwang JH, Moon JS, Lee DH. Environmental tobacco smoke and children's health. *Korean J. Pediatr.* Feb. 2012; 55: 35-41
 4. Karen J. Marcadante, Robert M. Kliegman. *Capitol 105-Otitis media din Nelson Essentials of Pediatrics* 2015, editia 7:105-106
 5. Nuntigar Sonsuwan, Patcharin Watcharinyanon, Kittisak Sawanyawisuth. What are the leading causative pathogens in acute otitis media with tympanic membrane perforation?. *International Journal of Pediatric Otorhinolaryngology* 2016; 90: 20-22
 6. Petri Koivunen. Otitis media in children: detection of effusion and influence on hearing. *Oulun Yliopisto, Oulu* 1999
 7. Prof. Dr Valeriu Popescu, Mihaela Raduț- Ștefănescu. *Otita medie din Algoritm diagnostic și terapeutic în pediatrie, vol II, București, 1999, 184-196*
 8. Baculard, F. (2007) Epidemiology of Acute Otitis Media and Its Complications in the Child. *Médecine thérapeutique/ Pédiatrie*, 10, 154-157.
 9. Uhari, M., Mantysaari, K. and Niemela, M. (1996) A Meta-Analytic Review of the Risk Factors for Acute Otitis Media. *Clinical Infectious Diseases*, 22, 1079-1083. <http://dx.doi.org/10.1093/clinids/22.6.1079>
 10. Daly, K.A., Brown J.E., Lindgren, B.R., Meland, M.H., Le, C.T. and Giebink, G.S. (1999) Epidemiology of Otitis Media Onset by Six Months of Age. *Pediatrics*, 103, 1158-1166. <http://dx.doi.org/10.1542/peds.103.6.1158>
 11. da Costa, J.L., Navarro, A., Neves, J.B. and Martin, M. (2004) Household Wood and Charcoal Smoke Increases the Risk of Otitis Media in Childhood in Maputo. *International Journal of Epidemiology*, 33, 573-578. <http://dx.doi.org/10.1093/ije/dyh071>
 12. Hounkpatin, S.H.R., Avakoudjo, F., Lawson Afouda, S., Yemadjro, F.S.R., Adjibabi, W. and Vodouhè, S.J. (2011) Prevalence of ENT Disorders in the Borgou Regional Hospital in the North-Benin. *La Revue africaine d'ORL et de Chirurgie cervico-faciale*, 11, 47-51.
 13. Zakzouk, S.M., Jamal, T.S. and Daghistani, K.J. (2002) Epidemiology of Acute Otitis Media among Saudi Children. *International Journal of Pediatric Otorhinolaryngology*, 62, 219-222. [http://dx.doi.org/10.1016/S0165-5876\(01\)00617-6](http://dx.doi.org/10.1016/S0165-5876(01)00617-6)
 14. Sophia, A., Rita, I., Rebekah, G., Brahmadathan, K. and Rupa, V. (2010) Risk Factors for Otitis Media among Preschool, Rural Indian Children. *International Journal of Pediatric Otorhinolaryngology*, 74, 677-683. <http://dx.doi.org/10.1016/j.ijporl.2010.03.023>

Correspondence to:

Magdalena Iorga
 Universitatea de Medicina si Farmacie "Grigore T. Popa"
 Spitalul de Urgenta pentru Copii "Sfanta Maria"
 Strada Universității 16,
 Iasi, Romania
 E-mail: email: magdaiorga@yahoo.com

BLUNT ABDOMINAL TRAUMA IN CHILDREN – A PRACTICAL REVIEW

Flavius Bulgaru^{1,2*}, Constantin Tica³, Florin-Daniel Enache³

Abstract

Blunt abdominal trauma is a major morbidity and mortality factor in all age groups, and especially in children it is the most common cause of intraabdominal injury. In the past two decades, the use of computer tomography images and nonoperative treatment of haemoperitoneum are important steps in the therapeutic management of abdominal trauma in children. The advantages of the conservative approach are reduced cost of hospitalization, faster discharge by avoiding non-therapeutic celiotomies, fewer intraabdominal complications and reduced transfusion rates associated with a global improvement in mortality rates.

This paper is a review of blunt abdominal trauma in children and a comparative study was carried out between the literature and the methods of therapeutic management used in the Clinic of Pediatric Surgery of "Sf. Apostol Andrei" Emergency Clinical County Hospital of Constanta.

Keywords: abdominal trauma, blunt abdominal trauma, abdominal injury, splenic injury, liver injury, hollow viscus injury, children

Introduction

Blunt abdominal trauma is a major morbidity and mortality factor in all age groups, and especially in children it is the most common cause of intraabdominal injury [1,2]. The identification of intraabdominal lesions is still very difficult, many lesions may occur after the initial assessment and treatment. In the past two decades, the use of computer tomography images and nonoperative treatment of haemoperitoneum are important steps in the therapeutic management of abdominal trauma in children. The advantages of the conservative approach are reduced cost of hospitalization, faster discharge by avoiding non-therapeutic celiotomies, fewer intraabdominal complications and reduced transfusion rates associated with a global improvement in mortality rates [3,4].

In addition to the CT exam, which is the first option in this pathology, laboratory tests and ultrasonography help the diagnose. However, it is important to note that anamnesis and a correct clinical examination, through primary and secondary emergency assessment, prompt resuscitation and

close monitoring, are essential maneuvers that make the difference between life and death.

Purpose

A review of blunt abdominal trauma in children and a comparative study was carried out between the literature and the methods of therapeutic management used in the Clinic of Pediatric and Orthopedic Surgery of "St. Apostol Andrei" Emergency Clinical County Hospital of Constanta.

Material and method

We have studied over 150 articles from the literature using online search engines and PubMed, Med-Line, Clinical Key, Ovid databases. Terms such as *abdominal trauma*, *blunt abdominal trauma*, *abdominal injury*, *splenic injury*, *liver injury*, *hollow viscus injury* have been used. Scientific articles, controlled randomized trials, protocols, meta-analyses, and reviews have been checked. This review allowed us to make a synthesis of conservative management of abdominal trauma in children compared to the diagnostic and treatment techniques of the Clinic of Constanta.

Results and discussions

In children, accidents caused by motorised vehicles represents about 60% of causes for blunt abdominal injuries. Then falls and bicycle injuries are second [5]. 10% of cases from accidents represent lap belt injuries [6]. There is a significant percent of children without history of accidents or the details are concealed by the parents. The management of these cases is very difficult and attention must be paid not to miss important injuries [7].

Following the retrospective statistical study we observed that out of 565 polytrauma children hospitalized between 2012-2016, only 248 associated abdominal trauma. The frequency is higher in urban than in rural areas (145 cases in urban areas versus 103 cases in rural areas). Like in adults, first place in children trauma etiology is occupied by road accidents, followed in frequency by falls from heights, play accidents or aggression. Causes that generated polytrauma and polytrauma associated with abdominal trauma are listed in order of frequency (Table 1).

¹2nd Surgery Clinic, "Sf. Apostol Andrei" Emergency Clinical County Hospital of Galați

²"Ovidius" University of Constanta, Faculty of Medicine, *PhD Student

³Pediatric Surgery Clinic, "Sf. Apostol Andrei" Emergency Clinical County Hospital of Constanta

E-mail: flavius_bulgaru@yahoo.com; tica.constantin@yahoo.com, dr.enache@chirurgiecopii.ro

Table 1. Etiology of polytrauma in our study.

Etiology	No. of cases of polytrauma associated with abdominal trauma	Other lesions associated with abdominal trauma
Road accidents	153	196
Falls from heights	83	106
other causes	12	15

Injury patterns in children differ from those in adults because of the size of the patients. When compared to adults the abdominal organs are closely packed together. Children have a thin abdominal wall, with relatively little abdominal muscle or fat mass, which can absorb some of the impact. The ribcage is very elastic, offering less protection to the liver and spleen. Also, the diaphragm is placed more horizontally, thus displacing the liver and spleen downwards, which further increases the vulnerability of the intra-abdominal organs. This is because the child's ribs do not absorb the force that adult ribs absorb while fracturing. Fractured ribs are rare in children [1]. Children have a relatively small pelvis placing the bladder more intra-abdominally and thus less protected. All these factors contribute to the vulnerability of the abdomen in children [8].

Principles of acute trauma care do not differ between children and adults, but in children even "simple" interventions such as placement of an intravenous catheter can be more difficult because of the smaller size of the vessels. For all these reasons, the child with possible severe trauma can therefore pose a significant challenge for physicians.

Hypothermia develop rapidly in children because of large skin area. Acidosis and coagulopathy, combined with hypothermia represent a fatal triad. In conclusion, hypothermia should be avoided whenever possible, during case management.

There are some differences in responses to stress between children and adults. Hemodynamic stability can be easily maintained in children only with discreet signs for a long period of time, before they rapidly develop severe hypovolemic shock. Bradycardia is very dangerous in children and it must be considered as a lethal sign.

In the emergency room injured children undergo primary survey, following through the ATLS/APLS principles: ABC (DEFG) and following the idea - treat first what kills first [9]. A patent airway, with in-line cervical spine immobilization, is secured and adequate ventilation established. This is followed by restoration of satisfactory circulating blood volume [1].

Usually, the examination of the abdomen is not a part of the primary survey, but may be included in maintaining under control the circulation, if there are signs of haemodynamic instability despite ongoing fluid resuscitation. Vital parameters are age-dependent. At a loss of more than 15% of the total circulating volume, it will appear the signs of hypovolemic shock. Severe hypotension will occur only after an acute loss of 25% of the total circulating volume. In case of hypovolemic shock, a bolus

of 20 ml/kg warm isotonic crystalloid is administered. This process can be repeated. In the first stage an amount of 25% of the circulating volume is assured, after the second maneuver 50% of the volume has been replaced. In comparison to the adults, in children, in case of hypovolemic shock there might be an increased systolic pressure due to the shock response.

A precise history of the mechanism of injury is important in the management of blunt abdominal trauma. The initial clinical assessment of children with abdominal injuries is often difficult. The most important signs and symptoms in awake patients are as follows:

- ✓ Pain
- ✓ Tenderness
- ✓ Gastrointestinal hemorrhage
- ✓ Hypovolemia
- ✓ Evidence of peritoneal irritation.

However, large amounts of blood can accumulate in the peritoneal and pelvic cavities without any significant or early changes in the physical examination findings. Bradycardia may indicate the presence of free intraperitoneal blood [10].

Physical examination may be unreliable in up to 30 per cent of children, particularly when the child has a reduced level of consciousness [11].

On physical examination, the following injury patterns predict the potential for intraabdominal trauma:

✓ Lap belt marks: children in accidents involving moderate to high speed frontal deceleration while being restrained by a seat belt are at high risk of sustaining a constellation of injuries known as the 'lap belt complex' [12,13]. This consists of a flexion-distraction injury to the lumbar spine (a fracture is possible), ecchymosis of the abdominal wall, and injury to the intestine [13].

✓ Ecchymosis involving the flanks (Grey Turner sign) or the umbilicus (Cullen sign): Indicates retroperitoneal hemorrhage, but is usually delayed for several hours to days

✓ Abdominal distention

✓ Auscultation of bowel sounds in the thorax: May indicate a diaphragmatic injury

✓ Local or generalized tenderness, guarding, rigidity, or rebound tenderness: Suggests peritoneal injury

✓ Fullness and doughy consistency on palpation: May indicate intraabdominal hemorrhage

✓ Creptitation or instability of the lower thoracic cage: Indicates the potential for splenic or hepatic injuries [14].

The inspection of the abdomen should look for bruising, movement with respiration, lacerations, distension, and seat belt marks. There is a high probability that major lesions of the internal organs can occur without any external signs.

Gentle palpation should be carried out to reveal any areas of tenderness. Care should be taken not to hurt the child because their continued cooperation is important during repeated examination [1].

A maneuver that must be carried out during the assessment of a potential abdominal trauma child is the gastric drainage. In children with serious injuries air swallowing and dilatation of the stomach is common. Gastric distension can mimic an abdominal lesion and goes to rerespiratory distress. Also venous circulation can be compromised. Clinical signs of abdominal trauma may change rapidly after the insertion of a gastric catheter [14]. Gastric intubation also reduces the risk of aspiration of food contents in unconscious children.

In a complete evaluation for multiple trauma, rectal and vaginal examination are routine in adults, but in children these maneuvers are mandatory only if rectal, spinal or urethral injuries are suspected. Tenderness, boggy, or a floating prostate are important signs, but may be difficult to ascertain with confidence in a child who is bound to be frightened by this examination [1].

If there are signs of rectal bleeding, a careful examination must be done under general anesthesia. Superficial injuries to the rectal mucosa or anal canal will resolve with conservative management. Full thickness injuries below the internal sphincter can be treated by primary repair whereas injuries above the internal sphincter may need a diverting colostomy [15].

After the examination of the genital area, a urinary catheter is mandatory for monitoring the liquid output and the evolution of the state of the patient during initial treatment. One has to be very careful with children who may have urinary tract lesions. These lesions may be present if there are signs of trauma, ecchymosis or swelling of the genital organs or perineum. If blood is present in the meatus or there is a visible haematuria, for sure we speak of urinary tract lesions. This state also goes with the inability to void or sensation of voiding without the passage of urine. Is better to avoid catheterisation in case of suspicion of an urethral injury, not to create more harm than good, to transform a partial tear of the urethra in a complete one [1].

During a complete evaluation, the physical examination is doubled by investigations, done during the primary survey and especially during secondary assessment. First of all an intravenous catheter during the first stage of assessment is mounted for different purposes:

- Cell count;
- Blood grouping and cross-matching;
- Electrolytes;
- Specific tests for:
 - o Pancreatic or small intestine trauma – serum amylase
 - o Liver lesions – transaminase

Beware of the fact that elevated amylase in the serum may be present if there are lesions of the parotid glands [16].

In a prospective study of 49 children younger than 12 years of age who were being evaluated for child abuse (without any physical sign of abdominal injury), four had elevated transaminase levels, of whom, three had liver

lacerations documented by subsequent abdominal computed tomography (CT) scans [16].

Urinalysis is another important test during the evaluation of an abdominal trauma child. Haematuria is an important marker not only for kidney lesions, but also for other abdominal injuries that not include the genitourinary tract. In one study of 378 consecutive children undergoing abdominal CT following blunt abdominal trauma who were evaluated for haematuria, 66% were found to have haematuria (220 had occult haematuria and 36 had gross haematuria). Organs injured in those with haematuria were: spleen (37%), liver (33%), whereas renal injury was seen only in 26% [17]. In another study of children with post-trauma haematuria with normal radiology of the genitourinary tract, 77% had an underlying hepatic, splenic, or pancreatic injury [18].

It is proven that if there are less than 4 red blood cells seen on microscope, this is the result of the catheter passage [19]. The literature has different opinions concerning kidney trauma and the quantity of haematuria:

- Stalker et al. more than 50 red blood cells (RBC) seen on microscope - significant of renal injury [20];
- Lieu and et al. said that greater than 20 RBC was significant [21];
- Taylor et al. believed that asymptomatic haematuria usually indicates insignificant urinary tract injury [22];
- Carroll and McAninch – haematuria is important but non-specific and not a predictor of the severity of the injury [23].

The literature says that in addition to the mechanism of injury and physical examination, the amount of haematuria is a factor in the decision of CT imaging [24,25].

Diagnostic peritoneal lavage in children is not very used today. The usage of this technique has rapidly declined because of the fact that many lesions of the solid organs in children are managed more and more conservatively. This maneuver may be used in the following cases [10]:

- Lesions of the spinal cord
- Patients with shock, which cannot be explained and with polytrauma
- Multiple trauma with a possible abdominal injury
- Intoxicated patients with a possible abdominal injury
- Patients with a possible abdominal lesions who will suffer a longterm anesthesia.

There are many disadvantages in using this technique in children: it is very painful, that's way it must be done under general anesthesia and itself can cause other abdominal lesions. The only time when this procedure is useful is the last point of the above paragraph, the necessity of excluding an abdominal lesions before a surgical procedure of other kind in a polytrauma patient [1].

Imaging tests complete the assessment of children with potential abdominal injury. Ultrasonography is a very useful, rapid, portable, noninvasive and accurate investigation to see if there is free intraabdominal fluid in the peritoneum [26]. The current focused abdominal sonography in trauma (FAST) examination protocol consists of 4 acoustic windows (pericardiac, perihepatic, perisplenic, pelvic) with the patient supine. An examination is

interpreted as positive if free fluid is found in any of the 4 acoustic windows, negative if no fluid is seen, and indeterminate if any of the windows cannot be adequately assessed [10,27].

This test is sensitive, but it alone cannot put the diagnosis of organ lesion, so it is useful only as an indication of a CT scan. Also is useful if there is a suspicion of intraabdominal bleeding in a trauma child that doesn't answer to fluid resuscitation.

Radiographs of the trunk (thorax, abdomen and pelvis) must be done during primary assessment of children with potential abdominal injury. A X-ray of the abdomen is useful to see the position of the stomach and also the models of intestinal gas distribution – paralytic ileus or oedema of the intestinal wall; presence of gas directly in the peritoneum.

Indirect signs of solid organ injuries (spleen, liver) may be suspected when there are rib fractures, displacement of the diaphragm or other neighbourhood organs or pleural effusion in the base of the lungs [28,29].

A normal chest or pelvic X-ray can't exclude itself a lesion of the abdomen in children.

Computed tomography has remained the first in the management of paediatric abdominal trauma since 1980, when Rance and Bear, first reported its use in stable trauma children [30].

This investigation can provide very detailed images of the solid organs, duodenum and genitourinary system and it

is used in determining the operative intervention or conservative management of haemoperitoneum [31].

There are some specific situations when CT scan is needed in the assessment of abdominal trauma child:

- Unexplained blood loss
- Unreliable physical examination
- Potential brain injuries
- Signs of intraabdominal fluid on X-rays and ultrasonography [32].

Until about four decades ago, in the 80s, laparotomy was the elective method in treating patients with haemoperitoneum. Because of opening of peritoneal cavity, lesions of the spleen and liver would often go to splenectomy or partial hepatectomy [1].

With conservative treatment and proper resuscitation and fluid therapy, it has been proven that many solid organ lesions may heal without surgical intervention. This practice avoids potentially fatal sepsis, especially after splenectomy in children [33].

In our study, conservative treatment had an important role in the management of abdominal trauma in children, with more than two thirds from the total of 248 cases (see Figure 1). These cases were carefully selected after different factors: haemodynamic stability, without visceral organs lesions or only in cases with grade I and II of spleen injuries or cases of grade I to grade IV hepatic injuries, some cases of kidney injuries and retroperitoneal haematoma. All children with signs of bowel perforation (6 cases) underwent laparotomy.

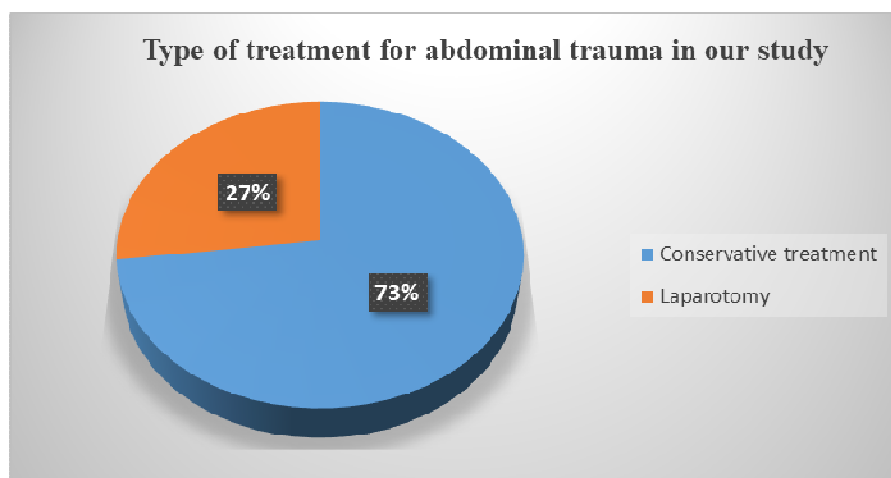


Figure 1. Type of treatment for abdominal trauma in our study.

The stability of the patients are vital. Those patients who require transfusion less than 40% of blood volume can be managed conservatively [34].

Other authors consider that the level of haemoglobin is not dropping below 7 mg/mm³, these children can be treated nonoperatively [35]. If the child is unstable and also

requires more than 40 ml/kg of blood, requires surgical intervention [1].

Proper resuscitation and specialised monitoring and intensive care is vital for the conservative treatment of these difficult cases. So these children suffering abdominal injuries must be treated in a trauma center with pediatric department.

Conclusions

- In our study, more than two thirds of cases with abdominal trauma were treated conservatively;
- All cases with visceral organs injuries were treated by laparotomy;
- The unique features of traumatized children, both physiologically and anatomically, require specific

trauma regional centers nationwide to serve the whole country;

- Specific protocols for the management of the trauma child should be developed, different from those of the adult due to the specific physiological and anatomical elements of the child.

References

1. Rance CH, Singh SJ, Kimble R. Blunt abdominal trauma in children. *J. Paediatr. Child Health* (2000) 36, 2–6.
2. Schacherer N, Miller J, Petronis K. Pediatric Blunt Abdominal Trauma In The Emergency Department: Evidence-Based Management Techniques, in *Pediatric Emergency Medicine Practice* (2014), 11:10, 1–24.
3. Stassen NA, Bhullar I, Cheng JD, Crandall ML, Friese RS, Guillaumondegui OD, Jawa RS, Maung AA, Rohs TJ, Sangosanya A, Schuster KM, Seamon MJ, Tchorz KM, Zarzuar BL, Kerwin AJ. Selective nonoperative management of blunt splenic injury: An Eastern Association for the Surgery of Trauma practice management guideline. *J Trauma Acute Care Surg.* 2012;73:S294–S300.
4. Sartorelli KH, Frumiento C, Rogers FB, et al. Non-operative management of hepatic, splenic, and renal injuries in adults with multiple injuries. *J Trauma.* 2000;49:56–61.
5. Cooper A, Barlow B, DiScala C, String D. Mortality and Truncal Injury. The Pediatric Perspective. *J. Pediatr. Surg.* 1994; 29: 33–8.
6. Clarnette TD, Beasley SW. Handlebar Injuries in Children: Patterns Prevention. *Aust. N. Z. J. Surg.* 1997; 67: 338–9.
7. Cooper A, Floyd T, Barlow B et al. Major blunt abdominal trauma due to child abuse. *J. Trauma* 1988; 28: 1483–7.
8. Kramer WLM, ten Duis HJ, Ekkelkamp S, Kimpen JJJ, Leenen LPH, Patka P. *Handboek kindertraumatologie.* p331–378 De Tijdstroom uitgeverij; 2007.
9. APLS: The Pediatric Emergency Medicine Resource 4th Ed. January 25, 2005.
10. Legome EL, Geibel J. Blunt Abdominal Trauma: Practice Essentials, Pathophysiology, Etiology. *Medscape*, Updated: Mar 15, 2016.
11. Du Priest RW Jr, Rodriguez A, Shatney CH. Peritoneal lavage in children and adolescents with blunt abdominal trauma. *Am. Surg.* 1982; 48: 460–2.
12. Glass RB, Sivit CJ, Sturm PF, Bulas DI, Eichelberger MR. Lumbar spine injury in a paediatric population: difficulties with computerized tomographic diagnosis. *J. Trauma* 1994; 37:815–9.
13. Newman KD, Bowmen LM, Eichelberger MR. The lap belt complex: Intestinal and lumbar spine injury in children. *J. Trauma* 1990; 30: 1133–8.
14. Maksoud JG Jr, Moront ML, Eichelberger MR. Resuscitation of the injured child. *Semin. Pediatr. Surg.* 1995; 4: 93–9.
15. Slim MS, Makoroun M, Shamma AR. Primary repair of colorectal injuries in children. *J. Pediatr. Surg.* 1981; 16: 1008–11.
16. Coant PN, Kornberg AE, Brody AS, Edwards-Holmes K. Markers for occult liver injury in cases of physical abuse in children. *Pediatrics* 1992; 89: 274–8.
17. Taylor GA, Eichelberger MR, Potter BM. Haematuria; A marker of abdominal injury in children after blunt trauma. *Ann. Surg.* 1988; 208: 688–93.
18. Freshman SP, Wisner DH, Weber CJ. 2-D echocardiography: Emergent use in the evaluation of paediatric precordial trauma. *J. Trauma* 1991; 31: 902–5.
19. Sklar DP, Diven B, Jones J. Incidence and magnitude of catheter induced haematuria. *Am. J. Emerg. Med.* 1986; 4: 14–16.
20. Stalker HP, Kaufman RA, Sledge K. The significance of haematuria in children after blunt abdominal trauma. *AJR* 1990; 154: 569–71.
21. Lieu TA, Fleisher GR, Mahboubi S, Schwartz JS. Haematuria and clinical findings as indications for intravenous pyelography in pediatric blunt renal trauma. *Pediatrics* 1988; 82: 216–22.
22. Taylor GA, Eichelberger MR, Potter BM. Haematuria: A marker of abdominal injury in children after blunt trauma. *Ann. Surg.* 1988; 208: 688–93.
23. Carroll PR, McAninch JW. Staging of Renal Trauma. *Urol. Clin. North Am.* 1989; 16: 193–201.
24. Bass DH, Semple PL, Cywes S. Investigation and management of blunt renal injuries in children – a review of 11 years experience. *J. Pediatr. Surg.* 1991; 26: 196–200.
25. McAleer IM, Kaplan GW, Scherz HC, Packer MG, Lynch FP. Genitourinary trauma in the pediatric patient. *Urology* 1993; 42:563–7.
26. Patrick DA, Bensard DD, Moore EE, Terry SJ, Karrer FM. Ultrasound is an effective triage tool to evaluate blunt abdominal trauma in the pediatric population. *J. Trauma* 1998; 45: 57–63.
27. Ingeman JE, Plewa MC, Okasnski RE, King RW, Knotts FB. Emergency physician use of ultrasonography in blunt abdominal trauma. *Acad. Emerg. Med.* 1996; 3: 931–7.
28. Eichelberger MR, Randolph JG. Pediatric trauma: An algorithm for diagnosis and therapy. *J. Trauma* 1983; 23: 91–7.
29. Maksoud JG Jr, Moront ML, Eichelberger MR. Resuscitation of the injured child. *Semin. Pediatr. Surg.* 1995; 4: 93–9.

- | | |
|--|---|
| <p>30. Rance CH, Bear JW. Computed tomography in the management of paediatric abdominal trauma. Aust. N. Z. J. Surg. 1980; 50: 506–12.</p> <p>31. Ein SH, Shandling B, Simpson JS, Stephens CA. Non operative management of the traumatised spleen in children. How Why? J. Pediatr. Surg. 1978; 13: 117–9.</p> <p>32. Taylor GA, Eichelberger MR. Abdominal CT in children with neurological impairment following blunt trauma. Ann. Surg. 1989; 210: 229–33.</p> | <p>33. Feliciano PD, Mullins RJ, Trunkey DD, Crass RA, Beck JR, Helfand M. A decision analysis of traumatic splenic injuries. J. Trauma 1992; 33: 340–7.</p> <p>34. Umali E, Andrew HG, White JJ. Critical analysis of blood transfusion requirements in children with blunt abdominal trauma. Am. Surgeon 1992; 58: 736–9.</p> <p>35. Polhgeers A, Ruddy RM. An update on paediatric trauma. Emerg. Med. Clin. North Am. 1995; 13: 267–89.</p> |
|--|---|

Correspondence to:

Flavius Bulgaru
Str. Lozoveni nr. 65
Galați
Tel. 0745526149
Email: flavius_bulgaru@yahoo.com

IDIOPATHIC INTRINSIC PYLORIC STENOSIS – A VERY RARE CAUSE OF GASTRIC OUTLET OBSTRUCTION IN SMALL CHILDREN

Lucian Vida^{1,2}, Aurel Mironescu^{1,2}, Șerban Rogoz³

Abstract

This is the report on the case of a 2 year old boy, known from the age of 1 month with recurrent symptomatology indicative of an intermittent gastric outlet obstruction. The imaging studies confirmed the gastric outlet obstruction syndrome, in the presence of a dilated and plicated stomach suggesting an intermittent gastric volvulus. During the surgery a pyloric fibrotic stenosis was discovered, therefore a pyloromyotomy was performed, followed by a Heineke-Mikulicz pyloroplasty and gastropexy. After the surgery, the patient's condition improved fast, with complete remission of all symptoms.

The few cases of pyloric fibrous stenosis described in children were secondary, either of toxic etiology (ingestion of caustic or corrosive substances, nonsteroidal anti-inflammatory drugs) or associated with peptic ulcer disease. In our case no certain etiology could be

Keywords: idiopathic, pyloric fibrous stenosis, gastric outlet obstruction, small children

Introduction

The gastric outlet obstruction (GOO) that occurs during infancy and childhood can have multiple causes; the most common is, by far, the hypertrophic pyloric stenosis (HPS) with an incidence of 1 - 4 to 1000 newborns. Other causes of this syndrome, such as congenital (pyloric atresia and prepyloric gastric antral web) or acquired conditions (ingestion of caustic or corrosive agents, nonsteroidal anti-inflammatory drugs overdose, peptic ulcer disease, chronic granulomatous disease, eosinophilic gastroenteritis, Jodhpur disease) are very rare, about 1 in 100 000 live births (1).

The diagnosis of HPS is easy to make and is confirmed by the ultrasound measuring of the pylorus. The diagnosis of a non-HPS GOO can be established by upper gastrointestinal (GI) series, upper GI endoscopy or ultrasound exam; in most of the cases, the etiology is determined at surgery.

The treatment of GOO depends on its cause; in most cases it is surgical and it rarely is non-operative (in case of peptic ulcer disease or inflammatory diseases). The

pyloroplasty has proved to be successful in the treatment of the pyloric fibrous stenosis, and its outcomes were excellent.

We report the case of a 2 years old boy who presented with an intermittent non – HPS GOO, with an early onset at 1 month of age. During the surgery, a pyloric fibrous stricture without any inflammatory component at the histopathological examination was detected.

Case presentation

A 2.6 year old boy was referred to our ward following recurrent episodes of forceful postprandial non-bilious vomiting occurring shortly (at about 10 minutes) after food intake, associated with diffuse abdominal pain and epigastric distention. The last vomiting episode dated 4 weeks before the presentation and was relieved after 2 weeks by drug treatment with antiemetics and antispasmodics.

The boy's medical history showed numerous episodes of non-bilious postprandial vomiting since the early age of 1 month, which usually responded to symptomatic treatment with Esomeprazole and Trimebutine maleate; the ultrasound measurements of the pylorus showed no hypertrophy of the muscular wall or channel narrowing and therefore ruled out the diagnosis of HPS. There was no history of caustic or corrosive agent ingestion; oral nonsteroidal anti-inflammatory drugs (Ibuprofen) were given only after 3 months of age and only in the recommended doses.

When admitted in our service the boy's condition was relatively good; the physical examination showed an epigastric distention with a mild tenderness during palpation; the rest of the systemic examination did not show any abnormality. The laboratory studies didn't show electrolyte imbalance; serum urea and creatinine were normal.

The upper GI series showed a free passage of contrast agent through the esophagus and a subdiaphragmatic located cardia, without any gastroesophageal reflux in the Trendelenburg position. The stomach was grossly distended and plicated, with significant pyloric narrowing and delayed gastric emptying (Figures 1 and 2).

¹Brașov Medicine Faculty of "Transilvania" University, Brașov

²Department of Pediatric Surgery, Brașov Children's Hospital

³Department of Pathology, Brașov Children's Hospital, Brașov

E-mail: lucian_vida@yahoo.com; aurel.mironescu@gmail.com



Figure 1 – Frontal view from the upper GI series showing a grossly distended and plicated stomach, with significant pyloric narrowing and delayed gastric emptying.



Figure 2 – Lateral view from the upper GI series showing the mediogastric plication of the stomach.

The upper endoscopy performed in another institution did not display esophageal or gastric peptic lesions, or other intraluminal lesions.

The diagnosis of pyloric stenosis was made and the boy was planned for elective surgery. At the operation, the stomach was distended and thick-walled while its left side was redundant, creating a mediogastric plication; the pylorus was normal-sized. No extraluminal compression was noted. After performing a gastrotomy proximal to the pylorus, the pyloric canal was explored and subsequently an

obvious intrinsic stenosis was detected at this level. A longitudinal pylorotomy was performed, cutting through a fibrous pyloric ring located in the muscle thickness. Heineke-Mikulicz pyloroplasty with an epiploic patch was done, followed by a left-side gastropexy. The pyloric biopsy showed a submucous fibrosis process at the gastroduodenal junction; a thickened muscularis mucosae was noted, containing collagen bundles intersecting with the muscle fibers and also entering the submucosa (Figures 3, 4 and 5). No inflammatory cells were detected.

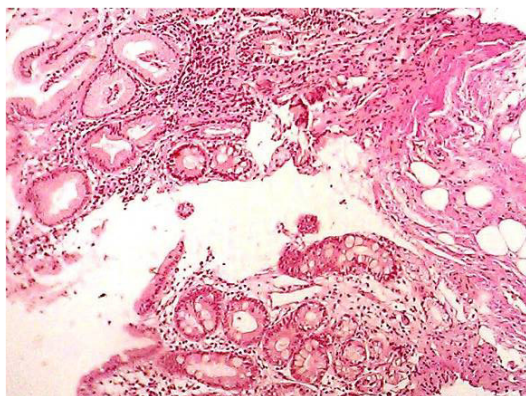


Figure 3 - Microscopic aspect of the pyloric biopsy, showing the gastroduodenal junction with duodenal mucosa on the left and gastric mucosa on the right. The muscularis mucosae contains collagen bundles intersecting with the muscle fibers, also entering the submucosa. Van-Gieson staining, 10×.

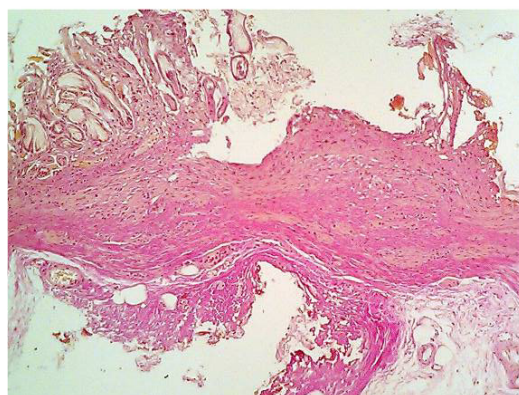


Figure 4 - Microscopic aspect of the pyloric biopsy, showing the yellowish muscularis mucosae fibers intermingled with thick red collagen bundles. The submucosa (on the left) also contains a large amount of collagen bundles. Van-Gieson staining, 4×.

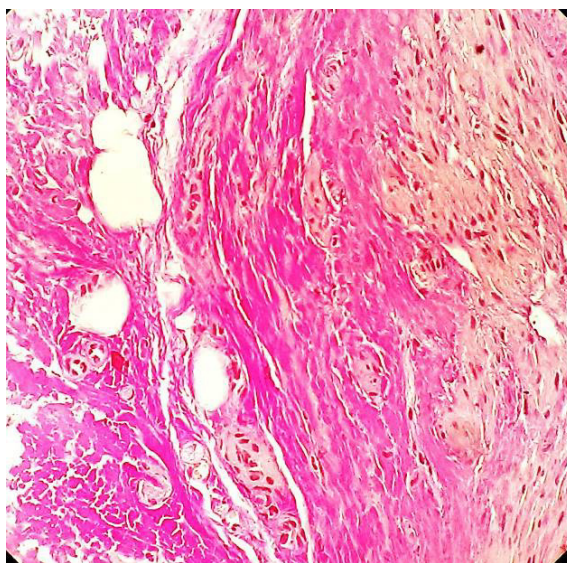


Figure 5 - Red collagen bundles in the muscularis mucosae and submucosa, intersecting with the yellowish smooth muscle fibers. Absence of inflammatory cells. Van-Gieson staining, 40×.

The post-operative period was uneventful, the patient gradually resuming oral feeding beginning with the 4th day after surgery, without vomiting. At 3-month follow-up the condition of the child was good, with complete remission of previous symptoms.

Discussions and conclusions

The GOO presents with forceful, non-bilious, incoercible or recurrent vomiting, loss of weight, abdominal pain and epigastric distention, with preserved appetite. The most common cause of GOO in infancy is the hypertrophic pyloric stenosis (HPS), with an incidence of 1-4 to 1000 newborns, which typically manifests between 4 and 10 weeks of age. There may be other conditions which can produce the GOO symptoms in this age group, but they are quite rare, i.e. 1 in 100 000 children (1); they include either congenital diseases such as pyloric atresia, gastric antral web, gastric duplication, heterotopic pancreas (2), or acquired conditions such as peptic ulcer disease (3), chronic granulomatous disease (4), caustic or corrosive agents ingestion (5), nonsteroidal anti-inflammatory drugs overdose, gastric volvulus, eosinophilic gastroenteritis and Jodhpur disease (6).

The onset of vomiting can be early, at birth, when the condition is congenital, or can be delayed in case of acquired diseases.

The diagnosis of GOO can be made by upper GI series, which reveal a dilated, often plicated stomach with a narrowed pyloric canal and a delayed gastric emptying. In case of HPS the ultrasound exam is the most appropriate since it allows for direct visualization and measurement of the pyloric channel and muscular wall, thus establishing the imaging diagnosis. The upper endoscopy may determine the etiology of a non-HPS GOO by visualising either lesions associated with a peptic ulcer disease, an antral web, polyps or other intraluminal masses / lesions.

It is essential to ascertain the cause of the pyloric stenosis because the therapeutic measures differ: medicamentous, with corticosteroids, for chronic granulomatous disease (4), endoscopic pneumatic dilatation for peptic stenosis (7), extramucosal pyloromyotomy for HPS, diaphragm excision with pyloroplasty for antral web, or pyloroplasty for peptic stenosis and Jodhpur disease respectively.

In our case the onset of symptoms was at the age of 1 month; at that time the diagnosis of HPS was ruled out by ultrasound imaging. Regarded as a gastroesophageal reflux disease, the illness was treated accordingly with Esomeprazole und Trimebutine maleate but the course of disease was oscillating, with periods of alleviation followed by recurrence of symptoms consisting in vomiting and colicky abdominal pain. Consequently additional imaging studies were performed, such as upper GI series which excluded the gastroesophageal reflux disease but displayed signs of GOO, and upper endoscopy which didn't detect any esophageal or gastric lesions suggesting a peptic disease. An intermittent gastric volvulus was also taken into account, based on the atypical plicated appearance of the stomach during upper GI series.

As mentioned, the definitive diagnosis was made only by directly assessing the pyloric fibrous stricture during surgery and subsequently by histopathologically confirming it.

A very rare similar form of GOO was described by Sharma *et al* (1) under the name of Jodhpur disease, with 22 cases reported so far. The average age of presentation is 2.9 years with predilection of male sex (6). Its features include narrowing of the pyloric canal, increased gastric emptying time and a large-sized stomach; the US evaluation does not show pyloric muscle hypertrophy and the gastroscopy reveals no intraluminal pathology. Histopathologically there is a normal structure of the pylorus, without inflammatory, fibroproliferative or neoplastic cells. Regarding our patient, most of the above aspects were present except that the

pyloric biopsy displayed thickened muscularis mucosae, containing collagen bundles intersecting with the muscle fibers and also entering the submucosa. The complete absence of inflammatory cells excluded the acquired inflammatory trait, which distinguishes our case from the one reported by Ratan et al (8). As is the case with Jodhpur disease, pyloroplasty proved to be very efficient in treating this illness.

In those cases in which other known congenital or acquired causes of a non-HPS GOO are ruled out, the rare

event of an idiopathic fibrous pyloric stenosis should also be considered; this pathologic entity has not been reported in literature until now.

As it happened in our case, the empiric antacid and symptomatic treatment only prolongs the child's illness and delays the definitive surgical treatment, e.g. pyloroplasty. Therefore, we stress the importance of establishing the etiology of a GOO, even though this can be difficult to achieve (9). In this regard, upper GI series and endoscopy can be of great help.

References

1. Sharma KK, Agrawal P, Toshiniwal H. Acquired gastric outlet obstruction during infancy and childhood: a report of five unusual cases. *J Pediatr Surg* 1997;32:928–930.
2. Ormarsson OT, Haugen SE, Juul I. Gastric outlet obstruction caused by heterotopic pancreas. *Eur J Pediatr Surg* 2003;13:410–413.
3. Azarow K, Kim P, Shandling B, et al. A 45-year experience with surgical treatment of peptic ulcer disease in children. *J Pediatr Surg* 1996;31:750–753.
4. Perdereau S, Touzot F, Robin L, et al: Recurrent pyloric stenosis in a 7-year-old child with chronic granulomatous disease. *Arch Pediatr* 2013;20(12):1337–1339.
5. Shukla RM, Mukhopadhyay M, Tripathy BB, et al. Pyloric and antral strictures following corrosive acid ingestion: A report of four cases. *J Indian Assoc Pediatr Surg* 2010;15(3):108–109.
6. Sharma KK, Ranka P, Goyal P, et al. Gastric outlet obstruction in children: an overview with report of Jodhpur disease and Sharma's classification. *J Pediatr Surg* 2008;43(10):1891–1897.
7. Chan KL, Saing H. Balloon catheter dilatation of peptic pyloric stenosis in children. *J Pediatr Gastroenterol Nutr* 1994;18:465–468.
8. Ratan SK, Dhua AK, Sinha S, et al. Acquired nonspecific cicatrizing inflammation causing pyloric stricture and gastric outlet obstruction in infancy: is it Jodhpur disease? *Trop Gastroenterol* 2013;34(4):274–277.
9. Hameury F, Mcheik J, Lardy H, et al. Acquired non hypertrophic pyloric stenosis in children. *Arch Pediatr* 2007;14(4):330–333.

Correspondence to:

Lucian Vida
Department of Pediatric Surgery
Braşov Children's Hospital
Braşov, 45 Nicopole Street, 500063
Romania
Phone +40 740304603
E-mail: lucian_vida@yahoo.com

ULTRASOUND DIAGNOSIS AND CORRELATION BETWEEN OBSTETRICAL TRAUMA AND NEUROLOGICAL DISORDERS

Marioara Boia¹, Daniela Cioboata², Florina Doandes²,
Nicoleta Lungu², Oana Costescu², Aniko Manea¹

Abstract

Introduction Obstetric traumas are neonatal disorders of multiple causes, often unpredictable, with implications for the clinical development of the newborn. Incidence is estimated at 2-7 % live births, decreasing due to improved health care. Mortality 2-3% of all neonatal deaths, 5-8 / 100,000 through physical trauma, 25 / 100,000 through hypoxia. **Objectives** The authors propose a review of severe forms of brain injury resulting from birth traumas, correlated with ultrasound monitoring and clinical evolution. **Results** Depending on the degree of somatic and neurological maturity, respectively gestation age and birth weight, the conditions observed or caused by perinatal insult may be different. Also, the type of mechanical insult (physical or hypoxic) can cause different injuries depending on the intensity or degree of neurological immaturity. Both short-term prognosis and long-term neurological prognosis depend on the early diagnosis of these lesions (subarachnoid hemorrhage, subdural hemorrhage, massive cerebral infarction, perinatal hypoxic-ischemic encephalopathy, grade IV intraventricular hemorrhage), the early establishment of the treatment and, if appropriate, the integration of the baby into the follow-up program and neurological dispensary. **Conclusions** Cerebral trauma due to obstetric causes is still an important cause of infant morbidity and mortality. The most serious brain injuries secondary to severe perinatal insult are: subdural hemorrhage, massive cerebral infarction and severe perinatal hypoxic-ischemic encephalopathy, grade IV intraventricular hemorrhage.

Keywords: ultrasound diagnosis, neurological lesions

Introduction

Obstetrical traumas - mechanical, hypoxic, ischemic lesions to which the newborn was subjected in the labor and delivery process, are the major cause of death in the neonatal period. The incidence is 2-7 % of living newborns and mortality - 2-3% of all neonatal deaths, 5-8 / 100,000 through obstetrical trauma and 25 / 100,000 through

hypoxia. [1]

Brief history

In ancient Greece, Hippocrates (460-377 B.C.) wrote: "no head injury is not too severe to despair, or too trivial to ignore", making a distinction between epilepsy and neonatal seizures.

A link between obstetrical trauma and neonatal neurological disorders was made in 19th century by Little (in 1843) that considered cerebral diplegia was associated with a traumatic birth and prematurity and asphyxia to be predisposing factors. Gowers in 1888 reported as etiologic factors asphyxia, transversal presentation and primiparity. In 1931, Ehrenfest noticed that 35% of newborns with laborious birth presented nystagmus, and 12% had retinal hemorrhage.

Risk factors: macrosomia, mechanic/dynamic dystocia, prolonged expulsion, abnormal presentation, prematurity, applying the forceps at birth, using vacuum extraction.

Classification of posttraumatic neurological lesions

In the premature infant, the posttraumatic neurological lesions are hypoxic-ischemic lesions of the periventricular white matter (focal and diffuse cerebral ischemic lesions, haemorrhagic necrosis of basal nuclei and thalamus) and the peri/intraventricular haemorrhage.

In term newborn, mechanical injuries during labor and birth induce asphyxious necrosis of the gray matter and cerebral haemorrhage (epidural, subdural, subarachnoid haemorrhage; periventricular and intraventricular haemorrhage; cerebellum hemorrhage).

The role of transfontanellar US

The transfontanellar ultrasounds are effective in evaluating term and premature newborns with brain lesions and allows early diagnosis and monitoring of brain lesions as long as the anterior fontanelle allows. Echographic signs are closely correlated with the anatomo-pathological data.

¹Universitatea de Medicina si Farmacie "V.Babes Timisoara", Disciplina Puericultura –Neonatologie
²Spitalul Clinic de Urgenta pentru Copii" Louis Turcanu" Timisoara , Clinica Neonatologie-Prematuri
E-mail: marianaboia@yahoo.com; daniela.cioboata@yahoo.com, florina_doandes@yahoo.com, nico_lungu2001@yahoo.com, oanabilav@yahoo.com, aniko180798@yahoo.com

Intracranial haemorrhage (ICH)

The traumatic injury of the newborn's brain is conditioned by mechanical trauma during the process of delivery, with the production of tentorial and vascular ruptures with extensive supra or subtentorial haemorrhages. The incidence of intracranial haemorrhage in newborns is directly correlated with weight loss:

- 50-60% in those with BW under 1000g,
- 10-20% in those with BW 1000-1500g. [1]

ICH are rarely present at birth: 50% occur on the first day after birth, 80-90% occur up to the third day after birth and 20-40% progress during the first week of life. [2]

Epidural hemorrhage are rare in the newborn, up to 2% of total ICH, but are difficult to diagnose, the symptoms are developed later. They are often associated with linear fractures of the cranial bones that occur after the application of forceps or vacuum extractor in a laborious labor. [3,4]

More frequent in term newborn, in fetal disproportions, when pelvic structures are extremely rigid, are the subdural haemorrhages. When the duration of labor is too short, it does not allow sufficient expansion of the pelvic structure, and when is too long, the fetal head is subject to prolonged compression.

Clinical variants of subdural haemorrhage: injury of the cerebellar tentorium with the inferior sagittal sinus rupture, hematoma in the posterior cranial fossa due to the tentorium laceration with the right, transverse sinus or Galen vein rupture, or rupture of superficial cerebral connecting veins.

Clinical signs occur within the first 24 hours after birth: focal or generalized seizures, disturbance of consciousness, irritability, neurological focal signs (hemiparesis, tonic convulsions, pupil dilatation on the same side as the hematoma). Evolution is severe, so diagnosis needs to be established quickly.

Transfontanelar ultrasound reveals large, hyperechogenic formation adjacent to the fronto-parietal

lobes (large hematomas of convexity), echodense image between the two hemispheres (interhemispherical, subdural fluid collections), hyperechogenic subtentorial image located above the cerebellar hemispheres – (hematomas in the posterior subdural fossa - rarely encountered). [5]

Subdural haemorrhage complications are severe: cerebellum and brainstem compression, obstruction of preponine cisterns, IV ventricle and aqueduct.

More common in premature newborns than in term newborns (29% in premature under 2000g) [3] is subarachnoid haemorrhage. If the haemorrhage is limited, it is asymptomatic. The extended form has a severe evolution: seizures, precoma or coma, hydrocephalus.

Transfontanelar ultrasound has low sensibility for diagnosis: the brain has an increased echogenity to the periphery or, it can reveal, hyperechogenic enlargement of the Sylvius aqueduct in coronary incidence. [5].

Peri/intraventricular haemorrhage, more frequently in premature babies, occasional in term newborns, can determine severe neurologic sequels. The incidence is 50% in GA < 30 weeks and BW < 1500 g, and frequency, inversely proportional with BW.

There are 4 degrees of severity:

- First degree (I)– subependymal haemorrhage;
- Second degree (II)– intraventricular (iv) haemorrhage - less than 50% of the lateral ventricle (LV) volume;
- Third degree (III)– iv haemorrhage - over 50% of the LV volume- Fig. 1 [5];
- Fourth degree (IV)– iv and intraparenchymal haemorrhage- Fig. 2 [5].

Obstetrical trauma is associated with ~ 10% of cases with peri/iv haemorrhage of third or fourth degree. Fourth degree IV Haemorrhage is the most severe form. In 80% of newborn babies, the haemorrhage occurs in the first 72 hours after birth [2].

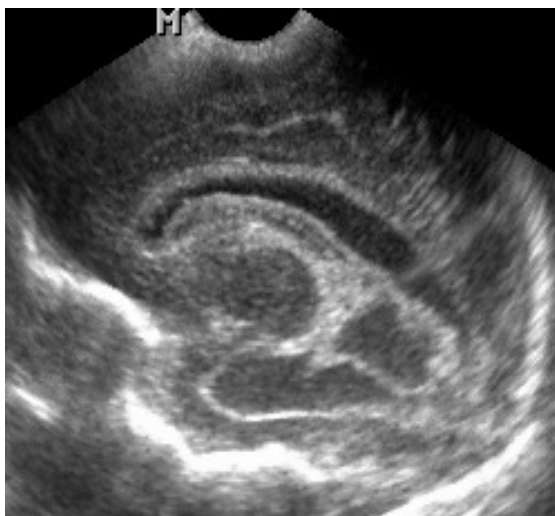


Fig. 1. Dilated lateral ventricles, the blood occupies more than 50 % of the LV volume. The anterior horns, and especially the posterior horns are dilated and so the aspect of colpocephaly can be observed.

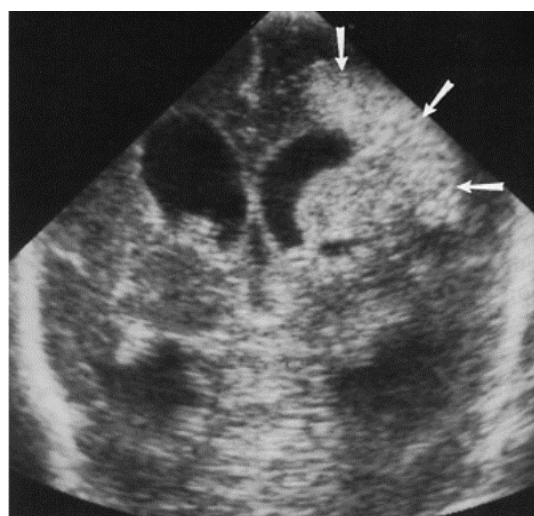


Fig. 2. Fourth degree intraventricular haemorrhage. Extended blood lesion inside frontal and occipital lobes on the same side with the intraventricular haemorrhage.

Hidrocephalus is the most severe complication of severe peri/intraventricular haemorrhages (75% of survivors). First ultrasound sign is dilatation of the trigone and occipital horns. At round 2 weeks after the haemorrhage, appears small, hyperechogenic areas - particles with a low amount

of proteins floating in the CSF (cerebrospinal fluid) – Fig 3,4 [5]. Obstruction, on several levels: LV near Monro's foramen, in the cerebral aqueduct of Luschka and Magendie, in the pericerebral cisterns.

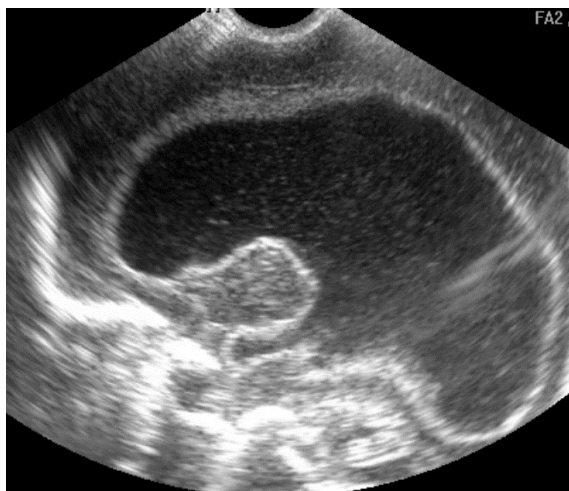


Fig. 3,4. Severe Hydrocephalus with small, hyperechogenic areas - particles with a low amount of proteins floating in the CSF.

Cerebellar haemorrhage

Cerebellar haemorrhage is a severe form of haemorrhage. 15-25% in premature babies with GA <32 weeks and BW <1500g, strongly associated with severe intraventricular haemorrhage [3].

Clinical signs: repeated apnea episodes, severe bradycardia (through bone marrow compression by cerebellar mass), decreasing hematocrit and hemorrhagic CSF. In prematures, onset in 1-21 days of life, with rapid evolution towards death in the first 12-36 hours.

Transfontanelar ultrasound reveals echogenic increase of the cerebellum, inhomogeneous echogenicity, asymmetrical, that can cover the entire cerebellar mass in severe forms.

Hypoxic ischemic encephalopathy

Frequent disease in neonatal medical practice with major implications concerning short term and long term health condition. US is efficient in the evaluation of newborns with hypoxic-ischemic post-traumatic cerebral lesions. The basis of clinical signs are major neuropathological aspects: focal and diffuse ischemic cerebral lesions and the hemorrhagic necrosis of the basal nuclei and thalamus.

Focal and diffuse ischemic lesions are more frequently in term newborn than premature babies and they are responsible for 10-15% of neonatal seizures. The

prevalence is 15-20% in the newborn with hypoxic ischemic encephalopathy [6].

Ischemic lesions in the distribution territory of one of the major cerebral arteries, especially middle cerebral artery (over 50%), determinates cerebral infarcts.

Ultrasound investigations (Fig 5,6) reveals hyperechogenic zones of different dimensions well outlined, diffuse in the cerebral cortex, the absence of arterial pulse, the absence or poor delimitation between gyrus and sulcus. Cerebral infarction cause neurological sequelae or death in 90% of patients with echographic modifications of the cerebral parenchyma.

Complications of cerebral infarction are:

- cerebral atrophy - echographic: the increase of the interhemispheric fissure, the increase of the distance between gyri (increased dimension of the sulcus);
- ventriculomegaly - in 19-20% of cases;
- parenchymal calcifications;
- multicystic encephalopathy [2].

Hemorrhagic lesion of the basal nuclei and thalamus within a perinatal hypoxic-ischemic encephalopathy are rarely encountered in medical practice. It appears both in preterm newborns as well as in term newborns. Typical echographic signs (Fig 7,8) are: hyperechogenicity in the area of the basal nuclei, especially at the level of the caudate nucleus and thalamus, and decrease of arterial pulse.



Fig. 5. Severe form of cerebral infarction in the distribution territory of the anterior cerebral artery.



Fig. 6. Cerebral atrophy –characterized by the increase of the interhemispheric fissure, the increase of the distance between gyri and ventriculomegaly.



Fig.7,8. Hemorrhagic lesion of the basal nuclei and thalamus.

Conclusions

Obstetrical brain injury represent an important cause of infant morbidity and mortality. In the premature infant, the hypoxic-ischemic lesions of the periventricular white matter and peri/iv haemorrhage are the main brain injuries, while in term newborn, mechanical injuries during labor and birth

with asphyxious necrosis of the gray matter and cerebral haemorrhage.

Term prognosis and neurological long-term prognosis depend on the early diagnosis of these lesions, on the early establishment of treatment and, if necessary, the integration of the child in the follow-up program and neurological monitoring.

References

1. Nicolas Nunes R., Hamilton M., Cardeal D., Traumatic brain lesions in newborns, Arq. Neuro-Psiquiatr. Sao Paulo 2017; 75:170-188
2. T. Michael O'Shea, Karl C.K. Kuban et al., Neonatal Cranial Ultrasound Lesions and Developmental Delays at 2 Years of Age Among Extremely Low Gestational Age Children; Pediatrics 2008; 122: 662-669
3. Volpe JJ. Injuries of extracranial, cranial, intracranial, spinal cord and peripheral nervous system structures. In

- Volpe JJ – Neurology of the newborn, 2008, Elsevier Health Sciences: 959-984
4. Kokolakis M., Koutelekos I.; Birth related traumatic brain injury –nursing interventions; Perioperativ nursing 2015; 4:121-136
5. Boia M, Ghid practic de ecografie transfontanelara, Editura Eurobit, Timisoara, 2015.
6. De Vries L., Groenendaal F., Patterns of neonatal hypoxic–ischaemic brain injury; Neuroradiology 2010 Jun; 52(6): 555–566.

Correspondence to:

Aniko Manea
Spitalul Clinic de Urgenta pentru Copii” Louis Turcanu”
Timisoara, Clinica Neonatologie-Prematuri
Iosif Nemoianu Street no. 2,
Timisoara
E-mail: aniko180798@yahoo.com

A 10 YEARS SBS RETROSPECTIVE STUDY OF NEONATES AND CHILDREN

Henry Osakwe^{1,3}, Adrian Pavel^{1,4}, Maria Trailescu^{1,4},
Elisa Mussuto², Calin Popoiu^{2,3}, Eugen Boia^{2,3}

Abstract

Introduction: Short bowel syndrome (SBS) neonates have complex management challenges, meaning a significant health care extra cost. This is 10 years retrospective SBS study-based estimate of children and neonates in our hospital. Population estimate of the incidence and mortality rate of neonates with SBS is not so accurate because of the differences in the definition, follow-up and regional referral patterns. The introduction of total parenteral nutrition (TPN) led to a remarkable improvement in the survival of SBS patients, but unfortunately the most common cause of death in SBS patient's is also TPN-induced hepatic dysfunction. Even though the survival of patients with less than or equal to 40 cm of residual small bowel is now routine. The long term survival of infants with as little as 20 to 30 cm small bowel can be expected. The management goal of these patients is to reduce the duration of TPN and to maximize intestinal nutrient absorption. It is difficult to predict the duration and the type of nutritional support for patients with SBS. Some patients may require permanent parenteral nutrition on either a continuous or intermittent basis depending on the length of the residual bowel. **Objective:** To evaluate the direct and indirect evidence that adaptation occurs after an extensive bowel resection, to review the factors that influence adaptation and to assess the strategies used in attempts to optimize this process. **Methodology:** A retrospective medical record review of newborns and children with SBS treated at our hospital between 2007 and 2017. Medical records of patients studied were retrieved from our archives and analyzed. **Results:** a *p*-value less than 0.05 (*p*-value = 0.033) was obtained, being statistically significant proving that there is a direct correlation between the post-operation intestinal length and the duration of parenteral nutrition. **Conclusion:** The major predictors of weaning from PN are adjusted small bowel length and the amount of energy patient can derive from enteral feeding attempts, also as a result of new management strategies combined with a

multidisciplinary team approach, majority of patients will wean from PN despite short intestinal length.

Keywords: short bowel syndrome, incidence, parenteral nutrition, mortality, outcomes

Introduction

Short bowel syndrome (SBS) results from the alteration of intestinal digestion and absorption that occurs after extensive bowel resection. It is a complex disorder with nutritional, metabolic, and infectious consequences. The amount of resection or remaining bowel generally dictates the degree of malabsorption and consequently the need for specialized enteral nutrition or parenteral nutrition (PN). Intestinal failure in the context of SBS is defined as a dependence on PN to maintain minimal energy and fluid requirement for growth in children. The incidence of extreme SBS in the neonatal age group is around 3-5/100,000 birth/year. The prevalence has improved over the last 2 decades due to an enormous progress in intensive care medicine, while the prognosis of babies with severe intestinal disease and/or following major surgery has drastically improved. Short bowel syndrome occurs when the functioning gut mass is reduced below the amount necessary for adequate digestion and absorption of food and fluid. Although the absorptive function of the intestine does not always correlate with residual bowel length, SBS is usually defined anatomically as less than 30% of normal intestinal length (<75 cm) in children. In the failing intestine the inability to absorb nutrients, fluids, and electrolytes eventually leads to clinical deficiencies and if an increase in oral intake is not sufficient to compensate for this malabsorption, then PN support is required. Short bowel syndrome (SBS) is a devastating condition with a mortality rate of up to 40% in neonates and also with significant morbidity. The causes of SBS are the following: necrotizing enterocolitis 32%, atresia 20%, volvulus 18%, gastroschisis 17%, aganglionosis 6%, others 7%.

¹County Emergency Hospital Arad, Romania

²Children's Hospital "Loius Turcanu" Timisoara, Romania

³University of Medicine and Pharmacy 'Victor Babes' Timisoara, Romania

⁴West University 'Vasile Goldis' Arad, Romania

E-mail: henrysan2007@yahoo.com, adipavel72@yahoo.com, trailescumaria@yahoo.com, elisamussuto@gmail.com, mcpopoiu@yahoo.com, boiaeugen@yahoo.com

Institution based estimates of incidence and mortality was carried out using data from our hospital archives 10 years patient's records. Figure 1 shows the incidence of SBS in the general population (n=53) and in our reference SBS population (n=10) per year. While in SBS population the

distribution/year was quite homogenous, with mode and median equal to 1, in the general population the distribution shows a decreasing trend, with maximum peak in 2012 (9 SBS cases).

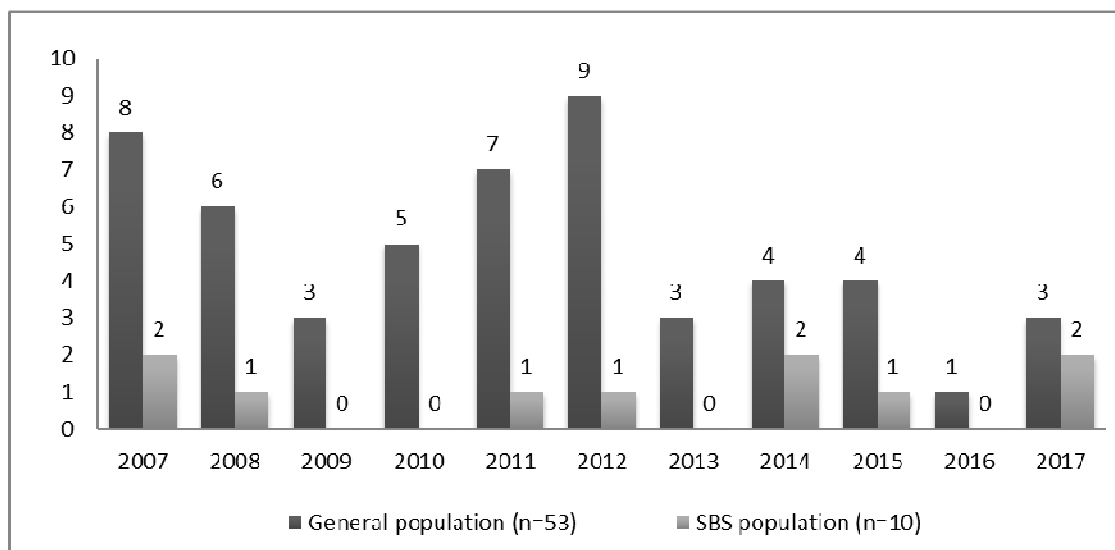


Figure 1. The incidence of SBS patient's (number) within the reference 10-years period of time, histogram.

In the general population, the incidence of SBS was much higher in the premature infants (less than 37 weeks) representing 35.84% (19 patients). In our reference group, however, the rate of premature patients was 40%, out of which 30% were male and 10% female, thus proving that SBS is multifactorial and not influenced by prematurity alone as a single factor. SBS fatality case rate was 3 out of 53 patients studied (5.66 %). The specific cause of death (for children less than 4 years old) was mainly cardio-respiratory arrest, acute respiratory insufficiency and

multiple organ failure Syndrome (MOFS). Table 1 defines the frequency rate of the main pathologies leading to SBS in the general studied population (n=53) and in the SBS studied population (n=10). In the general population study (n=53) gastroschisis was reported as the principal diagnosis in 17 patients (32 %), while in the specific population studied (n=10) gastroschisis was reported in 4 patients (40%). However, intestinal atresia represented 37 % in the general population cases studied (n=53) and just 20 % in the specific population cases studied (n=10).

Table 1. Comparison between rates of main diseases producing SBS in the general studied population (n=53) and the SBS reference population (n=10).

Frequency (%)	General studied population (n=53)	Disease	SBS studied population (n=10)	Frequency (%)
32.07547	17	Gastroschisis	4	40.0
7.54717	4	Volvolus	2	20.0
9.433962	5	Intussusception	0	0
37.73585	20	Small intestine Atresia/Stenosis	2	20.0
13.20755	7	Others (Necrotizing enterocolitis, etc)	2	20.0
100	53	TOTAL	10	100

Extensive intestinal resection leading to SBS is rarely necessary in older children.

Age was the first data analyzed and the mean age on admission in the SBS reference population was 896.7 ± 1818.87 hours. We calculated age in hours because majority of our patients (40%) were admitted in the first 24

h of life. Another 40% were admitted in the first one month, out of which 20% in the first week another 20% during the first month. Admission in the first 6 months of life and/or later in life was very rare. Table 2 illustrates the age on admission in both population studied.

Table 2. Age on admission in the general studied population (n=53) and the SBS reference population (n=10).

%	Nr of pts	Age	Nr of pts	%
30.18868	16	< 24 h	4	40
41.50943	22	1 - 30 days	4	40
9.433962	5	1 - 6 months	1	10
3.773585	2	6 - 12 months	1	10
3.773585	2	> 12 months	0	0
11.32075	6	unknown	0	0
100	53	TOTAL	10	100

Weight on admission was also studied and it was essential for subsequent postoperative follow-ups. Surprisingly, the mean weight calculated at 2522 ± 656.51 g falls within the normal weight range for newborns (2500 to 5000 g). However, when compared with the calculated mean weight for the general population (n=53) the value was much lower (mean weight value being 3640 ± 2948 g). SBS is the main cause of intestinal failure (IF) in children and has a higher morbidity and mortality rate. The adaptation changes that takes place after an extensive intestinal resection depends on the resected intestinal length, the location of the residual intestine and the nature of the disease responsible for the decision to resect a relatively large portion of the intestine. The length of residual intestine was measured in 10-cm segments from the ligament of Treitz advancing along the anti-mesenteric border of a slightly stretched intestine. The length of residual small bowel varied from 37 to 75 cm. Patients with residual intestine above 75 cm were excluded from the SBS reference group since their PN did not exceed a period of two weeks. While some patients received daily trace elements (added to the standard nutrient formulas) and lipids every other day, others received standardized formulas with or without lipids. During the immediate post-operation phase, continuous TPN was introduced until the first bowel movement occurred. This protocol assured an adequate circulating fluid volume with an acid-base and electrolyte balance. Patients received per kilogram body weight per day: dextrose, 3-4 g; lipids, 0.7-1 g. Nitrogen requirements were met by 0.10-0.15 g nitrogen contained in an amino acid solution (25 g of nitrogen per liter). Vitamins were administered separately twice a week. PN was delivered using a subcutaneous tunneled silicone catheter emptying into the internal jugular vein. EN was initiated gradually, starting with a strict non-fiber diet which was followed by a normal diet with or without intermittent or continuous TPN. Nutritional status was evaluated weekly.

The body weight, urine, stool and serum albumin, pre-albumin, and transferring were frequently analyzed.

Aim

To evaluate the direct and indirect evidence that adaptation occurs after an extensive bowel resection, to review the factors that influence adaptation and to assess the strategies used in attempts to optimize this process.

Methodology

A retrospective medical record review of neonates and children with SBS treated at the Children's Hospital "Louis Turcanu", between 2007 and 2017. First we analyzed the medical records of patients with preliminary diagnosis of SBS after an extensive intestinal resection in the *general population* (n=53), this was trimmed down further to a small cohort of patients that met our criteria for SBS referred to as *SBS population* (n=10). Dependency on PN for at least 25 days after surgery for congenital or acquired intestinal diseases and a minimal admission length of 30 days were parts of the criteria considered for a true short bowel syndrome. Microsoft Excel Worksheet was used for data collection and statistical analysis.

Results

Attention was focused first on the correlation between the length of the residual bowel (cm) and the duration of the exclusive/complementary PN and then the correlation between the length of the residual bowel (cm) and the initiation of total EN after surgery (days). In the reference SBS population (n=10) data analysis, the average length of the resected intestine was 122 ± 43.82 cm, these varied from 15 cm to 175 cm, while the mean length of post-operation residual intestine was 55.20 ± 11.28 cm, these varied from 37 cm to 75 cm. However, the average duration of PN alone was 40.1 ± 26.33 days, while the mean period of time needed to restore a complete EN was 42.5 ± 29.45 days. Using regression statistics, we calculated the

correlation (R) between the residual bowel length and the time needed for the restoration of a complete EN. Tables 3

and 4 illustrate the steps taken towards this calculation.

Table 3. Regression Statistics.

Multiple R	0.701299489
R Square	0.491820974
Adjusted R Square	0.428298595
Standard Error	8.994559521
Observations	10

Table 4.

	<i>df</i>	<i>SS</i>	<i>MS</i>	<i>F</i>	<i>Significance F</i>
Regression	1	626.3831921	626.3831921	7.742483625	0.02383128
Residual	8	647.2168079	80.90210099		
Total	9	1273.6			

Table 5.

	<i>Coefficients</i>	<i>Standard Error</i>	<i>t Stat</i>	<i>P-value</i>	<i>Lower 95%</i>	<i>Upper 95%</i>	<i>Lower 95.0%</i>	<i>Upper 95.0%</i>
Intercept	66.62054297	4.993603002	13.34117729	9.52577E-07	55.1052738	78.13581214	55.1052738	78.13581214
EN	-0.268718658	0.096573434	-2.782531873	0.02383128	-0.491417396	0.04601992	-0.491417396	0.04601992

Our p -value being equal to 0.023 is statistically significant at a $p < 0.05$, so it was assumed that with a confidence interval (C.I.) of 95% with 1 degree of freedom (df), the post-operation residual intestinal length has direct

correlation with the time needed for a complete restoration of EN.

The same formula and statistical calculation was used to find the correlation between post-operation intestinal length and the duration of PN, as illustrated in Tables 6, 7 and 8.

Table 6. Regression Statistics.

Multiple R	0.671784622
R Square	0.451294578
Adjusted R Square	0.382706401
Standard Error	9.346330998
Observations	10

Table 7.

	<i>df</i>	<i>SS</i>	<i>MS</i>	<i>F</i>	<i>Significance F</i>
Regression	1	574.768775	574.768775	6.579772104	0.033380701
Residual	8	698.831225	87.35390313		
Total	9	1273.6			

Table 8.

	<i>Coefficient</i>	<i>Standard</i>	<i>t Stat</i>	<i>P-value</i>	<i>Lower</i>	<i>Upper</i>	<i>Lower</i>	<i>Upper</i>
<i>s</i>		<i>Error</i>			<i>95%</i>	<i>95%</i>	<i>95.0%</i>	<i>95.0%</i>
Intercept	66.7460514	5.384809	12.395249	1.67411	54.328659	79.163443	54.328659	79.163443
pt	4	059	43	E-06	48	39	48	39
PN	-	0.112249	-	0.03338	-	-	-	-
	0.28793145	312	2.5651066	0701	0.5467788	0.0290840	0.5467788	0.0290840
	7		46		36	79	36	79

In this case a *p*-value less than 0.05 (*p*-value = 0.033) was obtained, being statistically significant, thus proving that there is a direct correlation between the post-surgery intestinal length and the duration of PN, at a confidence interval of 95%, with 1 degree of freedom. These results clearly demonstrated how the post-operation intestinal length can influence the quality of life and the evolution of a SBS pediatric patient. On the contrary, applying the same calculation, no statistically significant relationship was found neither between the length of the resected intestine and the duration of PN (*p*-value = 0.555, for *p* < 0.05, *df* = 1, *C.I.* = 95%) nor between the resected intestine and the time needed for restoration of a complete EN (*p*-value = 0.561, for *p* < 0.05, *df* = 1, *C.I.* = 95%).

Discussions

Pediatric SBS remains a management challenge with significant mortality. In order to improve the survival rate of patients we need to create an Advanced Intestinal Rehabilitation Center which includes dedicated surgery staff, gastroenterologists, neonatologists, nutritionists, pharmacists, nursing staff and social workers (3). Although absolute small bowel length is only slightly predictive of mortality, the percentage of normal bowel length (for a given infant's gestational age) is strongly predictive of mortality (if < 10% of normal bowel length) (1). The presence of the ileocecal valve (ICV) also strongly predicted weaning from PN; however, ICV was not predictive of survival. Death rate was just 5.66%, representing 3 out of 53 patients in the general population studied, while in the SBS population studied (*n*=10), there were no death observed.

Multiple nutritional, hormonal, and surgical therapies have evolved in the management of SBS patients in an attempt to improve life and decrease the duration of TPN dependency (5). Indirect evidence that intestinal adaptation takes place comes from the fact that patient's with very short bowel lengths can become independent of PN after a period of months or even years (12). Whether a patient can be weaned from PN is dependent on a number of factors. The length of small bowel and the presence of colon are very important. Other factors that are useful in predicting whether intestinal failure is permanent are the time on PN (>

2 years) and the amount of energy the patient can derive from enteral feeding (13). PN associated liver failure (PNALF) or venous thrombosis with loss of vascular access, result in failure of PN therapy (2). Patients who can no longer receive PN may still have intestinal transplantation as the only therapeutic option left (4). The result of transplantation due to intestinal failure using either an isolated intestine or composite grafts (liver and intestine or multi-visceral including intestine), has improved considerably but remains disappointing (6). The introduction of hepato-protective strategies and multidisciplinary management has significantly improved the outcome of neonates with SBS who require PN (7). Successful and reproducible strategies to increase adaptation remain elusive despite an abundance of experimental data (13). More than 90% of infants now survive after extensive small bowel resection with PN and the remaining small intestine will adapt with time (11). Home-based PN allows children to be treated in the best psychosocial environment (8). The residual small bowel length remains an important predictor for the duration of PN in infants and children with SBS. Prompt restoration of intestinal continuity is associated with low risk of intestinal failure and subsequent cholestatic liver disease (9). Early enteral feeding after surgery is associated with reduced duration of PN and less cholestasis (10). Cholestasis (conjugated bilirubin ≥ 2.5 mg/dl) remains the strongest predictor of mortality (9).

Conclusions

The major predictors of weaning from PN are adjusted small bowel length and the amount of energy that patient can derive from enteral feeding attempts, while the major predictors of mortality in pediatric SBS are cholestasis and age adjusted small bowel length. These data permit better prediction of outcomes of pediatric SBS and may help to direct future management of these challenging cases, while accurate estimates will assist clinicians in counseling parents, allocating resources, and planning clinical trials. Also, as a result of new management strategies combined with a multidisciplinary team approach, majority of patients will wean from PN despite short intestinal length.

References

1. Tilson MD: Pathophysiology and treatment of short bowel syndrome. *Surg Clin North Am* 60:1273–1284, 1980
2. Joyeux H, Solassol C: La nutrition artificielle: Suppléance intestinale et support régénératif dans les syndromes d'intestin court. *In* Actualités Chirurgicales,

- | | |
|---|--|
| <p>T. Chir. Abdominale et Digestive, Paris, Masson, 1981, pp 94–105</p> <p>3. Fleming CR, Beart RW, Berkner S, McGill DB, Gaffron R: Home parenteral nutrition for management of the severely malnourished adult patient. <i>Gastroenterology</i> 79:11–18, 1980</p> <p>4. Jeejeebhoy DN, Langer S, Tsallas G, Chu R, Kuksis A, Anderson GH. Total parenteral nutrition at home: Studies in patients surviving four months to five years. <i>Gastroenterology</i> 71:943–953, 1976</p> <p>5. Sheldon GF: Role of parenteral nutrition in patients with short bowel syndrome. <i>Am J Med</i> 67:1021–1029, 1979</p> <p>6. Weser E: Nutritional aspects of malabsorption. Short gut adaptation. <i>Am J Med</i> 67:1014–1020, 1979</p> <p>7. Colin R: Adaptation après résection étendue de l'intestin grêle chez l'homme: Utilisation optimale des réserves ou conséquence d'une régénération intestinale. <i>Gastroenterol Clin Biol</i> 6:153–155, 1982</p> <p>8. Joyeux H, Astruc B: <i>Traité de nutrition artificielle de l'adulte</i>. Montpellier, (eds) Société scientifique des traités de nutrition artificielle, 1980.</p> | <p>8. Joyeux H, Solassol C: Home parenteral feeding. <i>In</i> Topics in Gastroenterology. SC Truelove, HJ Kennedy (eds). Oxford, Blackwell Scientific Publications, 1980, pp 75–82</p> <p>9. Hill GL, Mair WSJ, Goligher JC: Gallstones after ileostomy and ileal resection. <i>Gut</i> 16:932–936, 1975</p> <p>10. Kelly T, Klein R, and Woodford J: Alterations in gallstone solubility following distal ileal resection. <i>Arch Surg</i> 105:352–355, 1972.</p> <p>11. Weser E, Fletcher JT, Urban E. Clinical conference: Short bowel syndrome. <i>Gastroenterology</i> 77:572–579, 1979.</p> <p>12. Williamson RCN, Chir M: Intestinal adaptation. I. Structural, functional and cytokinetic changes. <i>N Engl J Med</i> 26:1393–1402, 1978.</p> <p>13. Williamson RCN, Chir M: Intestinal adaptation. II Mechanisms of control. <i>N Engl J Med</i> 26:1444–1450, 1978.</p> |
|---|--|

Correspondence to:

Henry Osakwe,
County emergency hospital Arad,
Department of Pediatric Surgery,
Str. Andreny Karoly, Nr. 2 – 4,
Tel: 0724143432
E-mail: henrysan2007@yahoo.com

MANUSCRIPT REQUIREMENTS

The manuscript must be in English, typed single space, one column on A4 paper, with margins: top – 3 cm, bottom – 2,26 cm, left – 1,5 cm, right – 1,7cm. A 10-point font Times New Roman is required.

The article should be organized in the following format: Title, Names of all authors (first name initial, surname), Names of institutions in which work was done (use the Arabic numerals, superscript), Abstract, Keywords, Text (Introduction, Purpose, Materials and Methods, Results, Discussions and/or Conclusions), References, and first author's correspondence address.