CONTENTS

A SEVEN YEARS EXPERIENCE IN HIRSCHSPRUNG'S DISEASE TREATMENT

Radu-Iulian Spataru[1], Niculina Bratu[1], Monica Ivanov[1], Dan-Alexandru Iozsa[1]

Abstract

Introduction. Hirschprung's Disease (HD) is one of the main causes for the failure of meconium pass in the first 24-48 hours of life or later chronic constipation in infants or children. The diagnosis and the evolution after certain surgical treatment make HD a controversial topic for the pediatric surgeons where the success strongly relates to the postoperative issues.

Purpose. The feasibility and the safety of different diagnosis methods and operative techniques addressed in our team was the aim of our 7 years study.

Materials and methods. A retrospective study has been conducted over the cases of HD treated by our team in the last 7 years (January 2007 – June 2014). The study included 38 patients diagnosed by barium enema and/or suction rectal biopsy and further treated using 3 different operative techniques. Frozen tissue biopsy has been introduced in our team in the last year of our study and it has been used in 5 cases for intraoperative confirmation of the length of aganglionic bowel.

Results. Barium enema (used in 31 cases) was highly suggestive in diagnosis and preoperative imaging of the most cases of HD, but the gold standard for diagnosis is a rectal biopsy, which can be obtained safely using a mucosa-submucosa suction device (used in 14 cases). Modified Duhamel procedure was applied in 19 cases, Soave in 13 cases and De La Torre-Mondragon in 6 cases. The mean age was 28 months (the youngest patient having 7 weeks and the eldest 18 years old). The postoperative complications consisted in: residual septum, rectal bleeding, intestinal occlusion, enterocolitis, anastomotic stenosis, soiling and perianal rash.

Conclusions. The diagnosis quality in our clinic has increased after introducing the rectal suction biopsy and intraoperative frozen section biopsy. The use of the stapler device in the modified Duhamel procedure brings significant improvements regarding outcome. Soave is a valuable solution in total colonic HD and re-do surgery. De La Torre-Mondragon is an elegant procedure in the common type HD. Frozen tissue biopsy is a very safe method for intraoperative evaluation of the border between the aganglionic bowel and healthy colon.

Key words: Hirschsprung's Disease, surgical techniques, postoperative issues

Introduction

Hirschsprung's disease is the most common congenital anomaly in distal gut motility [1]. The intrinsic innervation of the gut wall is derived from neurons that are located entirely within the intramural ganglionic plexuses. There are two kinds of plexuses: myenteric (or Auerbach's) which lays within the muscularis externa between the circular and the longitudinal fiber layers, and there are two or more submucosal plexuses, the most superficial being the Meissner plexus [2]. HD is characterized by the absence of this intrinsic innervation in a variable length. The absence of propagation of the peristaltic wave is associated with the lack of submucosal and myenteric nervous plexuses making obstruction of the distal gut the primary clinical feature of HD [3]. Any child with history of chronic constipation or infant with failure of meconium pass in the first 2 days of life should be checked out for HD using appropriate diagnostic techniques [3, 4]. After the diagnosis of HD the surgical approach with the resection the aganglionic bowel segment is the current definitive treatment. On the other hand, the surgical approach over HD implies a lot of challenges in the matter of postoperative issues [1].

In our clinic, we recorded a significant improvement in the quality of diagnosis of HD by routine use of aspirative rectal biopsy and intraoperative frozen section histopathological examination. We also improved our surgical approach by replacing our classical Duhamel with the one-stage procedure using a stapler device and by introducing De La Torre-Mondragon surgical procedure.

Purpose

The aim of this study is to synthetize our last 7 years experience in HD management and to present the benefits or the disadvantages of different operative techniques used by our team. By using 3 different surgical approaches into treating HD patients and different diagnosis methods we've encountered varied aspects in the postoperative evolution. We are also claiming the importance of aspirative rectal suction biopsy and intraoperative frozen section biopsy.

[1]"Marie Sklodowska Curie" Emergency Clinical Hospital for Children, Bucharest
E-mail: radu_spataru@yahoo.com, nina.bratu@yahoo.com, mqmivanov@yahoo.com, dan.iozsa@yahoo.com

Materials and Methods

Our study focuses over the cases of HD treated by our team in the last 7 years (January 2007 – June 2014). We included in this retrospective analysis 38 patients who were diagnosed and surgically treated at different ages. The diagnosis was based by clinical picture, barium enema (26 cases), rectal suction biopsy (14 cases) and intraoperative frozen section biopsy (last consecutive 5 cases). In all cases, the diagnosis was confirmed by histopathological examination, using hematoxylin and eosin staining. We have used 3 different approaches: Modified Duhamel – one stage intervention using a stapler device (19 cases), Soave (13 cases) and De La Torre-Mondragon (6 cases). We have used modified Duhamel technique in common or high forms of congenital megacolon, and also in the majority of the cases admitted with an already performed colostomy. Soave procedure was preferred in high forms/ total aganglionosis and also in re-do pull-through surgeries. In the last years, based on the improved diagnostic means (rectal suction biopsy facility and intraoperatory biopsy) we introduced De La Torre-Mondragon technique. In present it is our surgical procedure of choice for patients with common type of HD.

Results

We have studied 38 cases of HD treated by a single team over the last 7 years. The sex ratio was 3.2:1 (29 males and 9 females). The mean age of intervention was 28 months. The youngest patient we have treated was 7 days and the oldest was of 18 years of age.

All cases showed constipation as major clinical sign. 8 patients experienced episodes of enterocolitis, previous to surgery. 12 children presented in emergency with acute signs of bowel obstruction. 15 cases suffered initial enterostomy (10 colostomies and 5 ileostomies), in 9 of them stoma being performed in other centers.

Barium enema was performed in 31 patients. In 9 cases the result was inconclusive (29%). In 6 patients repeated barium enemas were done, without obtaining suggestive images for HD.

In the last 14 cases we improved our diagnosis methods by introducing suction rectal biopsy. In 11 patients the results were positive for HD (78.6%). In 3 of them the result was unsatisfying, because of the quality of the obtained specimen (absence or not enough submucosa).

Frozen tissue biopsy was introduced in our clinic in the last year and was used in the last 5 consecutive cases. In all of them the length of the aganglionic segment was demonstrated.

In our series we encountered 5 difficult cases, misdiagnosed in other centers, with previous failed operations, in which the definitive diagnosis was established by serial open full thickness biopsies [12].

In all operated cases the diagnosis was confirmed by histopathological examination, using hematoxylin and eosin staining.

26 of our cases had common type of HD, 5 patients had a long colonic segment affected, 2 patients with short HD and 5 patients with total colonic HD.

We have used 3 different approaches: Modified Duhamel procedure using a stapler device (19 cases), Soave technique (13 cases) and De La Torre-Mondragon (6 cases).

After modified-Duhamel procedure we noticed the following complications [11]: 5 cases of minor rectal bleeding, subocclusive symptoms do to remnant septum with subsequent fecaloma formation in the rectal ampula in 4 cases, repeated enterocolitis in 3 cases, mechanical occlusion or adhesion in one case.

In patients who underwent Soave procedure we encountered 9 cases of significant perianal rash, and 7 cases with night soiling. We must mention that night soiling cannot be attributed to the technique itself, but to the length of the aganglionic segment and/or to the re-do surgery situation in 5 patients.

Analyzing the total/subtotal colonic HD cases that were operated using Soave technique we noted a medium frequency of stools in the first month after surgery of 7-15/day. Nevertheless, the frequency of stools decreased gradually in all cases as in after two years follow-up the frequency reduced to 4-6/day. In this group we noted 2 cases having postoperatory enterocolitis.

Despite the limited number of De La Torre Mondragon patients, we can affirm that this procedure gave us the best results, with only one complication reported – anastomotic stenosis successfully treated by serial dilatations.

Discussions

The rectum is always affected in HD, but the length of the additional involved proximal situated bowel varies widely [7].

In most of the cases, contrast enema, as the traditional way of diagnosis, may help the surgeon not only to presume the diagnosis of HD, but also to estimate the length of the aganglionic segment. In particular situations, as in neonates, in operated patients and in total aganglionosis forms, the diagnostic value of contrast enema diminishes considerable. This is the reason why the aspirative rectal biopsy has become a gold standard for the HD [8]. The procedure can be done at the bedside or in an ambulatory setting without the need for general anesthesia. Adequate tissue is obtained for analysis in the majority of patients. Repeated suction biopsies or full-thickness biopsies can be performed if the initial biopsy is equivocal.

A study made in 2005 [10] presents the sensivity and specificity of the three main diagnosis methods used in HD (see table 1). It mentions rectal suction biopsy with a sensivity of 93% and a specificity of 100%, contrast enema with a sensivity of 76% and a specificity of 97% and rectal manometry with a sensivity of 83% and specificity of 93%.

Other studies report a variability in contrast enema test, with a sensibility that can vary from 65% to 80% and a specificity of diagnosis from 65% to 100% [3, 6]. The normally innervated proximal colon may undergo progressive dilation, while anganglionic region may have a grossly normal or contracted appearance but it isn't effective in all forms of the disease – for example, in a total colonic the diagnosis is difficult to establish using radiologic

studies. Most cases are limited to the rectum and sigmoid colon [6, 7]. The length of the aganglionic small bowel and the age of the patient can influence the radiological findings in total colonic HD. The transitional zone can be false-positive in total colonic HD. The colon can appear normal. Total colonic HD may be assumed if the contrast enema study is normal but the patient remains symptomatic and other causes of distal bowel obstruction have been excluded [5]. On the other hand the barium enema is a good screening test for HD since it correlates with rectal biopsy as confirmation diagnosis [6].

In the investigation of neonates with functional large-bowel obstruction and older children with severe constipation, rectal biopsies remain the main diagnosis method. In our department we've used a RBI2 suction rectal biopsy device without manometric control. This technique's principle is getting small amounts of submucosa by direct suction of superficial rectal layers using an aspiration endorectal device. The correct gathered submucosa is sent to the Pathology Department for histological examination. The procedure can be done at the bedside or in an ambulatory setting without the need for general anesthesia. Adequate tissue is obtained for analysis in the majority of patients. Repeat suction biopsies or full-thickness biopsies under general anesthesia can be performed if the initial biopsy is equivocal [8]

An important mention would be that recent studies are trying to include full colonoscopy as a useful tool in determining the transition zone in transanal endo-rectal pull-through in HD (De la Torre-Mondragon technique) but none of them are concludent [9].

Conclusions

Introducing rectal suction biopsy in our clinic made possible reducing the age of intervention due to the early diagnosis of the disease and also the necessity of colostomies in common type and short HD cases. The relatively small percentage of positive results obtained in our series (78.6%) may be attributed to the learning curve of the procedure.

Frozen tissue histopathological examination should be a mandatory intraoperative step in evaluating the length of the affected colon segment, in order to decide the right spot for the future anastomosis. This quick procedure can prevent re-do surgery and future complications.

Soave procedure has been confirmed as the best choice for high forms of HD and for re-do surgery in misdiagnosed and mistreated cases. All cases of re-do surgery have reported variable night soiling as a complication.

De La Torre Mondragon became in our team the surgical procedure of choice for common type of HD, due to rapid postoperatory recovery and lack of complications.

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Correspondence to:
Radu Iulian Spataru
Maria Sklodowska Curie" Children Hospital
Bd. C-tin Brancoveanu nr. 20 Sector 4 Bucuresti
E-mail: radu_spataru@yahoo.com

DAILY PRACTICE OF MECHANICAL VENTILATION IN A PEDIATRIC INTENSIVE CARE UNIT - EXPERIENCE OF THE FIRST PEDIATRIC CLINIC TIMISOARA

Daniela Chiru[1,2], Craciun A[1,2], Tepeneu NF[1,2], David VL[1,2], Otilia Marginean[1,2], Ilie C[1,3]

Abstract

Aim. To assess how children requiring endotracheal intubation are mechanically ventilated in First Pediatric Intensive Care Unit (PICU), Timisoara. Material and methods. A four years observational study (January 2010 – December 2012) was conducted in the Fist PICU of Emergency Hospital for Children "Louis Turcanu" Timisoara and included all mechanically ventilated children $\geq$ 24 hours, aged 0-18 years. Results. One hundred eight patients met the inclusion criteria. The mean age of the patients was 27 months and median duration of mechanical ventilation was 9 days. The mean PRISM III score on admission was 17. The mean duration of mechanical ventilation was 9.36 days. Major indication for mechanical ventilation was acute respiratory failure. We used pressure-limited conventional modes of ventilation. Mean peak inspiratory pressure (PIP) values were constant < 30 cmH2O, with 12% of the patients having a maximum PIP $\geq$ 30 cmH2O, but < 35 cmH2O. There was little variability with positive end-expiratory pressure (PEEP) choice, with a mean value of 5 cmH2O. Mean levels of tidal volume (VT) was 8.16 ml/kg, and medium inspiratory fraction of oxygen (FiO2) was < 0.6. Arterial blood gases analyses showed normo- and hypocapnia. Sixty-seven percent of the patients fulfilled the oxygenation criteria for ARDS, but only half of them had bilateral pulmonary infiltrates. No mechanical complication as pneumothorax was noted. Ventilator associated pneumonia was encountered in 39% of patients. A total of 34 (32%) children died. Conclusions. Pressure ventilation modes were standard in our PICU. Describing the standard care and how mechanical ventilation is performed in children can be useful for future clinical trials.

Keywords: children, mechanical ventilation, modes of mechanical ventilation

Introduction

Mechanical ventilation is one of the most common procedures performed in pediatric intensive care units (PICU), with 20% to 64% of patients admitted to the PICU requiring ventilator support (1). The reasons for mechanical ventilation and management strategies vary, depending not only on disease state, but also on PICU's size, patient population served, clinician's experience and local protocols (2,3).

Many mechanical ventilation modes are currently used in clinical practice to provide respiratory support for a wide spectrum of patients, ranging from no lung disease to acute lung injury (ALI) or acute respiratory distress syndrome (ARDS). No data exist so far to determine the ventilatory mode that provides the greatest benefit with the minimum risk of ventilator-induced lung injury.

The definitions of ALI and ARDS for infants (older than one month of life), children, and adolescents are essentially similar to that already reported in adults (4-6). However, there are intrinsic differences between pediatric patients and adults, which often can affect management strategies. Infants and young children, as compared to older children, adolescents, and adults, have more compliant chest walls, higher sedation requirements, lower hematocrit (which may affect global oxygen delivery), higher baseline airways resistance, and lower functional residual capacity. Additionally, the still developing and growing lung may be at greater risk for ventilator-induced lung injury at a lower airway pressure than the developed lung of an adult (7).

By the end of the 20th century, pediatric intensivists had learned important insights about mechanical ventilation based on what works in adults. Outcomes over the past 2 decades have improved for adults with ALI/ARDS, managed with lung-protective ventilation strategies. The ARDS Network study (8) demonstrated that lower tidal volumes (VT) of 6 ml/kg with limited plateau pressures decreases mortality and increases the number of days without ventilator use, than traditionally high VT of 12 ml/kg predicted body weight. In addition, the application of PEEP for lung recruitment has improved also the outcomes in adults (9-11). Much less is known about pediatric mechanical ventilation practice in ALI/ARDS. A recent prospective, cross-sectional, observational Pediatric Acute Lung Injury Ventilation (PALIVE) study (12) enrolling fifty-nine pediatric intensive care units in 12 countries in North America and Europe reveals inconsistent mechanical ventilation practice in children with ALI. Attempts at creating a PEEP/FiO2 titration grid similar to the ARDS Network model (8) were unsuccessful, as routine pediatric practice demonstrated great variability in the application of PEEP in relation to FiO2.

We conducted this study to describe the standard care and how mechanical ventilation is performed in our PICU.

[1]University of Medicine and Pharmacy "Victor Babes" Timisoara
[2]Emergency Hospital for Children "Louis Turcanu" Timisoara
[3]Emergency County Hospital Timisoara
E-mail: dani.chiru@yahoo.com, ac_ro@ymail.com, nftepeneu@yahoo.com, david.vlad@yahoo.com, omarginean@ymail.com, constantinilie@umft.ro

Material and method

A four years observational study (January 2010 – December 2013) was conducted in the First PICU of Emergency Hospital for Children "Louis Turcanu" Timisoara and included all mechanically ventilated children ≥ 24 hours, aged 0-18 years. Preterm babies, patients with congenital immunodeficiency disorders, malignant or surgical diseases were excluded from the study.

Demographic data (gender, age, weight), reason for mechanical ventilation (MV), chronic functional status, route of mechanical ventilation (nasotracheal, orotracheal, or tracheostomy), need for reintubation, ventilation tube characteristics (cuffed versus uncuffed tube or tracheostomy), suction system (opened or closed), ventilator data, number of days on ventilator, hospital length of stay, complications of MV, outcome (discharge, transfer, death), and pediatric risk of mortality score (PRISM) III (13) were collected in all patients.

Ventilator parameters were collected at two different moments of MV: at the start of MV (time A) and after 72 hours of MV (time B). It was considered that a minimum period of 48 hours on MV would be necessary for comparison, since shorter periods of MV do not generally alter respiratory mechanics (14,15). Ventilator data were referring to: peak inspiratory pressure (PIP), positive end-expiratory pressure (PEEP), respiratory rate (RR), inspiratory fraction of oxygen (FiO_2), and tidal volume (VT). Values of VT were derived by measuring the exhaled tidal volume corrected by the body weight (ml/kg). The maximum and minimum values of PIP, PEEP and FiO_2 were noted during the entire period of MV for each patient.

Arterial blood gases were also collected at two different moments: one hour after starting MV (time C) and after 72 hours of MV (time D). PaO_2/FiO_2 ratio for ALI or ARDS diagnosis was calculated for each patient.

Endotracheal intubation (oral or nasal) was performed with pre-oxygenation and after rapid sequence induction using a sedative agent, an analgesic, and a paralyzing agent. It was also part of standard care to keep ventilated patients under continuous sedation and analgesia. Central venous lines were placed in the majority of ventilated patients for drugs infusions and for blood analyses. No arterial line was present. Enteral nutrition was achieved on nasogastric tube and was completed by parenteral nutrition.

The ventilator devices of our PICU are represented by two Viasys Avea and two iVent machines. Exhaled tidal volume measured by the ventilator device was used. The following modes of ventilation were available: pressure control ventilation (PCV), volume control (VCV), volume target pressure control (VTPC), airway pressure relieve ventilation (APRV), synchronized intermittent mandatory ventilation (SIMV) with pressure support (PS) and continuous positive airways pressure CPAP with PS.

This study was approved by the Hospital institutional review board.

Statistical analysis was performed using Microsoft Excel 2007 software. Results are expressed as percent (%), minimum, maximum, and mean ± standard deviation (M ±SD). Variables were compared using Student's t test for normally distributed variables. Comparisons were unpaired and all tests of significance were 2-tailed. Statistical significance was considered at p value < 0.05.

Results

A total of 108 pediatric patients needed ventilatory support for a minimum of 24 hours and met the inclusion criteria. Study population characteristics are shown in Table1. Seventy-four (68.51%) patients were males and the mean age was 2.3 years. Overall, 11 (10.18%) were neonates under 30 days; 61 (56.48%) were infants aged less than a year; 17 (15.74%) were small children (between the ages 1 and 3 years); 5 (4.62%) were between 3 and 6 years old; and 14 (12.96%) were over 6 years of age.

Seventy percent of the patients were orotracheal intubated. All endotracheal tubes were cuffed (Microcuff Kimberly-Clark) and all suction systems were closed. Reintubation, due to accidental detubation or tube obstruction with adherent secretions occurred in 13.88% of the patients.

The mean duration of mechanical ventilation was 9.36±8.52 days and the mean hospital length of stay was 24.7±18.66 days. Of all 108 patients, 34 died before discharge, resulting in 31.48% of deaths. The median value of PRISM III score on admission was higher in non-survivors than in survivors (17 vs. 22, p <0.01). Ventilator-associated pneumonia occurred in 34.24% of the patients. No barotrauma like pneumothorax was noted. Mortality rate was 31.48%.

The causes of PICU admission are listed in Table 2. Acute pulmonary conditions were the primary reasons for mechanical ventilation in 57.37% of the patients. Bacterial pneumonia was the most common primary diagnosis present in 18.51% of patients and bronchopneumonia was the second most common in 17.59% of patients. Among patients with acute respiratory failure, 16.66% had severe sepsis/septic shock. Nonpulmonary conditions, including neurologic diseases, cardiac diseases, and other diagnoses constituted 25.87% of patient condition.

Table 3 lists preexisting chronic medical conditions of the patients. Chronic neurologic diseases, represented mainly by cerebral palsy were found in 27.78% of patients, followed by malnutrition in 20.37% of patients. Chronic respiratory diseases (bronchopulmonary dysplasia and congenital pulmonary fibrosis) were present in 8.33% of patients.

At time A (start of MV), pressure assist-control (PC-A/C) mode was predominantly applied (89.91%), whereas pressure synchronized intermittent mandatory ventilation (PC-SIMV) was used in 10.18% of the patients. At time B (MV at 72 hours), PC-A/C was applied in 62.03% of patients, PC-SIMV in 12.03%, and CPAP in 14.81% of patients (Table 4).

Descriptive characteristics of ventilation parameters at time A and B are shown in Table 5. At time A, mean PIP was 25 cmH2O, PEEP was 5 cmH2O, ventilator rate (VR) was 32 b/min, FiO_2 was 0.58, and VT was 8.16 ml/kg.

Table 1. Study population characteristics

	N=108
Age (M ±SD) month (0-216)	27.65±51.00
Age, N (%):	
0-1 month	11 (10.18)
1 month-1 year	61 (56.48)
1-3 years	17 (15.74)
3-6 years	5 (4.62)
> 6 years	14 (12.96)
Sex, N (%)	
Male	74 (68.51)
Female	34 (31.48)
Intubation characteristics, N (%)	
Orotracheal	75 (69.44)
Nasotracheal	29 (26.85)
Tracheostomy	4 (3.70)
Endotracheal tube type, N (%)	
Cuffed	108 (100)
Uncuffed	0 (0)
Suction system, N (%)	
Closed	108 (100)
Opened	0 (0)
Reintubation, N (%)	15 (13.88)
Ventilator days (M ±SD)	9.36±8.52
Hospital length of stay (M ±SD)	24.7±18.66
Complications of MV, N (%)	
Ventilator-associated pneumonia	37 (34.25)
Pneumothorax	0 (0)
Outcome, N (%)	
Discharged	68 (62.96)
Death	34 (31.48)
Transferred to another hospital	6 (5.55)
PRISM III score (M ±SD)	17±6.83

Table 2. Cause of PICU admission

Cause of PICU admission	N (%)
Respiratory causes	**62 (57.37)**
Bacterial pneumonia	20 (18.51)
Bronchopneumonia	19 (17.59)
Pneumocystis jiroveci pneumonia	14 (12.96)
Neonatal respiratory distress syndrome	6 (5.55)
Meconium aspiration	1 (0.92)
Acute laryngitis	1 (0.92)
Pulmonary edema	1 (0.92)
	8 (7.39)
Cardiac causes	3 (2.77)
Congenital cardiac malformations	4 (3.70)
Congestive cardiac failure	1 (0.92)
Cardiac tamponade	**16 (14.80)**
Neurologic causes	9 (8.33)
Status epilepticus	5 (4.62)
Viral encephalitis	2 (1.85)
Bacterial meningitis	**18 (16.66)**
Severe sepsis	**4 (3.68)**
Others	1 (0.92)
Phenobarbital poisoning	1 (0.92)
Hemolytic-uremic syndrome	1 (0.92)
Severe depression	1 (0.92)
Guillaine-Barre syndrome	

Table 3. Preexisting chronic medical conditions

Concomitant diseases	N (%)
Malnutrition	**22 (20.37)**
Chronic respiratory disease	**9 (8.33)**
Bronchopulmonary dysplasia	7 (6.48)
Congenital pulmonary fibrosis	2 (1.85)
Chronic neurologic disease	**30 (27.78)**
Hydrocephaly	5 (4.62)
Cerebral palsy	14 (12.96)
Spinal muscular atrophy type 1	2 (1.85)
Duchenne muscular dystrophy	2 (1.85)
Hypoxic-ischemic encephalopathy	7 (6.48)
Others	**5 (4.62)**
Chronic renal disease	3 (2.77)
Hemolytic disease of newborn	1 (0.92)
Pierre-Robin syndrome	1 (0.92)

Table 4. Modes of mechanical ventilation

	Modes of MV	N (%)
A	PC-A/C	97 (89.91)
	PC-SIMV±PSV	11 (10.18)
B	PC-A/C	67 (62.03)
	PC-SIMV±PSV	13 (12.03)
	CPAP±PSV	16 (14.81)
	Without MV	12 (11.11)

Time A – Start of MV, Time B – MV at 72 hours

Table 5. Ventilator parameters

Ventilator parameters	Time of MV	N	Min.	Max.	Mean	Std.Dev.	p
PIP (cmH$_2$O)	A	108	19	33	25.18	2.70	*<0.01*
	B	96	14	32	23.42	4.10	
PEEP (cmH$_2$O)	A	108	3	8	5.07	0.83	0.075
	B	96	2,5	8	4.80	0.98	
VR (breaths/min)	A	108	18	60	31.91	11.13	0.158
	B	81	15	60	28.89	10.09	
FiO$_2$	A	108	0.21	1	0.58	0.20	*<0.01*
	B	96	0.21	1	0.45	0.18	
VT (ml/kg)	A	108	5	12	8.16	1.47	*<0.01*
	B	96	5	11	7.14	1.44	

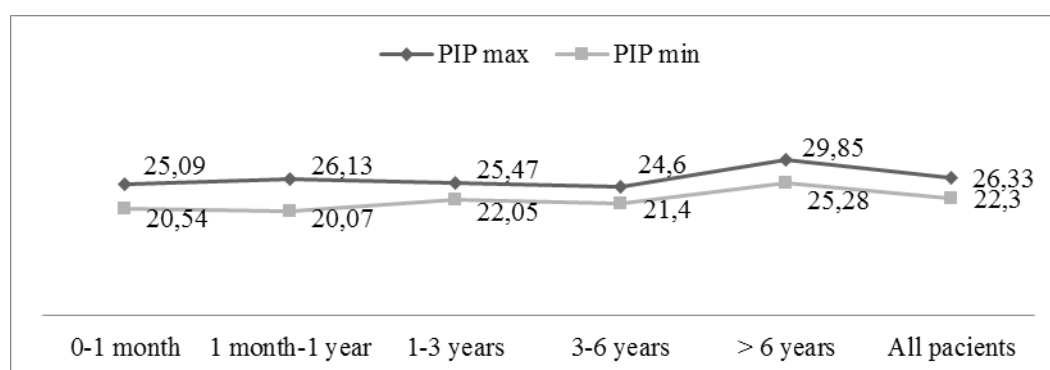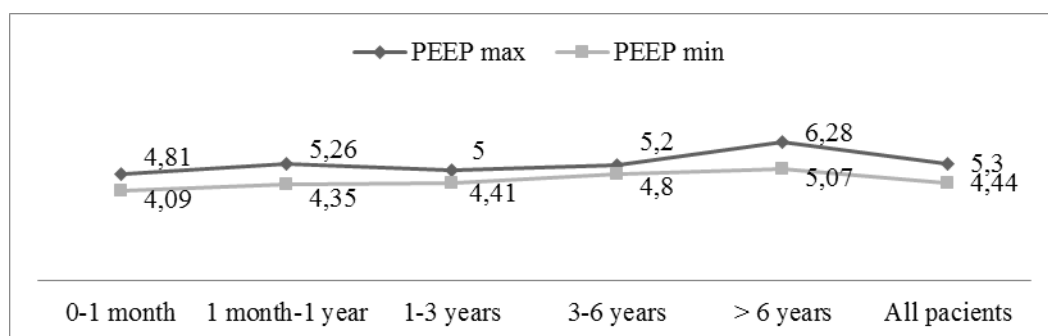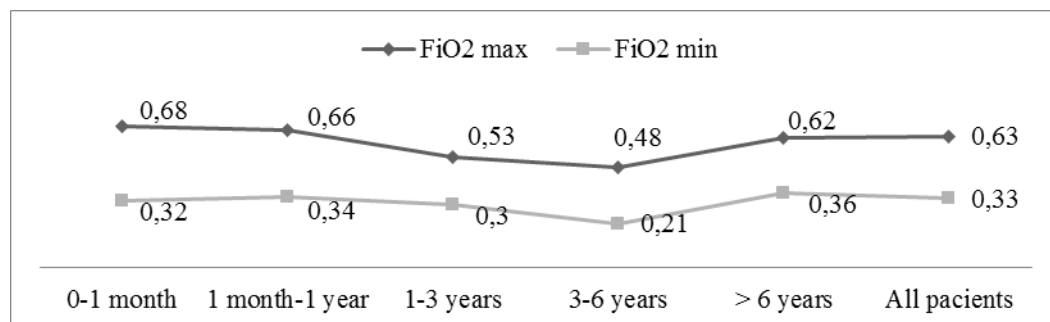Time A – Start of MV, Time B – MV at 72 hours

Figure 1. Maximum and minimum PIP

Figure 2. Maximum and minimum PEEP

Figure 3. Maximum and minimum FiO$_2$

Table 6. Arterial blood gases and PaO_2/FiO_2 ratio

	Time of MV	N	Min.	Max.	Mean	Std.Dev.	p
pH	C	108	7.13	7.63	7.38	0.09	0.286
	D	96	7.01	7.66	7.40	0.08	
PaO_2 (mmHg)	C	108	49	166	89.84	18.68	0.665
	D	96	51	149	89.50	15.52	
$PaCO_2$ (mmHg)	C	108	19	84	41,09	11,68	0,187
	D	96	21	82	39,55	9,16	
PaO_2/FiO_2	C	108	62	510	182.09	97.73	***<0.01***
(mmHg)	D	96	60	523.8	245.5	124.01	

Time C – one hour after starting MV, Time D – after 72 hours of MV
PaO_2 – partial pressure of oxygen, $PaCO_2$ –partial pressure of carbon dioxide

Values of PIP, FiO2 and VT were statistically improved at time B (p<0.01).

Mean PIP values were constant < 30 cmH2O in both times of determination. At time A, values of PEEP ≤ 5 cmH2O encountered in 75.92% of the patients and PEEP≤ 8 cmH2O in 95.38% of the patients. At time B, 80.2% of the patients had a PEEP ≤ 5 cmH2O. Values of FiO2 ≤ 0.6 had 69.15% of the patients at time A and 82.10% of patients at time B.

Maximum and minimum values of PIP, PEEP, and FiO2 by age groups are listed in Figures 1-3. The mean values of maximum PIP was < 30 cmH2O, with 12% of the patients having a PIP ≥ 30 cmH2O, but < 35 cmH2O. Two percent of the patients had a maximum PEEP ≥ 8 cmH2O. The mean values of maximum FiO2 was ≤ 0.65, and the mean values of minimum FiO2 was ≤ 0.35.

Arterial blood gases values at time C and D of determination and PaO2/FiO2 ratio are shown in Table 6. There was no statistical differences for pH (p=0.286), PaO2 (p=0.665), and PaCO2 (p=0.187) at time C and D of determination. Most patients (58%) were normocapnic and 22% of them were hypocapnic.

The mean value of PaO2/FiO2 ratio was < 200 at time A and < 300 at time B. ARDS was defined as bilateral pulmonary infiltrates, acute onset, PaO2/FiO2 ratio of 200 or less, and no suspicion of left heart failure (or a pulmonary capillary wedge pressure of 18 or less). Sixty-seven percent of the patients fulfilled the oxygenation criteria for ARDS, but only half of them had bilateral pulmonary infiltrates.

Weaning and extubation criteria and sedation protocols were not focused in this study.

Discussions

The patients enrolled in the study were hospitalized in a medical PICU and the practitioners are pediatric specialists with subspecialty in intensive care. This study reflects the real situation of mechanically ventilated children in our unit in the last 4 years. The weaknes of this study is that data extraction was performed in the last 4 years and practice changed in the last 2 years.

In our study, the main reasons for intubation and mechanical ventilation were quite variable, but almost 60% of the patients had acute respiratory failure. A much lower incidence, of 26% was reported by Khemani et al (1) in a multicenter clinical trial witch enrolled 12,213 children intubated and mechanically ventilated from 16 US PICUs.

Almost 30% of the patients associated chronic neurologic pathology, mainly represented by cerebral palsy, and 20% associated various degrees of malnutrition. The children with malnutrition were mostly recovered premature babies.

The mean age of the patients was 2.3 years; with 57% having less than one year old. Principi et al (16) and Randolph et al (2) reported almost the same incidence of mechanically ventilated infants.

The mean duration of mechanical ventilation was 9.36 days, corresponding to the same duration reported before both in children and adults (2,17). A shorter median length of ventilation of 4 days was reported in studies enrolled children hospitalized in medical and surgical PICUs (18,19).

The main route of intubation was oral in 70% of the cases; this route being performed in emergent intubation. There are studies reporting only orotracheal intubation and no nasotracheal intubation (20).

In all patients we used cuffed endotracheal tubes (Microcuff Kimberly-Clark), because they have several advantages: decrease the rate of ventilator-acquired pneumonia (21); reduces the need for tube exchanges (22,23); provides a perfect seal with the trachea even at low inflation pressure, without air leaks (22,24); and do not increase the risk of post-extubation stridor (22,23).

The mean PRISM III score on admission in PICU was 17, a higher value than previously reported (25,26), suggesting a more severe illness on admission. A PRISM score of 16 was found by Dahlem et al (27) in ARDS patients, and a score of 22 in non-survivor ARDS patients. Ventilator-associated pneumonia occurred in 34% of the cases, also a higher prevalence than reported (28), reflecting the level of health-care of this patients in a low socio-economic country.

The mortality of the study group was 31.48%, comparable with the mortality found by Zhu et al (25) for ARDS patients. Overall PICUs mortality was 2.5%.

We used exclusively pressure-limited modes of ventilation, even though other modes were available. The

most used mode was PC-A/C. As pressure ventilation was used, and no volume ventilation at all, more attention was paid to inspiratory pressure limits than to tidal volume control.

Mean PIP values were constant < 30 cmH2O, with 12% of the patients having a maximum PIP ≥ 30 cmH2O, but < 35 cmH2O. There was little variability with PEEP choice, with a mean value of 5 cmH2O. Only 2% of the patients had a maximum PEEP ≥ 8 cmH2O. Low levels of PEEP applied can be explained by the fact that patients had no central venous pressure monitored, as it is well known that high PEEP predominantly decreases cardiac output through a decrease in preload of right ventricle (29). In general, most patients who are managed without arterial lines are receiving modest ventilator support (1).

There was no direct connection between PEEP and FiO2, preferring low levels of PEEP and high levels of FiO2. This was also noted by Khemani et al (1) and Santschi et al (12). Mean FiO2 levels at the start o MV was < 0.6, and decreases at 0.45 after 72 hours of MV. The mean levels of FiO2 reported before varies between 0.35 and 0.5 (1,25,30).

In our study, mean levels of VT at the start of MV were 8.16 ml/kg, and decreased at 7.14 ml/kg after 72 hours of MV. Reported levels of VT in the era of "low VT" varies between 7.4 and 9.5 ml/kg (12,20,25,30).

Arterial blood gases showed normocapnia and hypocapnia, and as the mean PaO2/FiO2 ratio was < 200 at the start of MV and < 300 after 72 hours of MV, results that the ALI/ARDS strategies were not fully implemented. Kemani et al (30) proposed in 2011 a computer protocol for ALI/ARDS for children aged over one year old in a retrospective cohort study. The authors concluded that clinicians infrequently decreased FiO2, even when the PaO2 was high (>68 mmHg) and the protocol would have recommended more positive end expiratory pressure (PEEP) than was used in actual practice. Also, the clinicians often made no change to either PIP or VR when the protocol would have recommended to change, even when the pH was greater than 7.45 with PIP at least 35 cmH2O, being lost opportunities to minimize potentially ventilator induced lung injury for children with ALI/ARDS.

Conclusions

Pressure-limited ventilation modes were standard in our PICU. Protective lung strategies for ALI/ARDS were not fully implemented, as ventilatory settings resulting in normocapnia/hypocapnia were still being used. Describing the standard care and how mechanical ventilation is performed in children can be useful for future clinical trials.

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Correspondance to:

Dr. Daniela Chiru
Emergency Hospital for Children "Louis Turcanu"
I. Nemoianu Street, No.1, 300011, Timisoara
E-mail: dani.chiru@yahoo.com

EVOLUTIONARY TENDENCY OF NASAL CPAP USE IN TREATMENT OF RDS IN PRETERM INFANTS

Ramona Dorobantu[1]*, Valeria Filip[2], Constantin Ilie[1], Cătălin Dorobantu[2]

Abstract

Introduction: The non-invasive respiratory support, type CPAP, is widely used to support respiratory function in preterm infants and it is often the first choice in the neonatal intensive care unit.

Aim of the study: The aim of the study is to compare two therapeutic approaches to respiratory distress syndrome due to surfactant deficiency in premature infants.

Material and method: In this study were included all premature infants with gestational age up to 29 weeks, who were treated in the Intensive Care Unit within Oradea Maternity Hospital between 01st of January 2010 and 31st of December 2013. In the study were included 141 infants, divided into two groups: for the infants in the first group the prophylactic surfactant was administered within the first 30 minutes after birth and the infants in the second group received CPAP immediately after birth.

Results and Conclusions: This study presents the fact that the prophylactic surfactant reduces the duration of the CPAP respiratory therapy, of the mechanical ventilation and of the oxygen therapy. Most of these infants, from these two groups, didn't require CPAP conversion into assisted ventilation. The respiratory recovery was good in our study in both groups. The survival rate was of 68% in the first group, respectively 62,12% in the second group and the survival rate in the absence of oxygen at the corrected age of 36 weeks was of 62,66% in the first group and of 56% in the second group. The incidence of bronchopulmonary dysplasia was of 4% in the first group, respectively of 7,5% in the second group. The incidence of pneumothorax and of sepsis was higher in the group of infants with selective surfactant.

In *conclusion*, in premature infants with gestational age between 26-29 weeks with spontaneous breathing movements, the CPAP respiratory support must be used immediately after birth and the surfactant therapy should be introduced at the first clinical, laboratory and radiological signs of respiratory distress. Using this strategy, there are obtained the maximum benefits from this respiratory therapeutic method, reducing the incidence of respiratory morbidity.

Key words: preterm infant, CPAP, surfactant.

Introduction

The non-invasive respiratory support, type CPAP, is widely used to support lung function in premature infants, it is often the first choice in the neonatal intensive care unit.[1,2] In case of extreme preterm infants, CPAP is an alternative to mechanical ventilation and intubation[3], and in premature infants with gestational age over 30 weeks, CPAP is an alternative to oxygen therapy by head box .[4]

CPAP is an attractive option for the treatment of infants with respiratory failure because it keeps the spontaneous breathing, without need for endotracheal intubation, with the reduction of the incidence of pulmonary injuries.[5]

A continuous positive airway pressure (CPAP) can be provided with face mask, nasopharyngeal or endotracheal probes and single or double prongs. The use of positive pressure to the airways implies a great number of benefits, including the stabilization of airways, the increase of lung volume, the reduction in airway resistance, but also in respiratory effort.[6,7] However the increased PEEP values may increase the partial pressure of CO_2, with the reduction of tidal volume and with the increase of dead space. The increase of lung volume may lead to the reduction of the compliance and to the air leak syndrome. The increase of intrathoracic volume may also lead to the reduction of the cardiac activity. CPAP devices may cause skin abrasion and lesions of the nose.[8,9]

Other forms of non-invasive ventilation are IPPV, SIMV, HFOV by nasal prongs.

Currently the optimal time for initiating CPAP and surfactant therapy or for using the mechanical ventilation as a beginning therapy in extremely low birth weight infants is not clearly defined.[10,11] The respiratory support, type CPAP, can be provided with different techniques, as Bubble CPAP system (conventional CPAP) or as some new, modern and sophisticated systems. CPAP pressure is generated by two possible mechanisms: with variable flow and with constant flow. CPAP use involves team effort, experience and permanent medical assistance.[12-16]

[1]Victor Babeş University of Medicine and Pharmacy, Timişoara, *PhD Student
[2]Faculty of Medicine and Pharmacy, Oradea
E-mail: dorobanturamona@yahoo.com, valeriafilip@yahoo.com, constantinilie@umft.ro, dorojar@yahoo.com

Aim of the study

The aim of the study is to compare two therapeutic approaches to respiratory distress syndrome due to surfactant deficiency in premature infants: administration of the prophylactic surfactant, followed by extubation and CPAP vs. the administration of the selective surfactant and early CPAP.

Material and method

In this study were included all premature infants with gestational age up to 29 weeks, who were treated in the Intensive Care Unit within Oradea Maternity Hospital between 01st of January 2010 and 31st of December 2013. The information was taken from the consultation sheet and monitoring sheets of the infants. Of a total number of 172 premature infants with a gestational age up to 29 weeks, in this study were included 141 infants:

They were selected by the following criteria:
- infants with gestational age between 25 weeks 0 days and 28 weeks 6 days
- spontaneous breathing movements 5 minutes after birth
- clinical evidence of respiratory distress syndrome: cyanosis, moan, polypnea, indrawing, movement of the nasal wings
- radiological evidence of medium or severe form of RDS (respiratory distress syndrome)
- absence of congenital malformations

Exclusion criteria:
- severe asphyxia or Apgar score of 3 or less at 5 minutes
- endotracheal intubation for resuscitation
- ineffective respiratory movements
- genetic disease.

The infants in the first group received prophylactic surfactant in the first 30 minutes after birth and the infants in the second group received CPAP therapy immediately after birth.

Method

All infants were resuscitated in the delivery room using 100% O2, which was administrated in free flow or by ventilation with positive pressure by using a balloon and a mask. After they were stabilized and fulfilled the criteria of study groups, they were distributed in one of the two groups.

The infants *in the first group* were intubated and received a single surfactant dose in the first half an hour after birth, after that they were ventilated by using a balloon for 5 minutes, then they were extubated and it was continued the CPAP respiratory therapy.

The infants *in the second group* were treated only by early CPAP. In case of CPAP therapy failure and after pulmonary radiological examination, the infants received selectively a single surfactant dose that was administered by endotracheal probes.

The CPAP respiratory support was provided by Infant Flow System by nasal cannula, using the following parameters: initial FiO2= 40%, PEEP= 4, MAP= 7, based on the hemoglobin oxygen saturation (HbO2Sat) values. The second dose of surfactant was administered to those infants that still have clinical and radiological RDS criteria.

Criteria of CPAP conversion into assisted ventilation:
- FiO2 demand over 40% to maintain hemoglobin oxygen saturation (HbO2Sat) between 85%-92%,
- apnea, defined by over 4 spontaneously reversible apnea episodes in an hour or by 2 apnea episodes in an hour, which need ventilations by using a mask and a balloon.
- respiratory acidosis, defined as PCO2 over 65mmHg and pH < 7,2 in capillary blood

Detubation criteria and continuation of CPAP respiratory ventilation:
- FiO2 under 40% to maintain hemoglobin oxygen saturation (HbO2Sat) between 85-92%
- low ventilation pressure (PIP, PEEP, mean arterial pressure < 7cm H2O)
- PCO2 under 65mm/Hg and pH >7,2 in capillary blood

The results were evaluated at the corrected age of 1 week, 28 days, 36 weeks and then at their discharge from hospital.

At one week age the infants were evaluated regarding the necessity of orotracheal intubation and of assisted ventilation in the first 7 days of life. In this category are the infants who couldn't be detubated in an hour after surfactant administration and those who fulfilled the criteria of CPAP conversion into assisted ventilation in first hours after birth.

The evaluation at the discharge from hospital includes:
- death
- at corrected age of 28 days or 36 weeks: survival by respiratory support of CPAP-type, survival in the presence of O2 with FiO2>21%, survival in the presence of atmospheric air,
- incidence of pulmonary bronchodysplasia,
- air leak syndrome,
- pulmonary hemorrhage,
- intraventricular hemorrhage
- retinopathy of prematurity,
- necrotizing ulcerative enterocolitis,
- sepsis,
- total duration of mechanical ventilation,
- hospitalization period.

Results

172 premature infants with gestational age up to 26-29 weeks, cared for within the Intensive Care Unit between 01st of January 2010 and 31st of December 2013

Establishment of the group of infants eligible for the study:
- total number 172;
- eliminated - 31: infants intubated in the delivery room - 9, transferred infants from other hospitals - 12, other causes- 10.
- infants admitted in the study - 141
- first group – received prophylactic surfactant, then CPAP -75.

- second group – received early CPAP, then selective surfactant - 66

Clinical and demographic criteria are presented in Table 1:

Table 1: Clinical and demographic criteria.

	Prophylactic Surfactant	Early CPAP
G mean	955 grams	962 grams
GA mean	27,2 weeks	27.4 weeks
Apgar Score mean	3,98	4.07
Male	35	32
Female	40	34
Multiple pregnancy	6	5

Our study results concerning the infants present that the prophylactic treatment with surfactant immediately after birth isn't better than CPAP treatment regarding the necessity for the initiation of the assisted ventilation in first week of life. In our study 6 infants from the first group, who were treated by prophylactic surfactant need intubation and mechanical ventilation versus 8 infants from the second group treated with early CPAP. Multiple doses of surfactant needed 11 children in the first group, respectively 13 children in the second group. This study reveals that the prophylactic surfactant reduces the period of CPAP respiratory therapy, of mechanical ventilation and of oxygen therapy (Figure 1, 2).
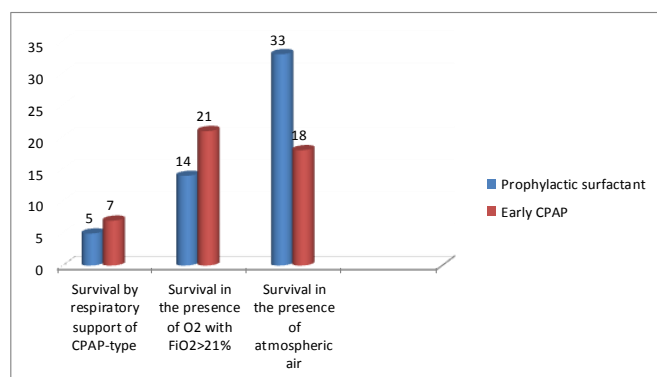
Figure 1: Results at the age of 28 days.
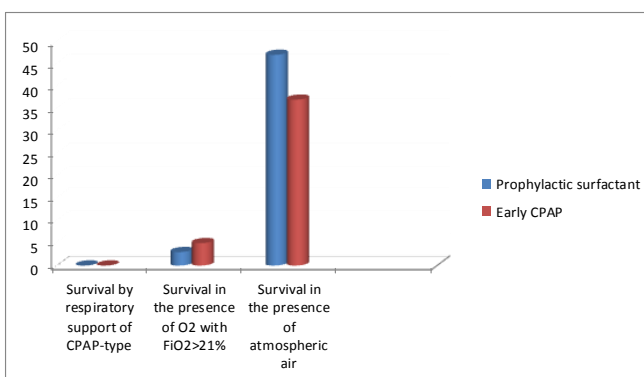
Figure 2: Results at the corrected age of 36 weeks.

Most of the infants of the two groups didn't need CPAP conversion into assisted ventilation. The difference between the two groups was according to the selected parameters. The group with early CPAP and selective surfactant needed the use of higher ventilation parameters than the first group (initial mean FiO2 42 % versus 34%; initial mean PEEP 4,1 versus 2,8) and the necessity for the CPAP respiratory support was longer (19,8 days versus 14,5 days).Only about half of infants in the second group needed surfactant administration (Table 2).

Table 2: Used ventilation parameters CPAP INFANT FLOW.

	Prophylactic Surfactant		Early CPAP
FiO2 initial mean	34%		48%
PEEP initial mean	2,8		4,1

The respiratory recovery was good in our study regarding the both groups. The survival rate was of 68% in first group and of 62,12% in the second group and the survival rate in the absence of oxygen at a corrected age of 36 weeks of life was of 62,66 % versus 56%. The incidence of pulmonary bronchodysplasia was of 4%, respectively of 7,5% in the second group. The incidence of pneumothorax and sepsis was higher in the group of infants with selective surfactant. The stabilization of the digestive tolerance occurred later in this group. Other complications of preterm birth weren't significantly different in the two groups (Figure 3). The duration of hospitalization was slightly lower in the group with prophylactic surfactant (Table 3).

The number of deaths was approximately equal in the two groups, 32% and 38%. The first causes of death were: intraventricular hemorrhage, infection and pulmonary hemorrhage (Figure 4, 5).

Figure 3: Differences of complications between the two groups.

Table 3: Mean duration of CPAP and hospitalization:

	Prophylactic Surfactant	**Early CPAP**
Mean duration of CPAP	14,5 days	19,8 days
Mean duration of hospitalization	56,2 days	62,5 days

Figure 4: Deaths.

Figure 5: Causes of death - total number of deaths.

Discussions

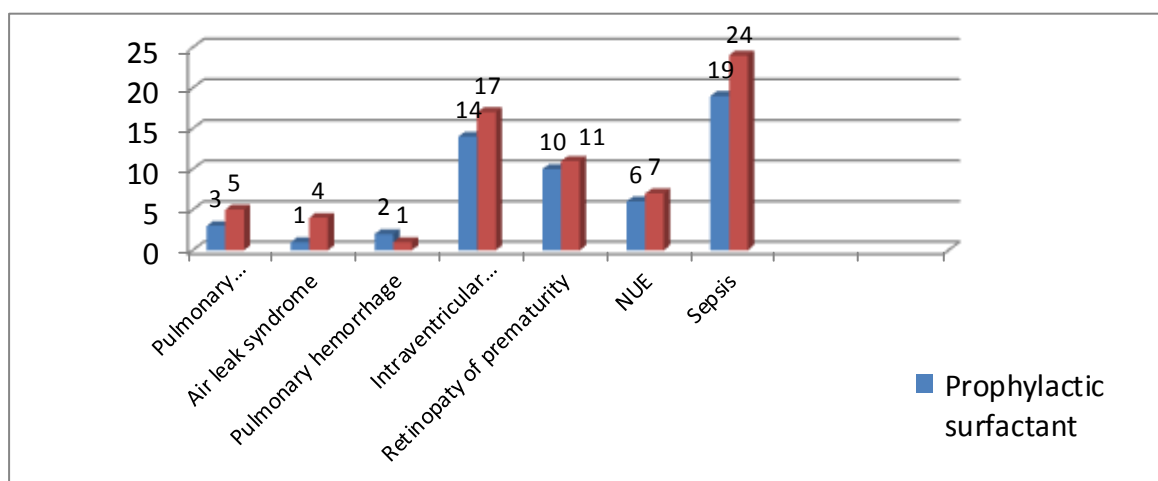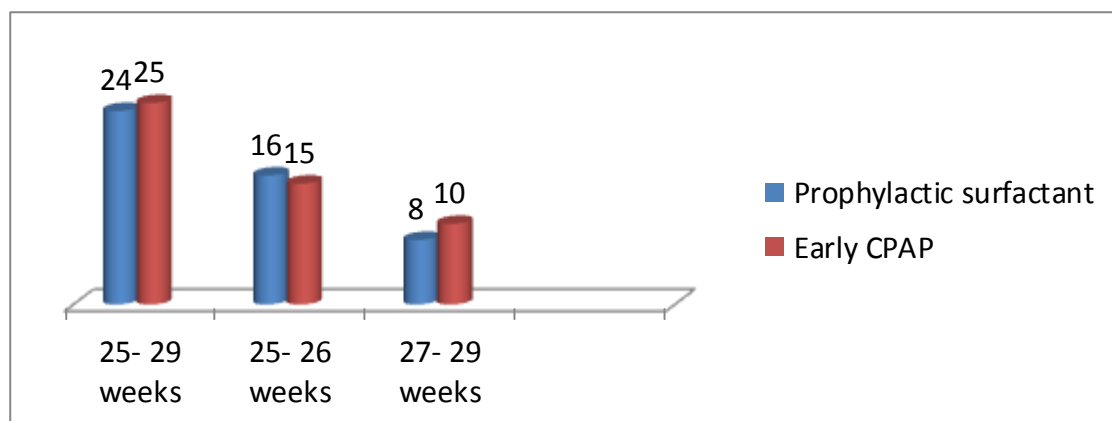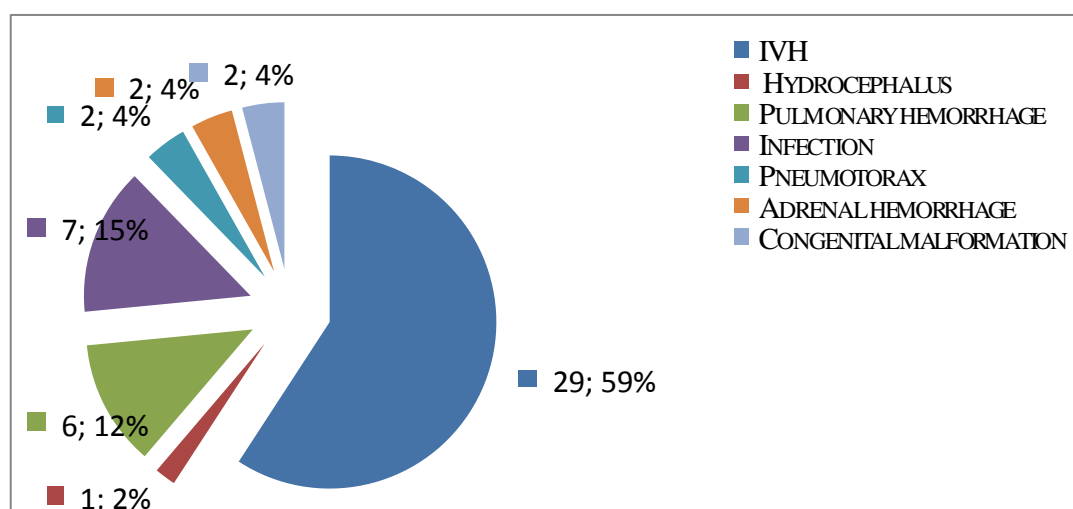The optimal time for the initiation of the CPAP therapy remains an unsolved problem. In COIN trial (CPAP versus orotracheal intubation)17, an international multicentre study, it was demonstrated, that the infants treated early with CPAP needed less ventilation days and had an oxygen dependence of more than 28 days, but less than 35 weeks of corrected age. However, these infants had a higher rate of air leak syndrome. In a subgroup selected at random from the above mentioned patients Roehretal demonstrated the improvement of the pulmonary mechanics in 8 weeks after birth in infants who benefit by early CPAP respiratory support versus those who were intubated and mechanically ventilated. In a review published by Verder and his collaborators, medium or severe RDS was treated by using INSURE technique (intubation, surfactant, detubation), followed by CPAP. They noticed that this technique improves the oxygenation, reduces the pulmonary bronchodysplasia rate and diminishes the period of mechanical ventilation in about 50% of cases.

A recent meta-analysis of 6 clinical studies, of that 3 randomized controlled clinical studies compares the results of two strategies of surfactant administration in infants with RDS or with SDR risk: the infants in the first group were treated with INSURE method then with CPAP, the infants in the second group were treated with selective surfactant, followed by intubation and continuous mechanical ventilation. The INSURE method was associated with a lower need for mechanical ventilation, with a lower incidence of pulmonary bronchodysplasia and a lower frequency of pneumothorax. However the number of surfactant doses per patient is significantly higher in those infants treated by INSURE procedure.18 The immediate detubation after the surfactant administration, followed by SNIPPV, which replaces the usual ventilation, was associated with the reduction of the need for oxygen, with the reduction of the period of intubation, of parenteral nutrition and of hospitalization.19 Another study presents that the detubation followed by SNIPPV is associated with the reduction of the need for oxygen and with an lower incidence of bronchodysplasia (73% versus 40%).20

Conclusions

In conclusion, in premature infants with gestational age between 26-29 weeks with spontaneous breathing movements, the CPAP respiratory support should be used immediately after birth and the surfactant administration must be performed at the first clinical, paraclinical and radiological signs of RDS. Using this strategy the benefits of this respiratory option are maximal, reducing the respiratory morbidity.

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Correspondence to:
Ramona Dorobantu
Spitalul Clinic de Obstetrica Ginecologie Oradea,
Str. Calea Clujului nr. 50,
Oradea, Romania,
E-mail: dorobanturamona@yahoo.com

THERAPEUTICALLY ASPECTS IN DDH – EARLY TREATMENT VERSUS LATE TREATMENT

AI Pavel[1], ES Boia[2]

Abstract

Developmental dysplasia of the hip (DDH) is the most common musculoskeletal disorder in infancy and varies in severity, ranging from neonatal hip instability with or without associated acetabular dysplasia to irreducible dislocation. Although the disease is described by Hippocrates, there is no standard protocol for diagnosis and treatment unanimously accepted.

Key words: Developmental dysplasia of the hip (DDH), ultrasound hip, early/late treatment of DDH.

Introduction

Ultrasonography is a method of choice for early diagnosis of developmental dysplasia of the hip (DDH) in newborns and infants (1,2,3,4). It is simple and noninvasive method for visualizations of the hip. While treating the DDH, it gives possibility for multiple performances and for monitoring (2,5,6). The treatment for hip dysplasia depends on the age of the patient and on the type of the hip disorder according to the Graf method (2,7). The goals of a screening program are early diagnosis in all patients who have DDH, when therapy is most effective and noninvasive. Radiographs are available and relatively low in cost. The main limitations are radiation exposure and radiography's inability to demonstrate the cartilaginous femoral head. Radiographs are of limited value during an first 3-4 months of infants life, when the femoral heads are composed entirely of cartilage, but they become more reliable for use in infants 4–6 months of age, with the appearance of femoral head ossification (8,9,10,11).

Purpose

The purpose of this paper is to demonstrate the differences between therapeutically results in the same type of DDH depending on time of initiation of treatment. The differences are therapeutic methods, duration of treatment, results and prognosis of the cases.

Materials and methods

Therapeutic aspects were studied 4 cases of infants with coxofemoral dislocation diagnosed and treated in the period 2011-2013. Two cases were diagnosed early ultrasonographic in the first month of life: I. M. male at age 3 weeks (hip type II D) and B. B. female at the age of 4 weeks (hip type IV) and was initiated early orthopedic treatment. The other two cases with hip dislocation were diagnosed radiological after the age of 5 months: D. C. female at the age of 5 months and N. A. female at the age of 6 months and orthopedic treatment started late.

To patients with type II D and type IV diagnosed in first month of life, I performed close reduction and fixed it ultrasonographic guided with Dr. Bernau - Tübingen hip abduction orthosis. Infants were followed clinically and ultrasonographic monthly. It is very important to collaborate with parents because they have to understand the severity of the disease and the importance of correct treatment.

The decision to stop the treatment was made when the hips has become type I A.

We found mature hips at all control hips ultrasound performed at 2 months after starting treatment, including the type IV. Such infants diagnosed early in the first month of life were cured clinically and ultrasonographic until the age of 4 months.

Subsequent the clinical and ultrasound controls were performed every 2 months until the age of 11-12 months.

Results

I will present case of newborn, I. M., boy – 3 weeks, diagnosed clinically and ultrasonographic with left hip dysplasia type II D (α angle 48,09°; β angle 77,88°) – picture 1a. I performed close reduction and fixed it ultrasonographic guided with Dr. Bernau-Tübingen hip abduction orthosis; the hip has become type I B (α angle 64,22 °; β angle 56,84°) – picture 1b. This case was followed clinically and ultrasonographic monthly, after one month (picture 1c) and two months of treatment (picture 1d), when the hip has become type I A (α angle 64 °; β angle 51°) and I stoped the treatment. Ultrasound control of the same hip at the age of 11 months, when he started to walk, founded mature left hip, type I A (α angle 69 °; β angle 51°) – picture 1e.

[1]University of Medicine and Pharmacy "Victor Babeş" Timişoara, România, PhD Student
[2]University of Medicine and Pharmacy "Victor Babeş" Timişoara, România
E-mail: adipavel72@yahoo.com, boiaeugen@yahoo.com
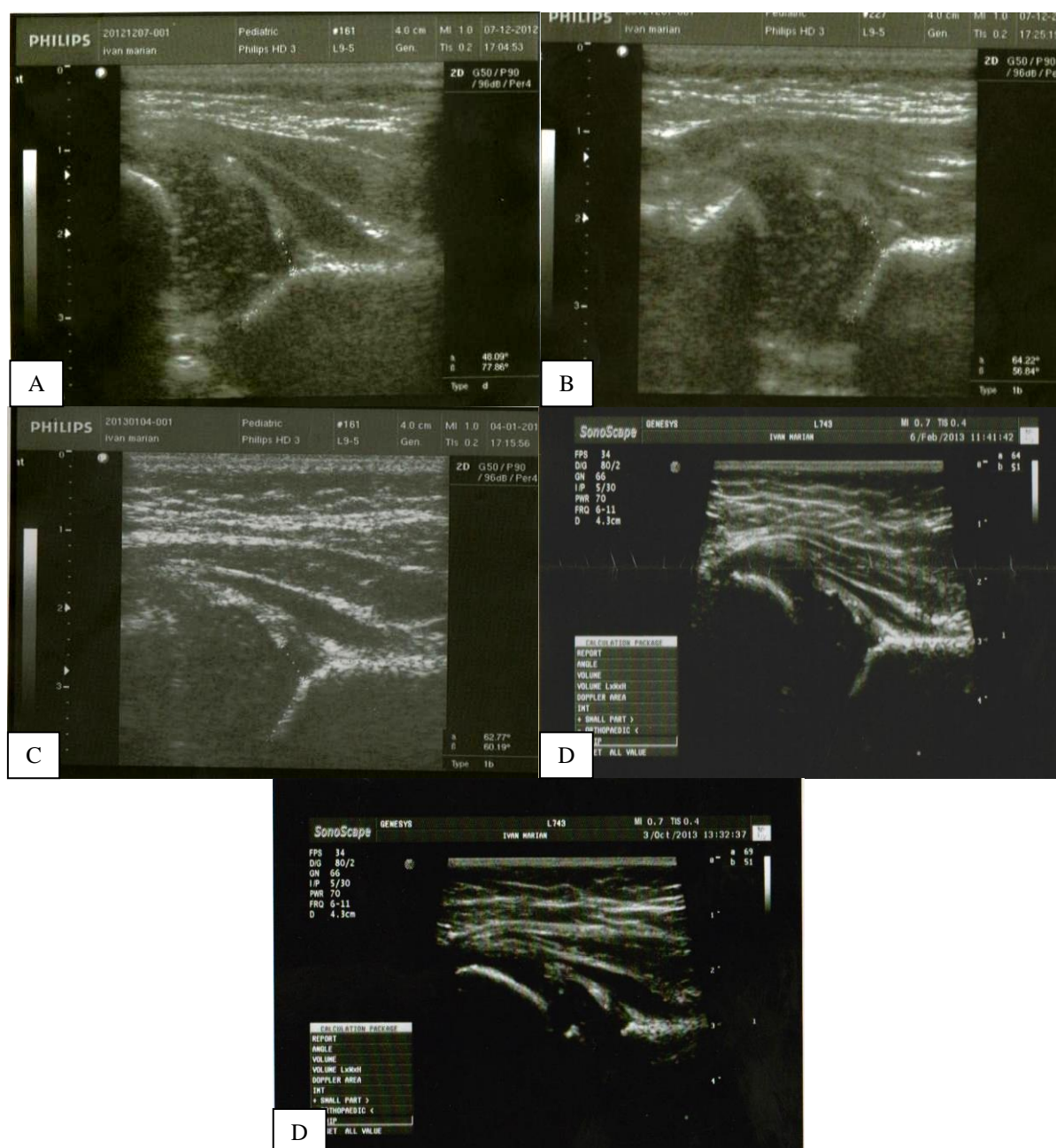
Picture 1. A – Initial aspect. B – After close reduction. C – After 1 month with Dr. Bernau-Tübingen hip abduction orthosis. D – After 2 months with Dr. Bernau-Tübingen hip abduction orthosis. E – Final aspect at the age of 11 months.

Next case presented is case of newborn, B. B., girl – 4 weeks, that I diagnosed clinically and ultrasonographic with right hip luxated, type IV, labrum interposed between the femoral head and joint capsule – picture 2a. After close reduction and imobilisation with Dr. Bernau-Tübingen hip abduction orthosis, the hip has become type II D (α angle 49°; β angle 77°) – picture 2b. This case was followed clinically and ultrasonographic monthly, after one month (picture 2c) and two months of treatment (picture 2d), when the hip has become type IA (α angle 61°; β angle 46°) and I stoped the treatment. I performed ultrasound control of the same hip at the age of 5 month (picture 2e), 6 month (picture 2f) and 1 year, when she started to walk, founded mature left hip, type IA (picture 2g).
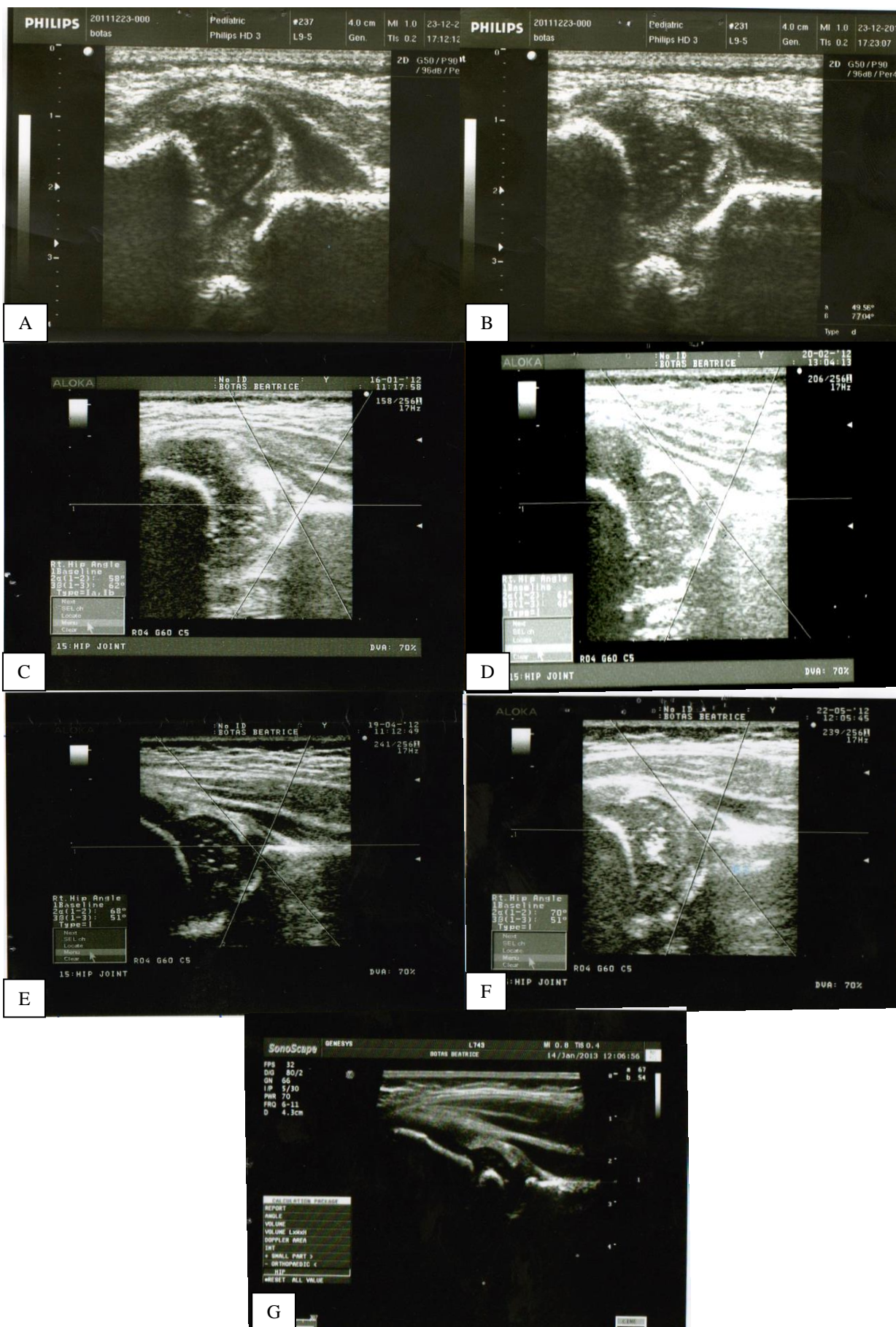
Picture 2. Girl – 4 weeks, with right hip luxated, type IV.

In these two cases diagnosed in the first month, after two months of imobilisation with Dr. Bernau-Tübingen hip abduction ortosis, the ultrasonographic aspect (hip type IA) allowed quit this and I continued treatment with hip abduction orthosis pantyhose for another 2 months. Such the duration of treatment was about 4 months, until the age of 4-5 months.

To patients diagnosed radiological after the age of 5 months, I performed close reduction under general anesthesia and fixed it by immobilization in the spica cast – Lorentz positions. Infants were followed radiologically at 6 weeks and immobilized in the spica cast, in general anesthesia into Lorentz successive positions.

First case was infant N. A. girl – 6 months, diagnosed radiologic with left hip luxated (picture 3a) that I performed close reduction under general anesthesia and immobilization in the spica cast – Lorentz positions, and radiologic control after close reduction and imobilisation (picture 3b). The next radiologic controls was made at 6 weeks (picture 3c) and 12 weeks from the close reduction (picture 3d), when the radiologic aspect shows a good position of the femoral head in the cotiloid cavity and a good coverage of the acetabular roof; I stop the imobilisation in the spica cast and I made imobilisation with Dr. Bernau-Tübingen hip abduction orthosis for 2-3 months. This pacient started to walk at the age of 1 year and 2 month. Radiologic controls at the age of 1 year and 8 months (picture 3e) respectively at the age of 2 years (picture 3f) suggests a possible avascular necrosis of the femoral head.
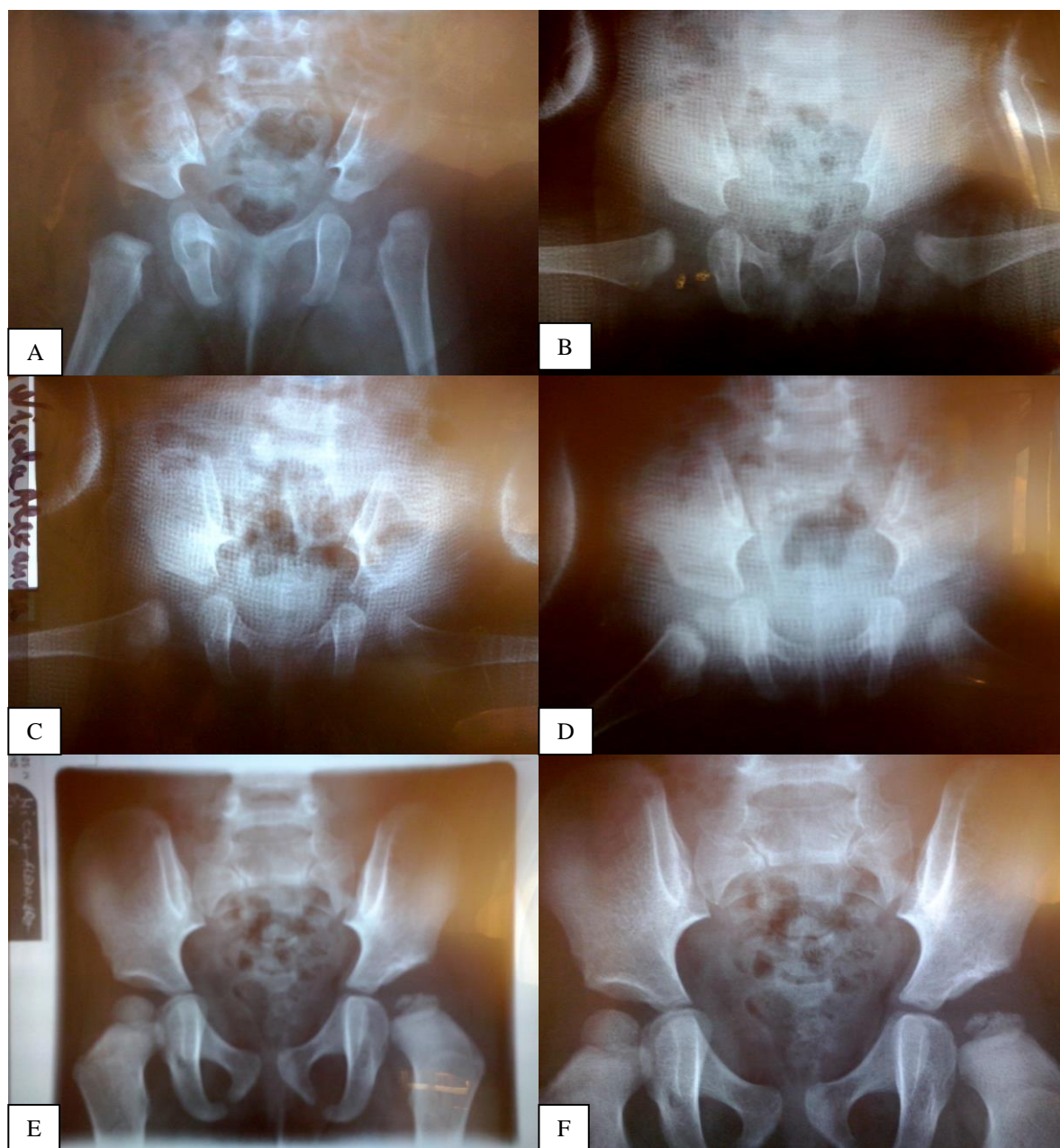
Picture 3. Girl – 6 months, diagnosed radiologic with left hip luxated.

The second case was infant D. C. girl – 5 months, diagnosed radiologic with left hip luxated (picture 4a) and ultrasound with left hip type IV (α angle 40°; β angle 88° - picture 4b) that I performed close reduction under general anesthesia and immobilization in the spica cast – Lorentz positions, and radiologic control after close reduction and imobilisation. The next radiologic controls was made at 6 weeks (picture 4c) and 12 weeks from the close reduction (picture 4d), when the radiologic aspect shows a good position of the femoral head in the cotiloid cavity and a good coverage of the acetabular roof; I stop the imobilisation in the spica cast and I made imobilisation with Dr. Bernau-Tübingen hip abduction orthosis for 2-3 months. This pacient started to walk at the age of 1 year. The last radiologic control at the age of 1 year and 4 months shows a good therapeutic results: a good position of the femoral head in the cotiloid cavity, a good coverage of the acetabular roof position and the appearance of ossification nucleus of the femoral head – picture 4e.
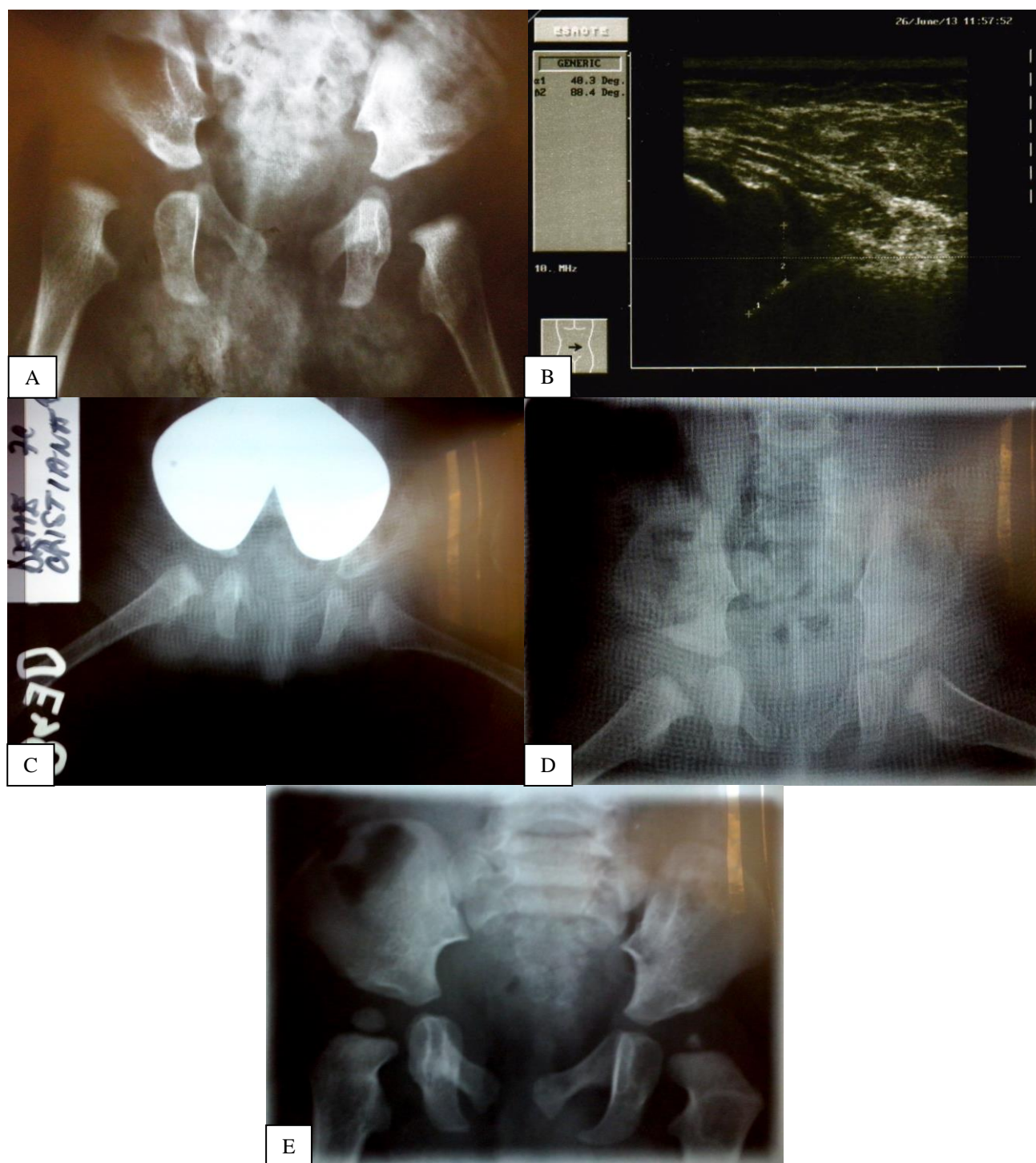
Picture 4. Girl – 5 months, diagnosed radiologic with left hip luxated and ultrasound with left hip type IV.

In these last two cases, after about three months of immobilization in the spica cast, the radiological aspect allowed quit this and continued treatment with Dr. Bernau-Tübingen hip abduction orthosis for another 2-3 months until the hip became the type IA ultrasonographic. Such the duration of treatment was about 6 months, until the age of 1 year.

Discussions

In our study newborns with type II D and IV hips were treated with a Dr. Bernau-Tübingen hip abduction orthosis and we found mature hips at all control hips ultrasound performed at 2 months after starting treatment, including the type IV. Early diagnosis in the first month of the congenital hip subluxation/dislocation allow early initiation of treatment with hip abduction orthosis which ensures quick healing in two months without sequelae.

Infants diagnosed after the age of 5 months required closed reduction under general anesthesia and immobilization in spica cast in Lorentz position for 3 months, followed by immobilization with Dr. Bernau - Tübingen hip abduction orthosis another 2-3 months, 5-6 months in total orthopedic treatment. Late diagnosis after the age of 5 months of the congenital hip subluxation / dislocation require orthopedic treatment last longer by immobilisation in spica cast device and healing may be sequelae (osteochondritis / avascular necrosis of the femoral head).

Conclusions

In our study newborns with type II D and IV hips were treated with a Dr. Bernau - Tübingen hip abduction orthosis and we found mature hips at all control hips ultrasound performed at 2 months after starting treatment, including the type IV. The subsequent ultrasound controls revealed healing without sequelae.

The treatment for hip dysplasia depends on the age of the patient and on the type of the hip disorder according to the Graf method. We can conclude that an early and proper orthopedic treatment for DDH, established in the first month of life, leading to cure of the disease in a very short time without sequelae.

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Correspondence to:
Pavel Adrian Ionel
University of Medicine and Pharmacy "V. Babes" Timisoara
P-ta Eftimie Murgu No.2, Timisoara, Romania
Telephone: 0740152345
E-mail: adipavel72@yahoo.com

RISK FACTORS IN THE OCCURRENCE OF ASTHMA IN CHILDREN

Adina Ungureanu[2], Ileana I[1,2], Chirila S[2], Andreea Gheorghe[2], Viviana Cuzic[1,2], Enache F[1,2]

Abstract

Asthma is still one of the most common chronic inflammatory disease of the airways who determines a high rate of morbidity and mortality in children population. This paper aims to highlight the main risk factors for asthma in children. It is a prospective study and was conducted on a sample of 199 cases with obstructive respiratory disease admitted in the Pediatric Clinic Emergency Hospital Constanta. After a four years period, we identified 126 cases of children that developed asthma. Assessment of risk factors for asthma showed high frequency for the following risk factors: male gender (57.1%), urban (60%), prematurity (29.51%), family atopy (53.2), artificial nutrition, exposure to cigarette smoke.

Keywords: asthma, wheezing, risk factors

Introduction

Asthma is the most common chronic disease of children. In Romania, 7-10% of children suffer from asthma, [1]but the disease is underdiagnosed. "In 2007, prevalences ranged from 2%–4% in Indonesia, Albania and Romania to 30%–32% in New Zealand, the United Kingdom and Costa Rica" [2].

A significant proportion of infants with wheezing have predisposition to asthma, attested by elevated IgE and positive skin test response to aeroallergens.[3,4,5,6] .

By the age of 6-9 years, the risk increases, especially if there is a history of asthma in the mother and / or eczema during the first year of life of the child.[7].

Material and methods

The study is a prospective study and was conducted on a sample of 199 cases with obstructive respiratory disease admitted to the Pediatric Clinic Emergency Hospital Constanta. Data were obtained from the records and history of children and parents. History: demographic data (sex, age, provenance), socioeconomic status, history of perinatal (birth weight, prematurity), artificial feeding in infancy, personal history of atopy, family prior history of asthma, atopy, recurrent wheezing, exposure to passive smoking, active smoking, the presence of air pollution in homes. They were followed for a period of 4 years, (with 6 month recalls), the outcome being the diagnosis of asthma.

For the statistical analysis we used relative risk to express the size of the effect and chi-square test to assess the statistical significance of the association between a studied risk factor and the development of asthma.

Results and discussion

The percentage of male patients who developed Asthma is 57.1% and it is consistent with data from the literature (Figure nr.1) [8] Distribution by area of origin shows the predominance of urban patients, representing over 60% of those who developed asthma, given according to the literature[9]. The disadvantaged social environments increase the risk of asthma and decreases access to adequate medical care. In the study group 24.6% of the cases had poor living conditions (Figure nr. 2)[9]

Analyzing according to gestational age group, resulting in a mean duration of 38.7 weeks pregnancy in children who developed asthma, 29.51% of cases had gestational age less than 37 weeks, statistically significant result ($p < 0.001$).

According to the weight at birth 30.15% of patients with asthma had lower birth weight of 2500g, data consistent with those in the literature [10, 11]. A. Bjerg et al., In a study conducted on a sample of 3,389 children in Sweden, shows that low birth weight (small airways, resuscitation) and antenatal exposure to cigarette smoke increases the risk for asthma 4-6 or at school-age children. [12].

Current to reduce the risk of atopic dermatitis, wheezing and asthma natural diet is recommended a minimum of 4 months of birth. Breast milk contains protective factors of infectious and Growth of cytokines and factors that prevent sensitization to environmental allergens such decreasing susceptibility to develop asthma [13]. Analyzing the distribution of values is apparent that in patients who developed asthma majority were breastfed for a short period of time, or 2 months. Family Atopy is a major criterion for suspicion of asthma had a lower incidence of 53.2% (Table nr.1) Compared with literature data that is present in 80% of children with asthma, atopy by maternal being a major risk factor for asthma. [14, 15].

Smoking during pregnancy increases in child 4 times the risk for wheezing and allergic sensitization. [16] Further impaired lung function, bronchial inflammation and asthma. [17] In our study, 22.2% of asthma cases were associated with smoking during pregnancy. Passive smoking is also associated with increased risk of lower respiratory tract respiratory infections in infancy and childhood small. Regarding parents' smoking behavior related to the study 31.2% of asthma cases have smoker parents that exposed them to passive smoking.

[1] County Emergency Clinical Hospital of Constanţa, Romania
[2] Faculty of Medicine, Ovidius University of Constanţa, Romania
E-mail: adinaungureanu2007@yahoo.com,
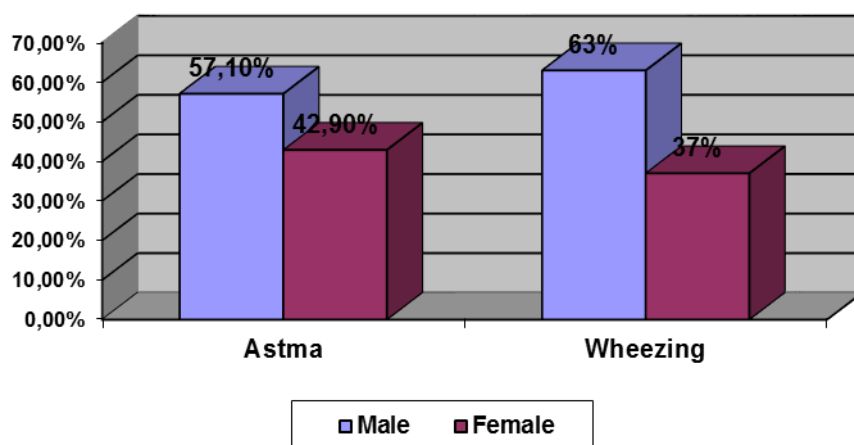
Fig.1 The gender distribution of the two groups of patients.
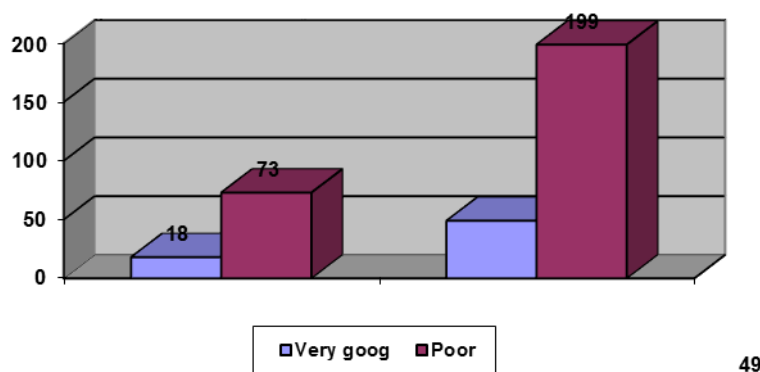
Figure nr. 2 Distribution of the backgrounds of the two groups of patients

			disease		Total
			Asthma	Wheezing	
Atopic parents	No	Count	59	33	92
		% within Disease	46.8%	45.2%	46.2%
	Yes	Count	67	40	107
		% within Disease	53.2%	54.8%	53.8%
Total		Count	126	73	199
		% within Disease	100.0%	100.0%	100.0%

Table nr. 1 Distribution of patients according to parental atopy

			Disease		Total
			Asthma	Wheezing	
Comorbidity	food allergy	Count	8	4	12
		% within Afecţiune	13.1%	8.9%	11.3%
	allergic conjuctivites	Count	5	5	10
		% within Afecţiune	8.2%	11.1%	9.4%
	eczema/dermatitis syndrome	Count	12	30	42
		% within Afecţiune	19.7%	66.7%	39.6%
	obezity	Count	9	0	9
		% within Afecţiune	14.8%	0.0%	8.5%
	allergic rinitis	Count	25	6	31
		% within Afecţiune	41.0%	13.3%	29.2%
	sinusitis and nasal polyposis	Count	2	0	2
		% within Afecţiune	3.3%	0.0%	1.9%
Total		Count	61	45	106
		% within Afecţiune	100.0%	100.0%	100.0%

Table Nr. 2 Distribution of patients according to associated comorbiditys

Allergic manifestations associated with increased risk of developing asthma are described in Table 2 syndrome eczema / atopic dermatitis was present personal history in 21.1% of cases. It is demonstrated the role of atopic dermatitis and allergic rhinitis in asthma occurrence in children. The natural history of allergic symptoms in children is the progression of the symptoms of food allergy in atopic dermatitis, allergic rhinitis and asthma later [18]. Studies show that 43% of children with atopic dermatitis develop asthma and allergic rhinitis 45%. [19] The severity of atopic dermatitis is of also a predictive risk factor: 70% of children with atopic dermatitis develops severe asthma, compared with 30% in those with mild respectively.

Allergic rhinitis studies reported 80-90% incidence of asthmatic children in our study there was a 41% of cases. Allergic rhinitis often precedes asthma occurrence in literature showing a rate of 32-64% of cases. [20] The diagnosis of allergic rhinitis can be hidden in the diagnosis of recurrent respiratory infection.

Conclusions

Assessment of risk factors for asthma in a group of 126 children with asthma showed frequency for the following risk factors: male gender, urban, prematurity, family atopy, artificial nutrition, exposure to cigarette smoke.

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Correspondance to:
Adina Ungureanu
University "Ovidius" Constanta
E-mail:adinaungureanu2007@yahoo.com

OUR EXPERIENCE IN TREATMENT OF CONGENITAL TALIPES EQUINOVARUS - SEVEN YEARS

Zeno A[1,2], Lazea Şt[1,2], Boia Es[1,2], Geanina Polosanu[2], Corina Stanciulescu[1,2], David VL[1,2], Iacob RE[1,2], Popoiu MC[1,2]

Abstract

Congenital talipes equinovarus, also referred to as clubfoot is one of the most common pediatric orthopaedic conditions requiring comprehensive treatment.

The aim of this study is to provide an overview of the cases of congenital talipes equinovarus that underwent treatment in the Clinic for Pediatric Surgery and Orthopedics of the Emergency Children's Hospital "Louis Ţurcanu" Timişoara, Romania between January 2007 and December 2013.

We retrospectively analyzed the clinical data of 321 patients with congenital talipes equinovarus.

They have been taken in consideration gender, groups of age, localisation, associated abnormalities, type of treatment (orthopaedic and/or surgical). The treatment was orthopaedic in all 321 patients and 100 patients had indication for surgical treatment. The Ponseti method had been introduced in our clinic three ago being treated with this method a number of 15 patients.

The results using Ponseti method were good and after the orthopaedic treatment the surgical treatment is less necessary, this method being also the most effective and least expensive treatment of clubfoot.

Key words: clubfoot, orthopaedic treatment, surgical treatment, Ponseti method, most effective, least expensive

Introduction

Throughout the time, walking research had been approached by numerous researchers from different specialities. Borelli (1682) is most likely worthy of determining the position of the gravity center. Demeny and Carlet (1891) introduced in the pressure control on the soil as well as chromatography. Braune and Fischer (1885) offered a mathematic approach of walking (1).

"Human stepping has the general characteristic of the quadrupeds, which move their limbs cross like. When man walks, he moves his four limbs as a horse, cross like; first stepping with the right foot and outstretching the opposite hand in the same time "said Leonardo DaVinci(1,2).

Congenital talipes equinovarus occurs in one in 1000 live births and is one of the most common birth defects involving the musculoskeletal system. Males are more commonly affected than females and up to 50% of cases are bilateral. When one parent is affected with clubfoot, there is a 3% to 4% chance that the offspring will also be affected. However, when both parents are affected, the offspring have a 30% chance of developing clubfoot (2).

Idiopathic clubfoot is an isolated deformity of the foot and leg that is identifiable in utero and consists of four components: equinus, hindfoot varus, forefoot adductus, and cavus. Clubfoot deformity may be associated with myelodysplasia, arthrogryposis, or multiple congenital abnormalities(3).

The diagnosis is simple, it is based on the described deformities, which are obvious at the inspection from the birth, and eventually underlined by the radiography.

Objectives

The main objective is to compare the morphological and functional changes in patients treated with Ponseti method to French method.

We retrospectively analyzed the clinical data of 321 patients with congenital talipes equinovarus.

Materials and methods

This study includes 321 patients with clubfoot (<1 month to >4 years of age) who were admitted and treated in our clinic during the January 2007 – December 2013 time frame. Patients data was obtained from hospital admission records, clinical observation forms, surgical records and imagistic studies. The analysis employed looked at demographic and anamnestic data, therapeutic methods, clinical evolution and treatment results.

The treatment of clubfoot applied in the Pediatric and Orthopaedic Surgery Clinic Timisoara includes consecutive cast immobilisations at 2-3 days, the immobilisation periods alternates with massage and physiotherapy: 3-4 weeks immobilisation, 1 week massage (Figure 1).

In case of the failure of the orthopaedic treatment surgery is indicated, performing Codivilla operation, ± arthrotomy, plantar aponevrotomy (Figure 2).

[1]University of Medicine and Pharmacy "Victor Babeş" Timişoara, România
[2]Emergency Children's Hospital "Louis Ţurcanu" Timişoara, România
E-mail: andrei.zeno@yahoo.com, lazeacalin@yahoo.com, boiaeugen@yahoo.com, polosanugeanina@yahoo.com, stanciulescucorina@yahoo.com, david.vlad@yahoo.com, radueiacob@yahoo.com, mcpopoiu@yahoo.com

Figure 1. Steps of cast imobilisation.
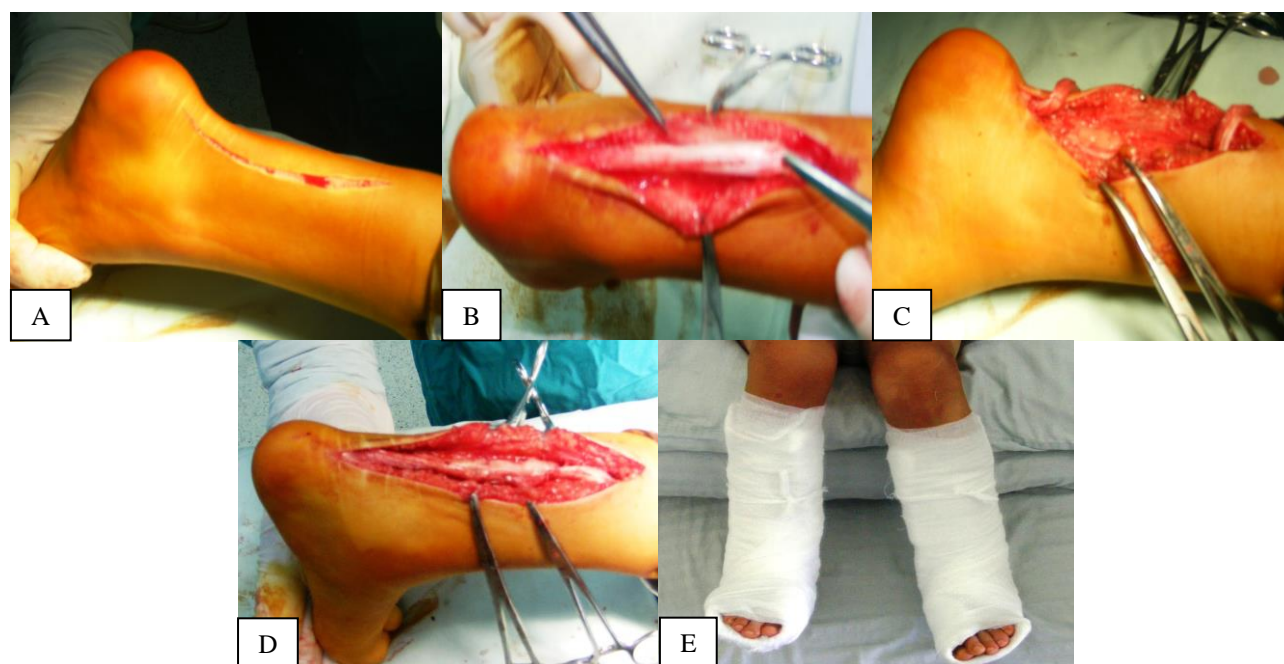
Figure 2. Steps of Codivilla operation. **A.** Slightly curved with concavity medial incision along the lateral aspect of the tendon relief achilian. **B.** Dissect and guide the tendon by locating the route of the future tenotomy in equin club foot the achillion tendon section is being made in a frontal "Z" incision. **C.** Dissect and guide the tendon by locating the route of the future tenotomy in varus equin club foot the achillion tendon section is being made in a sagital "Z" incision. **D.** Guide the foot at 90 degrees on the leg suturing the foot with the leg in easy hypercorrection. **E.** The cast immobilization postoperatory has to be kept for 30 days.
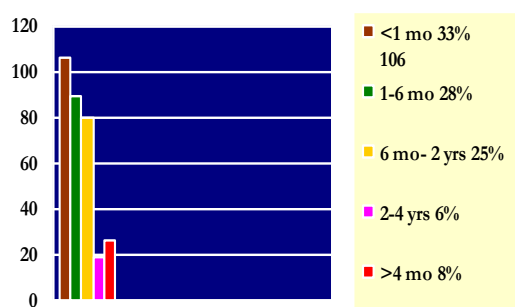
Figure 3: Patient distribution by age.

Results

Of the 321 patients included in the study, 87 are girls and 234 are boys (27% girls and 73% boys).

Figure 3 summarize patient distribution by age. 106 (33%) were less than one year of age at the time of admission. In 56% of cases (180 patients) the clubfoot was bilateral, in 77 patients the right foot was affected (24%) and

64 patients were with the left foot affected (20%). Table 1 indicates the associated disorders which were found at these patients.

Table 1. Associated disorders.

Associated disorders	No. patients
Talipes valgus	32
Congenital hip dysplasia	11
Arthrogryposis	7
Cleft lip, cleft palate	6
Scoliosis	7

The treatment used in the Pediatric Surgery and Orthopaedic Surgery Clinic Timisoara in children <1 year old initiate with 7-14 days of massage, gymnastics, recovery in elastic bandages and adhesive tapes. After 3-4 months continue recovery in splints and plaster casts. Finally after the age of 4 months surgery is indicated: the elongation of the achillion tendon and optionally the elongation of the tibialis posterior, minimal posterior tibio-talus capsulotomy, plantar aponevrotomy. In case of relapse or in children 1-2 years old the surgical treatment is used such as Codivilla, Ugo-Camera-Judet or Heymann intervations. Postoperative indicatios are cast immobilisations 1-3 months intervals, orthopaedic footwear, gymnastics, physiotherapy until the age of 5-7 years. In children >10 years old initially is indicated Codivilla intervention and duble or triple arthrodesis.

The orthopaedic treatment was applied in all 321 cases, surgery being indicated in treatment of 100 patients. 75 patients needed elongation of achilion tendon, in 10% of cases was used plantar aponevrotomy-capsulotomy, 3 patients plantar aponevrotomy and only 3% needed bone surgery (Figure 4).
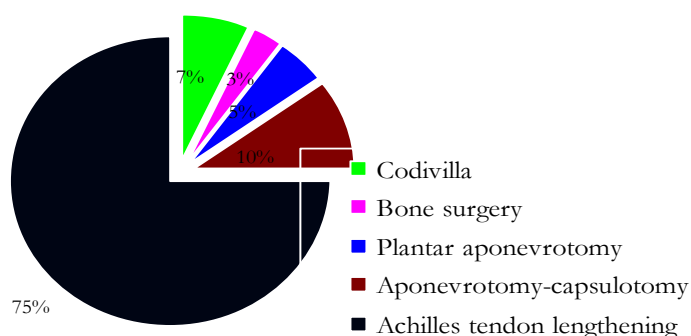

Figure 4. Patients distribution by surgical treatment.

The Ponseti method was applied in our clinic for the first time three years ago.

15 cases have been treated, at the moment when the treatment got started the patients were <1 month of age. The number of imobillisations varied on an average of 5/case. The period of imobillisation varied with an average of 2 months.

Discussions

Over the past decade, the Ponseti method has become the standard of clubfoot care around the world (4).

Hyounmin Noh and Soo-Sung Park (5) sustain that here is general agreement that the initial treatment for idiopathic congenital clubfoot should be nonoperative, regardless of the severity of the deformity, and should be started as soon as possible after birth. The goal of the treatment for clubfoot is to have a functional, pain-free, plantigrade foot with good mobility that does not require the patient to wear modified shoes (Hegazy et al. 2009). In 1950, Ponseti developed a method for treating congenital idiopathic clubfoot that uses manipulation and casting followed by PAT (percutaneus Achilles tenotomy) if pes equinovarus deformity remains (Ponseti 1992). This method is successful in almost 90% of cases (Herzenberg et al. 2002, Hegazy et al. 2009), and PAT should be the treatment for almost 85% of clubfeet (Morcuende et al. 2005).

They suggest that the clinical Pirani score, lateral tibiocalcaneal angle, and lateral talocalcaneal angle should be measured at the time of PAT because they may predict residual equinovarus deformities that might show even after Ponseti treatment of severe idiopathic clubfoot.

Lajja Desai, Florin Oprescu, Andrew DiMeo and Jose A. Morcuende (6) say that the adherence to the bracing protocol is the main factor for the longterm success of the treatment.

Given the potential devastating complications and discouraging long-term results, treatment preferences have since changed to primarily a non-operative approach through the Ponseti method. The method has become the standard of care and completely eliminates the need for extensive operative correction in over 98% of patients if applied correctly (7). The treatment involves manipulation, a series of castings, percutaneous Achilles tenotomy and foot bracing. With correct application of the procedure and appropriate patient adherence, complete correction can be achieved in as little as 16 days with an accelerated casting protocol.

According to Shawne Faulks and B. Stephens Richards (8) the Ponseti and French functional methods are equally effective.

Using gait analysis to evaluate the function of children treated with these techniques, there was no difference in cadence parameters between the two groups. More of the children treated with the French method walked with knee hyperextension, a mild equinus gait, and mild footdrop. In contrast, more of the patients in the Ponseti group demonstrated mildly increased stance-phase dorsiflexion and a calcaneus gait.

Matthew B. Dobbs and Christina A. Gurnett (9) believe that the avoidance of extensive soft-tissue release operations in the primary treatment should be a priority, and the use of surgery for clubfoot correction should be limited to an ''a la carte'' mode and only after failed conservative methods.

They suggest that although current treatment methods appear to be effective for most patients irrespective of etiology, knowledge of etiology may be helpful for prognosis, risk of comorbidities (ie, hip dysplasia), and response to treatment. Personalized treatment based on etiology may also allow reduced brace wear if risk of relapse correlates with etiology or genetic profile. The primary treatment goal is to provide long-term correction with a foot that is fully functional and pain-free. To achieve this, a combination of approaches that applies the strengths of several methods (Ponseti method and French method) may be needed.

According to A. Siapkara, R. Duncan (10) the overriding principle of management of congenital talipes equinovarus is to achieve and maintain a painfree, plantigrade and pliable foot. The few long-term results of surgical correction are disappointing. The initial results of treatment with the Ponseti regimen used across the world are encouraging. Longer term followup will be required to see whether the technique lives up to it's expectations. The management of resistant and recurrent deformities continues to remain a challenge.

Conclusion

The results using Ponseti method were good and after the orthopaedic treatment the surgical treatment is less necessary, this method being also the most effective and least expensive treatment of clubfoot.

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Correspondence to:
Stanciulescu Maria-Corina
Emergency Children's Hospital "Louis Ţurcanu"
Iosif Nemoianu Street 2-4, Timisoara, Romania
E-mail: stanciulescucorina@yahoo.com

CALCANEUS FRACTURES - CASE REPORT

Gocan H[1], Surd A[1], Rodica Muresan[1]

Abstract

The calcaneus is the bone in the back of the foot, commonly referred as the heel bone. This bone helps support the foot and is important in normal walking motions. Calcaneus fractures are almost always the result of high-energy injuries.Calcaneus fracture are extremly rare. We report two cases witch presented in the emergency room with posttraumatic pain, swelling, the loss of bimaleolar and achillian anatomical relation and functio laesa in the right lower limb. The calcaneus X- ray revealed the diagnosis. The fracture was surgically reduced and fixed using orthopaedic screws. In most cases the treatment is surgical, and has the following goals: restoring the congruence of the subtalar joint, restoring the height and width of the calcaneus, maintaining a normal articulation between the calcaneus and the cuboide bone and the correction of the varus following fractures. The recovery period of a calcaneus fracture is an important aspect in determining how well a patient will return to his pre-injury level of activity. The complications are frequent and vary from tendinitits, peronier stenosis, sural nerve damage, to local skin necrosis, surgical incision dehiscense, chronic pain, ostheomielitis, subtalar artrosis.

Keywords: Calcaneus fracture, surgery, pain

Introduction

The calcaneus is the bone in the back of the foot, commonly referred to as the heel bone. This bone helps support the foot and is important in normal walking motions. The joint on top of the calcaneus is responsible for allowing the foot to rotate inwards and outwards.

Calcaneus fractures are almost always the result of high-energy injuries. They usually occur as a result of a fall from a height, such as falling from a ladder. Other causes of a calcaneus fracture include automobile accidents and sports injuries.

Case report 1

We report the case of a 13 year old male patient who presented in the emergency room with posttraumatic pain, swelling, the loss of bimaleolar and achillian anatomical relation and functio laesa in the right lower limb. The calcaneus X- ray showed a longitudinal displaced fracture. The fracture was surgically reduced and fixed using orthopaedic screws, and the imobilisation was done using a cast for 30 days. As a post-operative complication we report local skin necrosis, for which free flap skin grapht was performed. The orthopaedic screws were removed after 30 days.

Case report 2

The second case report is of an 18 old male patient with the postraumatic pain, an open wound in the heel region with a protruding bone fragment and the traumatic section of the Achilian tendon, and functio laesa in the right lower limb. Clinical and radiological examination established the diagnosis of open calcaneus fracture with Achilian tendon section. The emergency treatment consisted in local antiseptic lavage, surgical reduction of the fracture with ostheosintesis using screws and the suture of the Achilian tendon. Imobilisation was done using a cast for 30 days.Post-operative care included triple-association antibiotics, with no following complications. The orthopaedic screws were removed after 30 days.

Discussion

Calcaneus fractures are extremely rare (aproximately 2% of all fractures) in the orthopaedic trauma pathology. Calcaneal fractures are categorized into two types: Intra- and Extrarticular fractures on the basis of subtalar joint involvement. Intrarticular fractures are more common and involve the posterior talar articular facet of the calcaneus. The Sanders system classifies these fractures into four types, based on the location of the fracture at the posterior articular surface. Extrarticular fractures are less common, and located anywhere outside the subtalar joint.[3] Extrarticular fractures are categorized depending on whether the involvement of the calcaneus is anterior (Type A), Middle (Type B) or Posterior (Type C).

All patients with a calcaneus fracture must also be examined for other high-energy injuries. Studies have shown a large number of patients who have a calcaneus fracture will also have fractures of the lumbar spine (10 to 15 percent). In most cases the required treatment is surgical, and has the following goals: restoring the congruence of the subtalar joint, restoring the height and width of the calcaneus, maintaining a normal articulation between the calcaneus and the cuboide bone and the correction af the varus following fractures.

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[1] Emergency Children's Hospital, Department of Pediatric Surgery, Cluj-Napoca

E-mail: muresanrodicaana@yahoo.com, adisurd@yahoo.com, horatiugocan@yahoo.com

Fig. 1. X-ray images:

Fig. 2. Intra-operative images:

The recovery period of a calcaneus fracture is an important aspect in determining how well a patient will return to his pre-injury level of activity. Patients will be required to keep weight off of the foot for as long as three months. The other critically important aspect of treatment is controlling swelling, especially in patients who have had surgery. The best ways to control swelling includes elevation, immobilization, and ice application.

The complications are frequent and vary from tendinitits, peronier stenosis, sural nerve damage, to local skin necrosis, surgical incision dehiscense, chronic pain, ostheomielitis, subtalar artrosis.

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Correspondance to:
Rodica Muresan
Emergency Children's Hospital
Department of Pediatric Surgery
Cluj-Napoca
E-mail: muresanrodicaana@yahoo.com

NECROTISING ENTEROCOLITIS IN PRETERM INFANTS WITH GESTATIONAL AGE≤32 WEEKS IN ROMANIA: INCIDENCE AND RISK FACTORS

Laura Olariu[1,2], Gabriela Olariu[3], Livia Ognean[4], Olariu S[3], Otilia Marginean[1,2], Boia ES[1,2]

Abstract

Introduction: Necrotising enterocolitis (NEC) is an acquired gastrointestinal disease associated with significant morbidity and mortality in preterm newborns. Taking into account the catastrophic development of this disease, it is necessary to focus research on prevention strategies and identify predictive risk factors for its occurrence. Aim: The aim of this study was to determine the incidence of NEC and to identify the main risk factors associated with NEC in preterm infants with gestational age(GA) ≤32 weeks admitted to neonatal intensive care units(NICUs) in Romania. Material and methods: This was a retrospective study based on the data collected in a standardised format for all preterm infants with GA ≤32 weeks born over a period of 2 years (january 2010-december 2011) and admitted to 12 tertiary-level NICUs in Romania. It was used data registered in the National Registry of Neonatal Respiratory Distress (NRNRD). A diagnosis of NEC was made based on clinical, radiological and/or histopatological evidence of stage II or III, acording to Bell's criteria. Logistic regression analysis was performed to determine the significant risk factors associated with NEC. Results: There were 1696 neonates under 32 weeks of gestation that met inclusion criteria; 1605 did not have NEC, while 91(5,3%) met criterion for NEC. Lenght of hospital stay and mortality were higher in neonates with NEC than those without NEC. Logistic regression analysis showed that smal for gestational age(SGA) and nosocomial infections were the most important risk factors for NEC. Other factors that were associated with an increased risk of NEC were bronchopulmonary displasia (BPD), use of nasal continuos positive airway pressure (CPAP), sepsis, apnea of prematurity, the lack of antenatal glucocorticoids and outborn pacients. Male gender and PDA were not statistical significantly correlated with NEC (borderline statistical significance). Conclusions: The incidence of NEC was higher in this study (5,3%). Low birth weight, nosocomial infections, BPD, CPAP, apnea and lack of antenatal glucocorticoids were associated with an increased risk of NEC in Romanian preterm infants under 32 weeks of gestation. Male gender and PDA were not statistical significantly correlated with NEC (at the limit of statistical significance).

Keywords: necrotising enterocolitis, preterm infants, risk factors

Introduction

Necrotizing enterocolitis(NEC) is an acquired inflammatory disease of the intestine, being the most common neonatal gastrointestinal emergency, that mainly affects preterm infants(1). NEC is a multifactorial disease that occurs in a high risk newborn. NEC incidence is inversely proportional to gestational age(GA), more than 90% of those affected are premature (2). With improving care at the end of the presurfactant era, the incidence of NEC declined briefly, but increased after surfanctant use became a standard of care. This reported increase is probably because of the increased survival of extremely low birth weight infants (3,4). The incidence of NEC ranged between 5%-7% and varies from country to country and between NICUs(5-8).

Because the etiology and pathogenesis of NEC are still incompletely understood, therapeutic options, morbidity and mortality were not significantly improved in the last decade of time. NEC is a major cause of mortality (between 10%-50%)(9-11) and morbidity, including recurrent sepsis, dependence on parenteral nutrition, need for surgery, survival with short bowel syndrome and neurodevelopmental delay in preterm infants.

Taking into account the catastrophic development of this disease, it is necessary to focus research on prevention strategies and identify predictive risk factors for its occurrence. The most important risk factor for NEC is prematurity and the greatest immaturity infants are at the greatest risk. Many putative risk factors have been associated with the development of NEC, both directly related to feeding practices(eg, time of feeding, use of nonhuman milk, the amount of used milk, use of fortifiants) and not related (eg, greater immaturity, smal for gestational age, respiratory distress syndrome, neonatal sepsis, mechanical ventilation, maternal pathology)(12). While many studies have identified individual risk factors related to the development of NEC, most studies include only a small number of infants with NEC, are single-institution reports, or were done in the presurfactant era. Many authors have focused on a single factor rather than exploring the additive effects of several factors(13-17).

[1] University of Medicine and Pharmacy "Victor Babes" ,Timisoara
[2] Emergency Hospital for Children "Louis Turcanu", Timisoara
[3] Neonatology Department of Municipal Emergency Hospital, Timisoara
[4] County Emergency Hospital, Sibiu
E-mail: tunealaura@yahoo.com; gabriela_olariu@yahoo.com; livia_sibiu@yahoo.com; raulolariu1981@yahoo.com; omarginean@ymail.com; boiaeugen@yahoo.com

Characteristics	Total	NEC(n=91)	No NEC(n=1696)	p-value
Maternal factors				
Type of delivery (n,%)				
Cesarean	754(44,7%)	41(45,6%)	713(44,7%)	0,874
Vaginal	931(55,3%)	49(54,4%)	882(55,3%)	
Maternal diabetes mellitus (n,%)	21(1,2%)	0(0,0%)	21(1,2%)	0,624
Maternal hypertension (n,%)	139(8,2%)	8(8,8%)	131(8,2%)	0,831
Maternal eclampsia(n,%)	68(4,0%)	4(4,4%)	64(4,0%)	0,782
Chorioamniotitis (n,%)	75(4,4%)	4(5,5%)	71(4,4%)	0,596
Antenatal steroid prophylaxis (n,%)	507(29,9%)	18(19,8%)	489(30,5)	0,030
Premature rupture of membrane (n,%)	425(25,1%)	22(24,2%)	403(25,1%)	0,842
Neonatal factors				
Location of birth (n,%)				
Inpatients	1346(79,4%)	63(69,2%)	1283(79,9%)	0,014
Outpacients	350(20,6%)	28(30,8%)	322(20,1%)	
Sex (n,%)				
Male	922(55,2%)	58 (64,4%)	864(54,7%)	0,070
Female	748(44,8)	32(35,6%)	716(45,3%)	
GA (mean±SD,weeks)	1696	28,26±3,57	29,76±7,15	0,000
Birth weight (mean±SD)		1078,19±338,72	1346,49±518,56	0,048
APGAR score at 1 minute (mean±SD)		4,62±2,52	5,41±2,49	0,003
Growth status at birth				
SGA (n,%)	576(34,0%)	49(53,8%)	527(32,8%)	0,000
AGA (n,%)	1038(61,2%)	40(44,0%)	998(62,2%)	0,001
LGA (n,%)	55(3,2%)	2(2,2%)	53(3,3%)	0,766

Table1. Demographic and clinical characteristics of preterm infants≤32 weeks of gestation with and without NEC

Parameters	Total	NEC (n=91)	No NEC(n=1696)	p-value
Given surfactant therapy (n,%)	240(14,2%)	12(13,2%)	228(14,2%)	0.786
Use of CPAP (n,%)	999(58,9%)	67(73,6%)	932(58,1%)	0,003
Use of MV (n,%)	251(14,8%)	14(15,5%)	237(14,8%)	0,872
PDA (n,%)	372(21,9%)	27(29,7%)	345(21,5%)	0,067
Apnea (n,%)	451(26,6%)	34(37,4%)	417(26,0%)	0,017
BPD (n,%)	120(7,1%)	15(16,5%)	105(6,5%)	0,000
Sepsis (n,%)	360(21,2%)	29(31,9%)	331(20,6%)	0,011
Nosocomial infections (n,%)	91(5,4%)	16(17,6%)	75(4,7%)	0,000
IVH (n,%)	640(37,7%)	38(41,8%)	602(37,5%)	0,416
Hospital length of stay (mean±SD,days)		47,12±29,32	33,64±26,51	0,000
Outcome (n,%)				
Survivors/discharged	1365(80,5%)	56(61,5%)	1309(81,6%)	0,008
Death	331(19,5%)	35(38,5%)	296(18,4%)	

Table 2. Comparison of treatment received and outcome among preterm infants≤32 weeks of gestation with and without NEC

Variables	B	SE	Wald	p-value
SGA	0,870	0,217	16,083	0,000
Nosocomial infections	-1,471	0,300	24,079	0,000
BPD	-1,037	0,300	11,937	0,001
AGA	0,740	0,217	11,593	0,001
Use of CPAP	-0,701	0.243	8,309	0,004
Death	-1,210	0,428	8,011	0,005
Sepsis	-0,558	0,233	6,353	0,012
Outbornpacients	0,571	0,236	5,887	0,015
Apnea	-0,530	0,224	5,601	0,018
Lack of antenatal steroid prophylaxis	0,575	0,269	4,579	0,032
Borderline variables				
PDA	-0,432	0,237	3,316	0,069
MV	0,407	0,226	3,242	0,072

Table 3. Variables associated with NEC, by multiple regression analysis

We performed this study to determine the incidence of NEC among preterm infants with GA≤32 weeks and to identify the main risk factors for NEC in a large unselected Romanian cohort of preterm infants. We used a national database of preterm infants under 32 weeks of gestation to investigate the risk factors.

Material and methods

This was a retrospective, observational study based on the data of all preterm newborns with GA≤32 weeks born between January 2010-December 2011 in Romania and admitted to the NICUs of 12 tertiary-level maternity participating in the NRNRD. Participating NICUs submitted data on these infants to the NRNRD upon their discharge or death. A standardised format was used for data collection. Each infant was considered a unique case and not duplicated in the registry. The database included consecutive preterm infants for each participating center, but not all centers contributed neonates for all 2 years (9 centers in 2010 and another 3 centers in 2011). Neonates who died in the first day of life, those under 23 weeks of gestation and those with congenital anomalies were excluded from the study.

The diagnosis of NEC was made based on the presence of clinical, radiological and/or histopathological evidence that fulfilled the stage II or III of Bell's criteria(18).

The potential risk factors considered were classified into 4 cathegory:
• neonatal factors: location of birth, gestational age, birth weight, sex, growth status at birth: being smal for gestational age (SGA, birth weith<10th percentile for respective gestational age), appropriate for gestational age (AGA, birth weith between 10th-90th percentile for respective gestational age), large for gestational age (LGA, birth weith >90th percentile for respective gestational age)(19,20), APGAR score at 1 minute
• maternal factors: maternal insulin-dependent diabetus mellitus, maternal hypertension, maternal eclampsia, chorioamniotits, antenatal steroid prophylaxis, premature rupture of membrane(over 18 hours), type of delivery
• factors related with resuscitation: surfactant therapy, use of nasal continuos positive airway pressure (CPAP), need for mechanical ventilation(MV)
• newborn diseases: presence of patent ductus arteriosus(PDA), intraventricular haemorrhage(IVH), apnea of prematurity, bronchopulmonary disease (BPD), sepsis, nosocomial infections, hospital length of stay, outcome (discharge, death).

The diagnosis of PDA was made based on the presence of a continuous heart murmur in the left second, intercostal space, hyperdynamic precordium, wide pulse pressure, bounding pulses and an increased pulmonary vasculature or cardiomegaly in the cest radiograph, or echocardiografic evidence of PDA. IVH was defined as the presence of haemorrhage in the intraventricular, periventricular or subependymal regions of the lateral ventricles of the brain as detected by cranial ultrasonography. Preterm apnea was defined as respiratory pause lasting 20 seconds or less, but accompanied by cyanosis or bradycardia. BPD was defined as needing oxygen therapy for more than 28 days and at 36 weeks of gestation. Sepsis was defined as the presence of clinical evidence of sepsis with positive microbiological culture in aseptically collected blood or cerebrospinal fluid specimens. Nosocomial infection was defined as a systemic infection manifested after the first 72 hours of life, caused by an infection transmitted vertically by existing microorganisms in the maternal cervico-vaginal canal or horizontally by contamination of the external environment.

Statistical analysis was performed using SPSS Version 17 Program. Results are expressed as mean± SD. Univariate analysis was used to compare the variables for the outcome groups of interest (pacients with NEC vs. patients without NEC). Comparisons were unpaired and all tests of significance were 2-tailed. Continuous variables were compared using Student's t test for normally

distributed variables. All p values< 0.05 were considered statistically significant. Chi-square test (or Fisher's exact test for variables with expected values <5) was used for univariate analysis of categorical variables. To establish the predictors for NEC it was used the binomial logistic regression, Wald model.

Results

There were 1696 neonates under 32 weeks of gestation that met inclusion criteria; 1605(94,7%) did not have NEC, while 91(5,3%) met criterion for NEC. From all 1696 preterm infants, 500(29,48%) were of gestation ≤28 weeks. A majority (79,4%) of the preterm infants were born to inpatients.

Univariate analysis showed no significant difference in the maternal factors between preterm infants with and without NEC, except for the use of antenatal steroid prophylaxis (Table 1). The proportion of mothers receiving antenatal steroids was significantly lower among childrens with NEC. The infants with NEC, compared with those without NEC, were of significantly lower birth weight and gestational age. Regarding neonatal factors, univariate analysis showed significant difference between infants with and without NEC for the following characteristics: GA, birth weight, SGA, AGA, APGAR score and outpatients. This factors were associated with an increased risk for NEC. Male gender and PDA were not statistical significantly correlated with NEC (borderline statistical significance).

Discussions

We conducted a retrospective, observational study to find the incidence and the risk factors for NEC in preterm infants≤32weeks of gestation. Our study population included preterm infants from 12 tertiary-level NICUs in Romania. NEC was defined based on the presence of clinical, radiological and/or histopathological evidence that fulfilled the stage II or III of Bell's criteria(17).

In our study, the incidence of NEC among preterm infants ≤32 weeks was 5,3%, much higher than that reported in other studies (Italy-3,1%, United States-2,6%, Australia-3,8%)(5,12,21), but lower than that reported in one big Malaysian study (6,2%)(22). Incidence of NEC varies significantly from country to country and between NICUs. Criteria for preterms inclusion in the studies may differ from one center to another. A study from United States had shown that NEC occurs in approximately 10% of infants born with a weight lass than 1500g with a large variation ranging from 2% to 22%, depending on the centre of inquiri(23). Another recent surveys on a large samples of VLBWIs in North America have shown an incidence ranging from 6,6% to 7,1%(7,8,11).

Similar to the findings of Canadian and Australian studies(8,12), the data from our study showed that low gestational age was a significant risk factor associated with NEC. This was different from the findings of Guthrie, Kosloske and Holman et al(3,21,24), which reported that decreasing birth weight was the main risk factor for NEC.

We also find that the use of antenatal glucocorticoids decrease the incidence of NEC, similar to the vast majority of previous studies(25, 25). A few studies found the opposite relationship (i.e., antenatal glucocorticoids increase the incidence of NEC)(21,27,28). The hypothesize could be that the protective effect of antenatal glucocorticoids might be birth-weight-specific and the number of doses may influence the effects. Repetitive doses of glucocorticoids may have different morphologic effects upon gastrointestinal development when compared to a single dose.

Several risk factors for the development of NEC identified by other studies such as apnea, BPD, sepsis, nosocomial infections, were also found to be associated with NEC in our study(22,29,30).

Use of CPAP was associted with the developing of NEC in this study, being different from other reports(31).

Contrary to other studies(5,32), PDA was not a significant independent risk factor associated with NEC in our study. Probably not all childrens in our study were diagnosed with PDA due to several factors: impossibility of ultrasound PDA diagnosis because of lack of cardiologists in many centers, there is no single diagnostic protocol in the country and also the time of diagnosis is very important.

The outborn pacients had in our study the risk for developing NEC, similar to another reports(33). The factors that could be associated with the higher incidence of unfavorable outcomes among outborn infants include ineffectiveness of stabilization procedures before or during transport, delays in commencing assisted ventilation or use of surfactant, risk of infections and delays in transport(34). In addition, transport itself is a stressor that can adversely affect this babys(35). There are many possible factors for the improved outcomes of preterm infants at tertiary centers, including availability of laboratory, radiologic, and specialist medical support, and more adequate staffing and equipment to provide optimal care in the delivery room and NICUs(34).

Our data confirm previous reports that NEC is an important neonatal problem associated with significant morbidity and mortality(3,4). In this study the mortality rate of infants with NEC was significant(38,5%), similar to the findings of other studies(3,7,8,23,24), and the newborns with NEC also had a longer hospital length of stay.

Conclusions

The incidence of NEC among preterm infants ≤32 weeks was higher(5,3%) in our study. Low birth weight, SGA, nosocomial infections, BPD, CPAP, apnea of prematurity and lack of antenatal glucocorticoids were associated with an increased risk of NEC in Romanian preterm infants under 32 weeks of gestation. Male gender and PDA were not statistical significantly correlated with NEC (borderline statistical significance).

In summary, NEC is still a common problem affecting preterm infants, with the incidence and mortality remained unchanged in recent years. A number of modifiable risk factors associated with NEC have been identified and it is possible that such factors might help us to plan optimal preventive strategies to reduce the incidence of NEC in preterm babys.

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Correspondance to:

Dr. Laura Olariu
Emergency Hospital for Children "Louis Turcanu"
Nemoianu Street, No.1, 300011, Timisoara
E-mail: tunealaura@yahoo.com

CLINICAL ASSESSMENT IN NEONATAL TRANSFUSION GUIDELINES

Mihaela Demetrian[1,2*], Silvia Stoicescu[3], Constantin Ilie[1]

Abstract

Background Packed Red Blood Cell (PRBC) transfusions are often administered to patients in the neonatal intensive care unit.

Aims The purpose of this study was to determine whether current blood transfusion clinical practice guidelines are as useful as clinical judgement in identifying patients in need of a PRBC transfusion.

Methods The study is a post-transfusion survey on premature newborns less than 32 weeks old that received a PRBC transfusion. These patients were divided into three groups, based on the criteria used for transfusion: (a) clinical practice guidelines; (b) clinical judgement/symptoms of need for PRBC transfusion; or (c) both. These three groups were further subdivided based on clinical response to transfusion. Demographic data and clinical variables were compared among the groups. 35 preterm infants who received transfusions were identified. Thirteen patients (37%) were transfused based on guidelines, 4 (11%) based on clinical judgement, and 18 (52%) based on both.

Results Neonates transfused based on guidelines alone were more likely to have received the transfusion in the first week of life, had a lower pre-transfusion hematocrit, were less symptomatic and had a higher likelihood of requiring mechanical ventilation. Neonates transfused based on clinical judgement were more likely to be on non-invasive ventilatory support and were more symptomatic. Neonates who improved after a transfusion had a lower pre-transfusion hematocrit (p=0.03), were more symptomatic (p=0.01) and were more likely to be on non-invasive ventilatory support (p=0.02) when compared to the group without clinical improvement. The group without improvement had an increase in oxygen requirement (+3.8±2.4) after the transfusion (p=0.0004).

Conclusion Guidelines on when to transfuse stable growing premature newborns with PRBC should be reevaluated to include more clinical judgement and perhaps be more restrictive for critically ill neonates.

Key words: preterm newborn, blood transfusion, guidelines, anemia of prematurity

Introduction

Newborns, especially premature infants from neonatal intensive care units (NICU) are among the most likely to be transfused of all hospitalized patients[1]. During the first 2 weeks of life, when blood losses are frequent, approximately 50% of Extremely Low Birth-Weight (ELBW) infants (<1000g) receive their first transfusion[2]. By the end of hospitalization over 80% of ELBW infants receive at least one transfusion[3,4]. Although the number of transfusions received by premature infants remains significant, it has dropped in the last 20 years mainly because of more restrictive transfusion guidelines[5,6].

The main objective of this study was to try and determine if the current NICU Packed Red Blood Cell (PRBC) transfusion guidelines are better than the clinical perception of symptoms in determining the need for transfusion. The secondary aim of this study was to find which symptom of anemia was most frequently associated with ordering a PRBC transfusion.

The hypothesis of the study is that infants that received PRBC transfusions based solely on guidelines did not have a significant clinical improvement and that the association of clinical perception is more predictive of the need for packed red blood cell transfusion.

Materials and methods

The study took place in 2010 (January – December) at the IOMC-"Polizu" Maternity neonatal intensive care unit (NICU). All preterm infants under 32 weeks old that received PRBC transfusions during this period were included. The guidelines used for PRBC transfusion were based on disease severity, as illustrated in Table I. We retrospectively analyzed transfusion criteria with the help of a questionnaire. Using the answer to Question 1: "Which is the indication for transfusion?" newborns were split into 3 groups: (a) newborns transfused based on the guidelines; (b) newborns transfused based on clinical perception and symptoms; and (c) newborns transfused based on both (guidelines and clinical perception). Patients were further subdivided into two subgroups, based on clinical improvement after the PRBC transfusion. The questionnaire also included other questions: "Was the transfusion beneficial for the newborn?", "Did you use other therapeutic measures?", "Which intervention was most beneficial to the patient".

[1]Victor Babeş University of Medicine and Pharmacy, Timişoara, *PhD Student
[2]Clinical Hospital of Obstetrics and Gynecology „Filantropia" Bucharest – Neonatal Department
[3]Carol Davila University of Medicine and Pharmacy, Bucharest, Mother and Child Institute – "Polizu" Maternity
E-mail: mdemetrian@yahoo.com, stoicescusilvia@yahoo.com, constantinilie@umft.ro

Clinical improvement was defined as a 10% decline of at least one of the following parameters: (i) fraction of inspired oxygen (FiO2), (ii) heart rate in the case of tachycardia (>160 beats/min), or (iii) episodes of apnea, bradycardia, or desaturation (ABD). These parameters were chosen because of their frequent association with the anemia of prematurity.

Table I. Packed red blood cell transfusions guideline in the NICU.

Transfusion recommendations		The volume of packed red blood cells transfused
Hypovolemic shock due to acute blood loss		Determined by the physician
Hct≤38%:/Hb≤12	MV with MAP> 8 and FiO2 > 40% HFV with MAP>14	10-15 ml/kg 2-4 hours
Hct≤35%:/Hb≤10 Hct≤30%:/Hb≤9	Average MV MAP≤8 and FiO2<40% HFV with MAP<14 Minimal ventilatory support NCPAP 4-5 and FiO2≤35%	10-15 ml/kg 2-4 hours
Hct≤25%:/Hb≤8	Without MV FiO2 21-40% and one of the following: - Tachycardia HR>180 or - Tachypnea RR>60 ≥ 24 or - Doubling of oxygen requirement - Weight gain <10 g/kg/day for 4 days if ≥120 cal/kg/day - Apnea/bradycardia (>9/12 hours or 2/24 hours that require BM ventilation - Lactate ≥2,5 mEq/l or metabolic acidosis pH<7,2 - Preoperative	15-20 ml/kg 2-4 hours 10 ml/kg x 2
Hct≤21%:/Hb≤6	Asymptomatic and with an absolute reticulocyte count <100.000/μl (2%)	20 ml/kg 2-4 hours or 10 ml/kg x 2

Hct=hematocrit, Hb=hemoglobin, MV=mechanical ventilation, MAP=mean airway pressure

Results

During the study period, 120 preterm infants under 32 weeks were admitted to the NICU, 35 of them receiving at least one PRBC transfusion; these 35 infants received a total of 129 transfusions. Thirteen patients (37.1%) received transfusions based solely on the guidelines, 4 (11.4%) patients were transfused based on the clinical perception of symptoms and 18 (51.4%) patients received transfusions based on both criteria (guidelines and clinical perception). There were no significant differences concerning gestational age and current weight among the 3 groups. The guideline-based group received more transfusions during the first 7 days of life compared to the other groups (p=0.006). These infants also required more intensive ventilatory support (p=0.019) and had a lower mean pre-transfusion hematocrit (p=0.002). Mean hematocrit did not differ significantly among the 3 groups during the first week of life (p=0.8). In the subsequent weeks of life the "transfusion trigger" hematocrit was significantly lower in the guideline-based transfusion group (p<0.05). Infants that were transfused based on the clinical perception of anemia symptoms or by using a combination of guidelines and symptoms had more episodes of tachycardia and ABD (p=0.001) when compared with the group that received transfusions according to the guidelines (Table II).

Table II. Comparison of clinical parameters among the three transfusion groups.

	Transfusion guideline	Symptoms	Symptoms and guideline	P value
Hematocrit pre-transfusion 1 (first 7 days)	32,6 ±2,5	29,2 6,8	30,6±5,6	0.8
Hematocrit pre-transfusion 2 (days 8-14)	28,6±7,3	30,4±3,8	33±2.6	0.002
Hematocrit pre-transfusion 3 (days15-28)	24.3±4.2	29.6±3.5	27.5±4.	0.02
Hematocrit pre-transfusion 4 (>28days)	22±3.9	22.8±4.9	27 (1 caz)	0.001
Mean FiO2 before transfusion (%)	37,6±21,7	47,5±24	25,5±6,3	0.025
Change of the FiO2 after transfusion(%)	- 10	- 5,8	- 2.5	NS
Number of infants with tachycardia	1 (7,7%)	6 (33%)	4 (100%)	0.002
Number of infants with ABD	3 (23%)	8 (44%)	4 (100%)	0.001
Number of infants with clinical improvement	11 (84%)	10 (55,6%)	2 (50%)	NS

Without taking into account the reasons for the transfusions, the 35 infants were subdivided into 2 subgroups based on the presence or absence of clinical improvement (Table III). There were no statistically significant differences concerning clinical improvement among the 3 groups, although we did observe a favorable trend for clinical improvement in the group that received transfusions based only on the guidelines. Preterm infants with clinical improvement after transfusion had a ~ 13% reduction in O2 requirement compared to a ~ 4% increase in O2 requirement in the group without clinical improvement (p=0.004). Most patients in the group that saw clinical improvement were treated with non-invasive ventilation (nCPAP) or oxygen therapy without mechanical ventilation (p=0.002). Patients with clinical improvement after transfusion also had a lower mean hematocrit (p=0.03, more episodes of ABD (p=0.002) and tachycardia (p=0.013) before the transfusions, compared to those that did not improve.

Table III. Comparison of clinical parameters between groups with and without clinical improvement after transfusion.

	Clinical improvement	Without clinical improvement	P value
Number of infants	22 (62,9%0	13 (37,1%)	
Pre-transfusion hematocrit (%)	28.9±6.5	33.2±2.6	0.03
Post-transfusion hematocrit (%)	36±3.9	34.3±3.4	0.01
FiO2 (%), pre-transfusion	41.3±24.7	40.9±19.9	0.2
Change of FiO2(%)	28.5±9.9	44.7±22.3	0.004
IPPV	6	14	0.03
NCPAP	2	1	0.6
MAP > 8 FiO2 >40%	2	5	0.8
MAP 6-8 FiO2 <40%	3	3	0.7
MAP 4-5 FiO2 <35%	6	2	0.02
Number of tachycardic patients	6 (34,2%)	0	0.02
Number of patients with ABD	7 (31.8)	0	0.01
Other interventions	14 (63.6%)	10 (76.9%)	0.6

Most (78%) patients in both of the groups also received other interventions, such as antibiotic therapy, increased ventilatory support, increased FiO2, aminophylline, inhaled bronchodilator therapy, and diuretics, simultaneously with red blood cell transfusion.

In the subgroup of patients that had clinical improvement and received multiple interventions, the clinical impression was that transfusions contributed to improvement in 72% of cases. In cases without clinical improvement after transfusion, other interventions in particular increased ventilatory support (54%) seemed to have benefited the patient.

Discussion

In our study, 35 of the 120 preterm infants (<32 weeks gestational age) that were admitted to the NICU received a total number of 129 PRBC transfusions for a variety of reasons. When deciding on an early transfusion, it is important to keep in mind that despite the progress made in transfusion practice, complications still exist[7,8]. Transfusion guidelines for neonates are still unclear and there is much controversy surrounding the optimal timingoftransfusions[9,10]. The hematocrit is generally kept at higher than physiologic values for ill neonates, although there is no clear evidence of benefit in doing so. Hematocrit alone is a poor indicator of tissue oxygenation[10,11]. There is no single, optimal biochemical marker or sign that can be used to ascertain the need for transfusion[12,13]. Without a reliable marker to guide optimal transfusion timing, clinical judgement seems to be the most important tool used by the medical staff when determining the need for a transfusion.

In our study, there were no statistically significant differences in clinical improvement among the three groups of infants; there was a positive trend in the group that received transfusion based on the guidelines. However, we believe it is important to include clinical signs and clinical judgment in the practice of red blood cell transfusion.

Many aspects of our transfusion guidelines should be reviewed. For example, according to the guidelines, all infants with "severe cardio-pulmonary disease" (HFV, FiO2> 40% NO, MAP> 8 cm H2O) with a hematocrit <40%, or infants with "moderate cardio-respiratory disease" (MAP 6 -8 cm, FiO2> 35%) with a hematocrit ≤ 35% should receive transfusions[14].

As shown in our study, 37% of infants in the group that did not show clinical improvement were ventilated with MAP>8cmH2OandFiO2>40% versus 14% in the group that showed clinical improvement (p=0.02), indicating little to no benefit after transfusion[15].

It is possible that the volume of transfused blood was detrimental to the infant due to lung overloading with a subsequent increase in oxygen requirement. This is a problem in the first week of life when preterm newborns are in the early stages of respiratory distress, due to surfactant deficiency. The guidelines for this subgroup (preterm critically ill in the first week of life) should be reviewed to assess the potential risks generated by volume overload, as they might outweigh the benefits of increased oxygen-carrying capacity.

More patients from the group with clinical improvement required minimal ventilatory support (MAP 4-5 cm H2O, FiO2<35%) compared to the group without clinical improvement (37% vs. 14%, p=0.002). Based on the current guidelines, these patients should not be transfused until the hematocrit drops below 30%, and in some cases<24% [14,16].

In our current guidelines tachycardia is used as a criterion only for stable growing newborns. However, we found that patients that were tachycardic before being transfused were 6 times more likely to achieve clinical improvement. We recommend that tachycardia be included in the guidelines for all categories. Most patients with clinical improvement required multiple therapeutic interventions and blood was the primary factor of improvement in 72% of the cases.

Conclusions

Based on our study, we recommend that PRBC transfusion guidelines currently used to assess ventilatory-dependent critically ill premature newborns should be used cautiously, in accordance with the complex physiology of neonatal respiratory pathology.

For stable growing infants, transfusion guidelines should be re-assessed to include more clinical judgement.

For all newborns, red blood cell transfusion guidelines should be revised to include more clinical parameters, with emphasis on the use of tachycardia as a "need to transfuse" trigger.

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Correspondence to:

Mihaela Demetrian
Clinical Hospital of Obstetrics and Gynecology „Filantropia"
Neonatal Department,
No. 11, Ion Mihalache Boulevard, District 1,
Bucharest, Romania,
E-mail: mdemetrian@yahoo.com

THE IMPACT OF PRETERM PREMATURE RUPTURE OF MEMBRANES ON NEONATAL OUTCOME

Mirabela Adina Dima[1,2,*], Nicoleta Ioniță[1,2], Daniela Iacob[1,2], Aniko Manea[1], Daniela Chiru[1,3], C Ilie[1,2]

Abstract

Preterm premature rupture of membranes eventuate when the amniotic sac breaks at least 4 weeks before a pregnancy has reached full term. The motive of this study was to evaluate the effect of preterm premature rupture of membranes on neonatal outcome and to establish correlations between mother's infection and gestational age, weight as well as hospitalization days of the newborn. A retrospective study was conducted over a period of 1 year in Bega Clinic of Obstetrics-Gynecology and Neonatology Timisoara. The study included 36 premature newborns admitted to Neonatal Intensive Care Unit, who meet the inclusion criteria. Confirming the diagnosis of neonatal sepsis includes the history of the neonate, clinical signs, symptoms and paraclinical investigations. The present work focuses on the history of mothers with PPRM over 16 hours, with or without infection, which indicates the need to look up for a possible neonatal infection. For laboratory tests: complete blood count, C-reactive protein, blood and vernix cultures were taken. Further research will analyze new markers of infection. Corroborating new findings with the data taken so far, helps us developing a novel clinical protocol and to improve the therapeutic management of this cases.

Keywords: preterm premature rupture of the membranes, premature infants, infection

Introduction

Premature labor often ends with an early birth. The labor is considered to be premature if it starts more than three weeks before the predicted birth date [1]. Preterm birth is a high risk for perinatal mortality and long-term morbidity as well as the health consequences outcomes. Preterm birth is among the top causes of death in infants worldwide [2]. One of the conditions that lead to premature birth is the rupture of the membranes. Premature rupture of the membranes (PRM) was defined as leakage of amniotic fluid that precedes the onset of uterine contractions and cervical changes. PRM is considered prolonged when it occurs more than 18 [3] or 24 [4] hours before labor. Preterm premature rupture of membranes (PPRM) is characterized as the tear of the amniotic sac during pregnancy before 37 weeks of gestation. It occurs in 3 percent of pregnancies and is the cause of approximately one third of preterm deliveries [5]. Before term, PPRM is frequently due to a uterus infection. Other factors that may be linked to PRM embrace the following: sexually transmitted infections like chlamydia and gonorrhea, low socioeconomic conditions, previous preterm birth, smoking during pregnancy. PPRM often conduct to significant perinatal morbidity, including neonatal sepsis, respiratory distress syndrome, and fetal death. Therefore, this study focuses on finding correlations between the PPRM and its direct consequences on the neonatal outcome.

Purpose

The purpose of the following study was to evaluate the impact of preterm premature rupture of membranes on neonatal outcome and to establish new correlation between mother's infection, and gestational age, weight and hospitalization days of the newborn.

Materials and methods

A retrospective study was conducted over a period of 1 year (January 2013 – January 2014) in the Neonatal Intensive Care Unit (NICU), Clinic of Obstetrics-Gynecology and Neonatology of the Emergency County Hospital Timisoara. There were selected 36 premature newborns admitted to NICU. One of the most important lot inclusion criteria was preterm labor due to preterm premature membrane rupture. Also, another eligible condition was that the membrane rupture occurs more than 16 hours before labor in all selected cases. All the parturient had a good follow up of the pregnancy and gynecological controls were performed regularly. Statistical analysis was performed using Microsoft Excel 2007 software.

[1]University of Medicine and Pharmacy "Victor Babeş" Timişoara, România – Department of Neonatology, *PhD Student
[2]Clinical Emergency Hospital – Bega University Clinic, Timişoara, România
[3]Emergency Hospital for Children "Louis Turcanu" Timisoara
E-mail: dima_mirabela@yahoo.com, ionita_nicoll@yahoo.com, danielariacob@yahoo.com, aniko180798@yahoo.com, dani.chiru@yahoo.com, constantinilie@umft.ro

Results and Discussions

Confirming the diagnosis of neonatal sepsis includes the history of the neonate, clinical signs and symptoms (which can be early or late offset, so, in this study it was not taking them into consideration), laboratory investigations and imagistic investigations. The present work focuses on the history of mothers with PPRM over 16 hours, with or without infection, which indicates the need to look up for a possible neonatal infection. For laboratory investigations: complete blood count (CBC), C-reactive protein (CRP), blood and vernix cultures were taken.

Leukocytopenia, also known as leukopenia, illustrates a decrease in the number of white blood cells (leukocytes), which places the neonates at high risk of infection [6]. In the present study, 25 newborns from all 36 cases had abnormal leukocytes count, with an absolute frequency of 69.44% (Tab.1).

Table 1. Relative and absolute frequency of the leukocytes values.

Leukocytes (values)	Relative frequency	Absolute frequency (%)
Normal	11	30.56
Decreased	22	61.11
Increased	3	8.33
Abnormal leukocytes count	**25**	**69.44%**

Thrombocytopenia develops in up to 50% of the newborns admitted to NICU and who require intensive care [7]. Newborn thrombocytopenia discovered at birth result from transplacental passage of maternal platelet alloantibodies and autoantibodies nearly always in babies who are very affected, particularly associated with infection [8]. The data below reveals a noticeable thrombocytopenia in a majority of 27 cases (75%) from a total of 36 premature newborns included in the study (Tab. 2).

Table 2. Relative and absolute frequency of the thrombocytes values.

Thrombocytes (values)	Relative frequency	Absolute frequency (%)
Normal	4	11.11
Decreased	27	75.0
Increased	5	13.89

Almost all newborns experience a mild decrease in hemoglobin concentration after birth. Anemia of prematurity represents a form of anemia affecting preterm infants with decreased hemoglobin values. Associating the sepsis with the physiological destruction of the erythrocytes their number drops and the capacity of oxygen transport will be low because of the disturbances in the iron metabolism. The study presented in this paper discloses low levels of hemoglobin in 41.67% of all cases (Tab. 3). Along with leukocytopenia and thrombocytopenia, anemia is a sign of neonatal infection.

Table 3. Relative and absolute frequency of the hemoglobin values.

Hemoglobin (values)	Relative frequency	Absolute frequency (%)
Normal	11	30.56
Decreased	15	41.67
Increased	10	27.78

C-reactive protein (CRP) is a ring-shaped pentameric protein found in the blood plasma and it is used mainly as a marker of inflammation [9]. CRP is the first specific investigation used when neonatal infection is assumed. In this work, there were 11 neonates representing 31.25% with positive CRP from a total of 36 premature newborns included in the study.

The second and also the most specific and sensitive laboratory investigation to determine the neonatal sepsis is the blood culture. Various studies are carried out in developed countries show that Gram positive bacteria such as Group B, and coagulase negative staphylococci (CONS) are usual isolates [10]. Klebsiella species is noted to be the commonest organism along with *E. coli*, *Staph. aureus*,

Staph. epidermidis, Group B Streptococci, *Entrobacter* sp., *Enterococcus faecalis*, *Pseudomonas* sp., *Proteus* sp., are seen in developing countries [11]. In the present study, the most common Gram-negative pathogens have been Klebsiella pneumoniae equalize 25.00%. Other important pathogens have been found to be Pseudomonas aeruginosa and Candida albicans (12.50%) found in blood culture. The most common Gram-positive isolate has been found to be Staphylococcus aureus, representing 37.50% of the cases with positive culture. Flavimonas orzyhabitans, also known as Pseudomonas oryzihabitans, is a nonfermenting yellow-pigmented, gram-negative bacterium that can cause septicemia. Interestingly, this type of microorganism was isolated from the vernix caseosa and was associated with mother infection and PRM of more than 24 hours.

From all cases included in the study, 8 blood cultures came out positive. One of the 8 was also positive on the vernix culture.

As shown in table 4 from a total of 11 mothers with PPRM and infection, only 3 prematures newborns were diagnost with neonatal sepsis, while another 5 premature newborns with sepsis belongs to the group of mothers with PPRM and whithout infection. Consequently the study concluded that there is no direct corelation between the presence of infection at a mother with PPRM and the neonatal sepsis.

Table 4. Correlation between maternal and newborn's infection.

Infection		Neonatal	
Maternal		+	-
		8	28
+	11	3	8
		27.3%	72.7%
-	25	5	20
		20.0%	80.0%

The gestational age average of the newborns is 30.19 weeks, with a standard deviation of 2.9 weeks. Gestational age was established according to the first-trimester ultrasound. One of the most important causes of preterm birth might be the preterm premature rupture of the amniotic sac. This condition encourages high risk of the newborn sepsis. This is the reason why this study focused on PRM as a precursor of preterm birth and neonatal infection.

An inverse relationship exists between gestational age of the infant resulted by mothers with infections, which is significantly decreased, versus newborns resulted from mothers without infections (T-Test for independent variables, p=0.046, α=0.05) (Tab. 5). Although the PRM is the cause of preterm birth in all cases, not all parturient had an infection clinically manifested. The longer the period between PRM and delivery, the higher the risk for infection is.

According to birth weight classification (Tab. 6) the infants included into the study were classified as very low birth weight with an average of 1502.78 grams and with a standard deviation of 518.83 g.

Weights of the infants resulted by mothers with infections are significantly decreased versus newborns resulted from mothers without infections (T-Test for independent variables, p=0.029, α=0.05 (Tab. 7).

Table 5. Comparison between mother's infection and newborn gestational age.

Maternal infection	No. of cases	Gestational age average	Std. deviation	Average std. error
Yes	11	28.82	2.442	0.736
No	25	30.80	2.915	0.583

Table 6. Birth weight classification (WHO Statistical Information Systems (WHOSIS). 2011).

Premature babies may be classified by weight independent of gestational age:		
Low birth weight	LBW	<2,500 g
Very low birth weight	VLBW	<1,500 g
Extremely low birth weight	ELBW	<1,000 g
Infants may also be classified by weight for a specific gestational age:		
Small for gestational age	SGA	Weight <10th percentile
Appropriate for gestational age	AGA	Weight 10-90th percentile
Large for gestational age	LGA	Weight >90th percentile

Table 7. Comparison between mother's infection and infant's birth weight.

Maternal infection	No. of cases	Weight average	Std. deviation	Average std. error
yes	11	1222.73	512.798	154.614
no	25	1626.00	480.867	96.173

Hospitalization is significantly raised in the case of newborns with infection (T-Test for independent variables p=0.011, α=0.05) (Tab. 8). One of the most important consequences of prolonged hospitalization is the risk for nosocomial infections overlapped an existing disease. Another concern for a long time admission is poor developmental outcome and augmented medical costs.

Table 8. Hospitalization days of cases with/without infection.

Infection	No. of cases	Hospitalization days average	Std. deviation	Average std. error
yes	8	33.25	29.149	10.306
no	28	11.69	16.835	3.182

Conclusions

The unfavorably outcome of the newborns resulted by mothers with infection and PPRM as a consequence, is given by prematurity and low weight at birth. Maternal infection and PPRM determines a premature birth in all analyzed cases. Considering the laboratory investigations taken abowe, it was concluded that only 8 (22.22%) from a total of 36 prematures newborns were diagnosed with neonatal sepsis although 31.25% revealed a positive CRP, 41.66% anemia, 69.44% abnormal leucocyte count and 75% trombocytopenia. Although there is unquestionable clinical information that suggests connections among mother and neonatal infection status, this study could not establish a certain statistical correlation between parturients infection and positive cultures of the newborns. Further research in this field will analyze procalcitonin and interleukin 6 levels for the diagnosis of early-onset infection of the neonates. The data gathered so far, enhanced with new markers of infection will help us developing a new clinical protocol and to improve the therapeutic management of this cases.

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Correspondence to:
Mirabela Adina Dima
Clinical Emergency Hospital – Bega University Clinic
12 Victor Babes St.
Timișoara, România
E-mail: dima_mirabela@yahoo.com

MONITORING OF CEREBRAL OXYGENATION USING NEAR INFRARED SPECTROSCOPY IN PRETERM NEONATES ON ASSISTED VENTILATION

Nicoleta Ioniţă[1,2*], Mirabela Adina Dima [1,2*], Alina Elena Agoşton-Vas[2], Constantin Ilie[1,2]

Abstract

In the Neonatal Intensive Care Unit (NICU) we deal with one of the most vulnerable patients, the premature born infants. Nowadays despite medicine evolution the percent of prematurity is high; due to developing therapeutic modalities their life expectancy increases but one of the major concern for us is their outcome. In this study we monitored for 48 hours a group of 42 neonates admitted in the NICU. Inclusion criteria: gestational age < 32 weeks, cardio-pulmonary resuscitation in the delivery room, no congenital malformations, the need for Surfactant administration and mechanical ventilation. We monitored vital signs and besides cerebral and somatic oxygenation using Near Infrared Spectroscopy (NIRS). This technique is based on the optical properties of the tissue due to the natural chromophores, hemoglobin, deoxyhemoglobin and cytocrome oxidase with different characteristic absorption spectra in the visible and near-infrared wavelength range. We used an INVOS 5100 device. We compared the values recorded using NIRS with the values showed on the monitor of the pulsoxymeter, blood gases and blood pressure. Our main goal was to prevent hyper or hypoxia. Guiding our therapeutical decisions and modifying ventilator parameters with good response on the cerebral oxygenation, we concluded that NIRS is a very useful noninvasive and real time method of investigation. Meanwhile we had no significant changes in the peripheral oxygenation. Avoiding hyper and hypoxia in premature neonates can improve their neurodevelopmental outcome.

Key words: premature infants, cerebral oxygenation, near infrared spectroscopy, brain, mechanical ventilation, outcome.

Introduction

The most vulnerable category of patients in the Neonatal Intensive care Unit (NICU) are premature infants. In Europe the percentage of premature births is 8% and in Romania is over the European range. Premature infants mortality is high, almost 40%. They are extremely vulnerable to all the environmental and medical aspects. These infants and especially their brain is very immature [10]. Nowadays the main concern in the NICU is to improve their outcome, that's why the intensive care protocols are looking forward to establish less manipulating and invasive therapeutic management [5,6]. As we mentioned premature infants' brain is not ready for the extrauterine life and its adaptation and development shows up with sequels. Most of these patients need resuscitation in the delivery room; the first therapeutic gesture is to administer oxygen. It can save their life but it can also be harmful. In the NICU it is very important to know when, for how long and how much oxygen to administer. Pulsoximetry and blood gases are routinely used in order to avoid hypo and hyperoxia. But recently was concluded from literature and clinical cases that it is not conclusive if we want to appreciate brain oxygenation. A promising method to investigate that is Near Infrared Spectroscopy (NIRS); it was first described by Jobsis in 1977 [1]. First reported studies on cerebral oxygenation in newborn infants belong to Brazy, Darrell, Lewis, Mitnick and Jobsis from 1985 [2,3]. Reynolds and colleagues (Edwards et al., 1988; Reynolds et al., 1988; Wyatt, Cope, Delpy, Wray & Reynolds, 1986) monitored sick newborn infants and they reported the changes in regional hemoglobin concentrations, cerebral blood flow and cerebral blood volume. This technique is based on the optical properties of the brain tissue due to the natural chromophores, hemoglobin, deoxyhemoglobin and cytocrome oxidase with different characteristic absorption spectra in the visible and near-infrared wavelength range [3]. To convert the changes in absorption and attenuation in concentration of the chromophores it is used the Modified Lambert Law.

Objectives

Human brain is one of the most complex organs and not even nowadays enough investigated. Moreover newborns' brain is immature and more susceptible because of prematurity. Although the etiology of brain damage is multifactorial and even partly unknown, hypoxia, hyperoxia and hemodynamic instability during the first days of life seem to play an important role. Our purpose is to improve our understanding regarding premature infants' brain and to develop our abilities and therapies in order to offer them a better neurodevelopmental outcome. NIRS is a modern and noninvasive method of monitoring and we want to take advantage of that. We monitored a group of premature neonates using an INVOS device and we had a real time monitoring of the brain oxygenation so we could intervene earlier, compared to the interventions guided on the routinely used methods of investigation.

[1]University of Medicine and Pharmacy "Victor Babeş" Timişoara, România – Department of Obtetrics-Gynecology and Neonatology, *Ph.D. Student

[2]Clinical Emergency Hospital – Bega Universitary Clinic, Timişoara, România

E-mail: ionita_nicoll@yahoo.com, dima_mirabela@yahoo.com, alinaelena.agoston@yahoo.ro, constantinilie@umft.ro

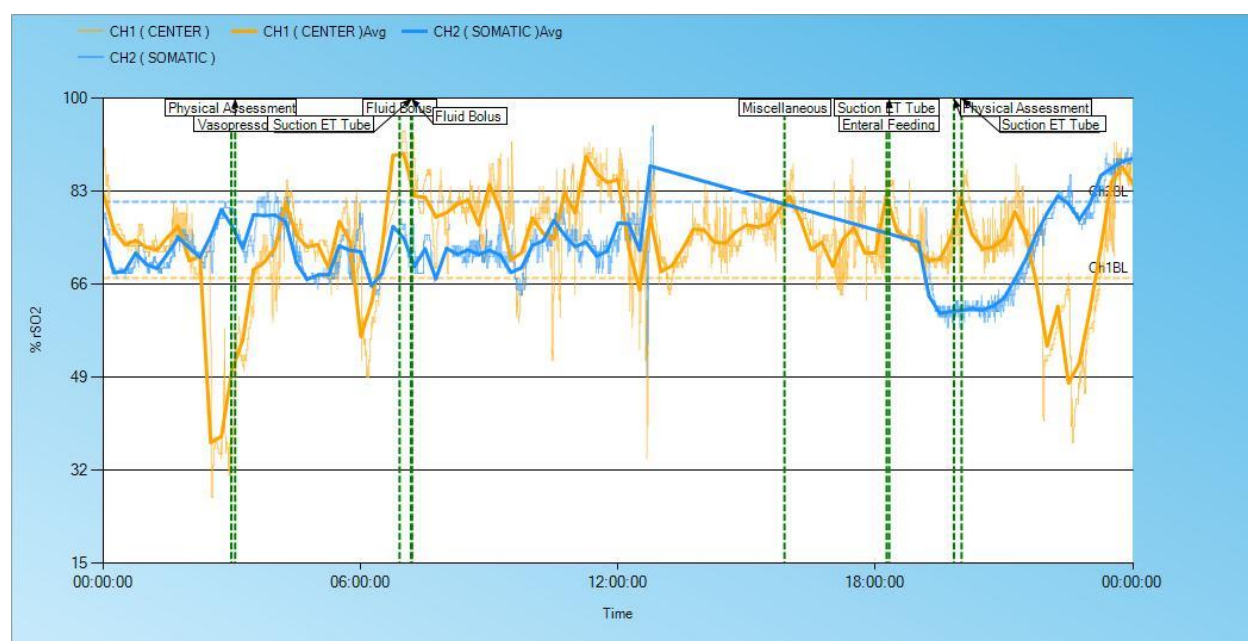**Fig. 1.** Cerebral oxygenation recorded in a premature neonate in the NICU

Fig. 2. Cerebral (yellow) and somatic (blue) oxygenation and the fluctuation at the performance of different gestures in the critical care of a premature neonate.

Fig. 3 NICU

Patients and method

We included in our study 180 neonates who were admitted in the NICU between January 2013 – January 2014. We chose for monitoring the neonates with gestational age < 32 weeks and birth weight < 1500 g. Our final study lot consists of 42 neonates; we will mention further the exclusion criteria. 80% of them born by cesarian section; all of them needed cardio-pulmonary resuscitation in the delivery room (VPPO2 +/- MCE); mean Apgar score 6/5. Maternal pathology: pregnancy induced hypertension (15%), premature membranes rupture > 24 hours (25%), untreated urinary tract infections (13%), genital infections most of them with Group B Streptococcus (18%), placenta praevia (18%) , normal inserted placenta detachment (11%). Over 30% of the neonates had maternal-fetal infections; from these cases 9% being no medical followed-up pregnancies. All the neonates included in the study lot were intubated and needed mechanical ventilation for at least 3 days; 26 (61%) of them needed curative Surfactant administration. After taken from the delivery room, each neonate was placed in the NICU in a preheated, humidified incubator. We placed on the right arm the pulsoximetry sensor. We used a Nellcore pulsoximeter. The umbilical vein and artery were catheterized, we intubated the infant and we administered Surfactant (Curosurf) 200 mg/kg as it is mentioned in the guides. Right after we connected the infant to the ventilator we placed on the right forehead [4] the INVOS sensors and we started to monitor the regional cerebral oxygenation (rScO2). Before that we cleaned properly the skin surface and we assured that there are no lesions, hemangioma or excessive hair under the sensor [7]. We used an INVOS 5100 (Somanetics) device, a memory stick was attached to the monitor and data were processed on a laptop IBM Think Pad T410 using SPSS Statistics 17.0. rScO2 was monitored from the first 3 hours of life and during 48 hours; we also monitored cerebral fractional tissue oxygen extraction (cFTOE). The reference limits for rScO2 were established between 55-85%. Blood pressure, heart rate, blood gases (arterial blood), peripheral oxygen saturation (pulsoximetry, SaO2) were also monitored [10] (Fig.3). Together with the SaO2, cFTOE can be calculated ((SaO2-rScO2)/SaO2). Somatic sensors are also available, we placed one on the renal area, but in this paper we will only dscuss the cerebral oxigenation aspects. We excluded from the study lot all the neonates with congenital cardiac malformations other than persistent ductus arteriosus (PDA), central nervous system or gastro-intestinal malformations; inconclusive recordings due to errors when placing the sensors (the skin was not well cleaned or for any other reason the sensor detached and environmental light penetrated), or we did not get parental written consent for the study. We also excluded 2 cases of neonates who died before 72 hours of life and 1 case of a neonate with gestational age < 28 weeks with large PDA who needed transfer for cardiac surgery. We selected from the INVOS menu the events which were to be performed during critical care of the neonates: miscellaneous, physical assessment, oral and endotracheal tube suction, repositioning, feeding, seizures, intravenous bolus and sedation. The nurses were trained in using the INVOS device and to select the event every time they noticed a change in the clinical status of the patient or every time they performed one of the gestures mentioned above.

Results

In the end we found conclusive for our study 24 of the recordings. We encountered problems in placing the sensors (they detached or the environmental light penetrated), not all the events were marked at the right time or the memory stick was not attached from the beginning. The 24 recordings are correct and clear. We find important to mention that all the neonates developed right after birth severe respiratory distress, metabolic and then respiratory

acidosis, hypotension, cardiac rhythm disorders (alternating tachycardia and bradycardia), hypoglycemia, apnea, seizures. Before intubation we had a peripheral oxygenation < 75% (SaO2) despite the administration of FiO2> 60%, tachycardia, hypotension, CO2 > 50%, pH< 7,25, NaHCO3⁻ = 12 (mean value), Becf = -14 (mean value). 30 minutes after intubation and after we connected the infant to a ventilator we repeated blood gases analyze and the parameters mentioned above were between ranges; SaO2 > 95%. We also started to administer medication [9]. Initial ventilatory parameters in the IPPV mode: PIP= 20 cmH2O, PEEP = 4 cmH2O, FR= 50 r/min, Ti/Te= 1 / 2, FiO2 = 80%. Our goal was to have a SaO2= 80 - 92%. Some of the premature infants (10) needed higher ventilator parameters: PIP= 22-24 cmH2O, PEEP= 5 cmH2O, FR= 60 r/min, FiO2= 90-100%. We had to maintain the neonates ventilated in the IPPV mode > 3 days; 9 of them were switched to SIMV mode after 24- 48 hours and extubated after 24-32 hours, having a favorable clinical evolution. When we started the monitoring of the rScO2, we had a mean baseline value < 65% (the preterm neonate was already on mechanical ventilation and the SaO2 > 95%). After 10-15 minutes of observation while the infant was also receiving medication and hemodynamic support the rScO2 values raised > 75 %. During hypotension episodes the necessary of cerebral O2 raised [2]; periods with a significant correlation between rScO2 (and cFTOE) and mean arterial blood pressure suggested more periods of lack of cerebral-vascular autoregulation; we noticed decreases of the rScO2 also during seizures, the SaO2 was also decreasing but the fluctuations were higher on the cerebral oxygenation and lasted longer. A heart rate > 200 bpm determined the sudden decrease of the rScO2 [1,2] from 75% to 30%, under the critical limit of 45%, while we had no significant changes on the SaO2 (95-98%). We decided to administer 10% calcium gluconate intravenous slow and we noticed that the heart rate was decreasing < 170 bpm simultaneously with the gradually increasing of the rScO2. This was a prove that we are having a real time monitoring of the cerebral oxygenation. Infants with PDA [8] had lower rScO2 and higher cFTOE values, compared with the neonates without

PDA. These neonates were periodically investigated by a cardiologyst who performed cardiac ultrasound; he did not decide in any of these cases to start the administration af Indomethacin or Ibuprofen [8]. We also confronted good peripheral oxygenation, but a persisting low rScO2 (under the baseline value of 65%); we lower the ventilator parameters and we noticed no significant changes in the SaO2 values (< 5%), while the rScO2 was increasing immediately. In 9 cases we had a larger variance of the rScO2 (persisting low values) despite a SaO2 > 92%, low ventilator parameters, normal heart rate, blood pressure and blood gases values. In evolution we noticed that these premature neonates developed IIIrd degree intraventricular hemorrhage and had a severe form of hypoxic-ischemic brain injury.

Conclusions

INVOS is a very reliable method of investigation. The sensors are easy to be applied and also the menu is at reach for all. We had no accidents such as skin burn after applying the sensors. A very important aspect for our neonatal critical care is that NIRS is a noninvasive and real time monitoring method which can be used as a trend. The recordings are not influenced by environmental noise, movements (we could manipulate the neonate while monitoring the rScO2, we changed the endotracheal tube etc), temperature and the sensor does not have to detect a pulse. Guiding on the values from the INVOS monitor we could intervene on time , before having laboratory results despite good values of the SaO2 or apparently stationary clinical status. We concluded that pulsoximetry which is routinely used in the NICU does not have sensitivity and organ specificity. As we previously mentioned premature neonates brain is very immature and too much oxygen or an aggressive mechanical ventilation (high ventilator parameters) can be harmful so using the INVOS device we could intervene on time, reducing the FiO2 or we improved therapeutic procedures. We find important to routinely use NIRS in the premature neonates' critical care in order to improve their neurological outcome.

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Correspondance to:

Nicoleta Ioniță

Clinical Emergency Hospital – Bega University Clinic

12 Victor Babes St

Timişoara, România

E-mail: ionita_nicoll@yahoo.com

25 YEARS EXPERIENCE IN PULMONARY HYDATID CYSTS TREATMENT

Ionescu S[1], Andrei B[1], Mocanu M[1], Pavel D[1], Licsandru E[1], Bratu N[1], Coman M[2], Stanescu D[2], Gurita[3], Tabacaru R[3]

Abstract

Pulmonary hydatid cyst is a common pathology in children coming from the rural areas. In this paper we evaluate the results of the surgical treatment over the past 25 years.It is a retrospective study about the management children with pulmonary hydatid cysts treated between 1988 and 2013 in our institution. Of 432 children with pulmonary hydatid cysts, 85% had unilaterally lesions while in 15% of cases both lungs were affected; the right lung was involved in 54% of the cases; in 74% of the cases there was a single cyst and in 26% there were multiple hydatid cysts. In 59 cases there were associated extrapulmonary hydatid cysts. The treatment consisted of cystotomy with wedge resection, membrane removal, drainage of the remaining cavity and of the pleural space in 87,5%, ideal cystectomy in 11,5%. Toracophrenolaparotomy was performed for associated liver and right pulmonary cysts in 1% of the cases. There were postoperative complications like: wound infection, prolonged bleeding and one death occurred in a 2 years old boy with multiple bilateral cysts. The drainage of the remaining cavity was prolonged.(in 8 cases. There was no recurrence of the hydatid disease. Pulmonary hidatid cyst is the most frequent surgical pulmonary disease in children in our country. All hidatid cysts were incidentally discovered. Our approach was lateral thoracotomy without rib resection. In bilateral lung localizations, the second intervention was performed 3 to 6 months after the first. The treatment of the pulmonary cysts had priority on the extrapulmonary localisations.

Key words: pulmonary, hydatid cyst, child, surgery, cystostomy, cystectomy

Introduction

Human echinococcosis is a zoonotic infection caused by the tapeworm of the genus Echinococcus. There are 4 known species of Echinococcus of witch 3 are of medical importance in humans. Echinococcus granulosus, causing cystic echinococcosis is the most frequent, Echinococcus multilocularis, causing alveolar echinococcosis is rare but most virulent and Echinococcus vogeli, witch is the most rare.

Along with the Mediterranean countries, south Africa and Middle east, (1) Romania is an endemic country for this parasite, with an incidence of 1¬-220 cases per 100000 inhabitants. Epidemiologic studies of cystic echinococcosis in Romania emphasize the need for improved preventive measures (2).

In the paediatric population, the hydatid cyst is more frequent in children coming from rural areas, due to a closer contact with dogs and/or sheep, goats or swine witch are the definitive and intermediate hosts respectively. Infestation can occur when exposed to water and food contaminated with faeces of a infected definitive host (1). In the paediatric age group pulmonary hydatid cysts need to be differentiated from other thoracic masses like congenital malformations, tumors, tuberculosis. There are studies that state that in the paediatric population pulmonary hydatid cysts are more frequent than the hepatic ones are (3).

Hydatid cysts may remain asymptomatic for a long time; the parasitic load, cyst site and size determine the degree of symptoms. Theoretically, echinococcosis can involve any organ. The liver is the most common organ involved, followed by the lungs. These 2 organs account for 90% of cases of echinococcosis.(4) As for the pulmonary cysts the symptoms can vary from total asymptomatic to irritative cough, haemoptysis, pain, coughing up of hydatid fluid, dyspnoea, spontaneous pneumothorax, allergic reaction like urticaria and erythema or purulent sputum when an infected cyst opens in a bronchus.

The morbidity of pulmonary cysts comes from compression of mediastinal structures; rupture into the pleural cavity or heart or into a great vessel and asphyxia, haemorrhage or anaphylaxis when intrabronchial rupture occurs.

Surgery is the primary treatment method of pulmonary unilocular hydatid cysts. Newer methods like puncture, aspiration, injection and reaspiration (PAIR) are still under evaluation (5;6). Chemotherapy is used as an adjuvant to surgery, to prevent relapse of the disease, in case of inoperable cysts, in multiple locations or in peritoneal cysts. There are two benzimidazloles available but in our country, we are more familiar with Albendazole, given orally at a dose of $10 – 15$ mg/kg/day, for a period of $3 – 6$ months.

[1] Department of Pediatric Surgery, "Maria Sklodowska Curie" Emergency Children Hospital
[2] Department of Radiology "Maria Sklodowska Curie" Emergency Children Hospital
[3] Intensive care unit "Maria Sklodowska Curie" Emergency Children Hospital
E-mail: nsionescu@yahoo.com, bogdansimona2003@yahoo.com, mmocanu@yahoo.com, danielapavel85@yahoo.com, elena_licsandru@yahoo.com, nina.bratu@yahoo.com, comar62ro@yahoo.com, ro.gurita@yahoo.com, radu_tabacaru@yahoo.com

Purpose
The aim of this paper is to present the results of various surgical treatment methods of pulmonary hydatid cysts in children that were used in the past 25 years in our clinic

Materials and Methods
For that matter we reviewed, in a retrospective study, the epidemiology, cyst's characteristics, diagnosis, treatment and complications in children with pulmonary

hydatid cysts treated in the Department of Pediatric Surgery of 'Maria Sklodowska Curie' Emergency Children's Hospital, Bucharest, between 1988 and 2013.

We also noticed that in the group of children with surgical thoracic pathology treated in our clinic in the mentioned period, the majority consisted of hydatid cysts, as you can see in figure 1.

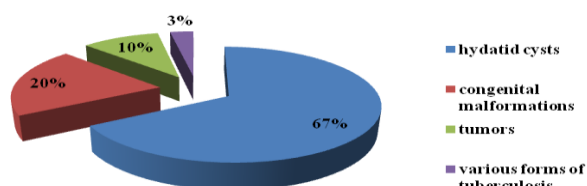**Fig. 2**.Surgical thoracic pathology in children treated in our clinic between 1988- 2013

Fig. 1. Patient distribution by location

Results
Our study comprises 432 children with pulmonary hydatid cysts with ages between 2 and 18 years. The majority of them came from a rural environment, 87% and only 13 % lived in a city area, but parents admitted to have around the house seep and/ or dogs (Fig. 2). This is consisted with literature data.

The hydatid cysts were incidentally discovered on pulmonary X-ray examination for pulmonary tract infection, cronic cough and thoracic deformation. We performed complementary investigations like blood count, abdominal ultrasound and when more details were needed , CT scan of the abdomen, thorax and cranium, IV urogram, ultrasound examination of soft tissues.
There was no significant sex difference, as both sexes were equally represented in our group.

In regard to cyst localization, we found only 15 % of patients with bilateral cysts, while the rest of them had one affected lung only. As it is mentioned in other studies, there are almost equal numbers of patients with right and left lung cysts: 54% on the right, 46 % on the left. A single cyst was identified in 74% of the patiens, while 26% had multiple.

There were 59 patients in witch extra pulmonary cysts were associated. Most of them were hepatic, 22 (37.3%) in the left hepatic lobe and 20 (33.9%) in the right hepatic lobe, but there were also peritoneal cysts (5- 8.5%), splenic cysts (4 − 6.7%), renal (4 − 6.77%), of the broad ligament 2 − 3.38%, one (1.7%) retroperitoneal and one of the quadriceps muscle.

The treatment consisted mainly of cystotomy, inactivation of the cyst with scolicidal agents - 20% hypertonic saline solutions or 95% ethanol, with wedge resection, membrane removal, lavage of the remaining cavity with physiologic serum and betadine, and after

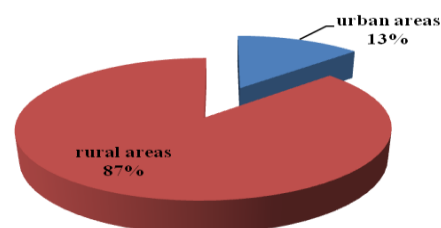identifying and suturing any visible bronchial fistulas, drainage of the remaining cavity and of the pleural space. This procedure was performed on the majority of patients, 87,5% respectively. We were able to perform ideal cystectomy in 11,5% of them. In both situations, the thorax was opened through a lateral thoracotomy without rib resection.

For the bilateral cysts we performed two different operations at 3-6 months interval, while in patients with pulmonary and extrapulmonary cysts we first operated on the lung and after complete recovery the extrapulmonary cyst was excized.
In one patient with right lung hidatid cyst located in the inferior lobe associated with hepatic cyst of the rihgt lobe, we performed thoracophrenolaparotomy and treated both cyst in the same session.
There was no need for sternotomy or lung resection in any of our patients.

There were several complications. Wound infection appeared in 14 patients witch required daily nursing but healed uneventfully in 10- 14 days, postponing with several days the discharge. Prolonged drainage was registered in 8 cases. While we usually keep the tubes in place for 2-4 weeks, these particular patients had prolonged drainage through the remaining cavity tube and could not be removed until week 8 post operatory. There was one case of post operatory bleeding that we had to explore in the operating room. On thoracoscopy there was no evident source of bleeding and the bleeding stoped spontaneusly on day 3 post operatory after lavage and drainage that continued for another 2 days.

We registered one death, in a 2 year old boy who had multiple bilateral pulmonary hydatid cysts, 7 on the right and 4 on the left. No autopsy was performed.

On long term follow-up, there was no relapse of the disease and on 4 to 6 months pulmonary reexpansion was complete in all of our patients, with no residual cavity visible on chest X-ray.

Discussions and/or Conclusions

Pulmonary hydatid cyst is the most frequent surgical pathology in children and most of the time the diagnosis in incidental, on thoracic X-ray examination, demanded for respiratory tract infection, cough, etc., as clinical signs are non specific. Of some value in the diagnosis process of the cysts and of its complications, are the total blood count, IgM antibodies abdominal ultrasound, CT scan.

The treatment is primarily surgical and consists of evacuation of the cyst and of it's membrane after inactivation with scolicid solutions. The approach by lateral thoracotomy, without rib resection, is suitable in the majority of cases, with rapid healing.

For patients with pulmonary bilateral cysts we choose a staged procedure, on 3 to 6 months interval. If there was a pulmonary cyst associated with an extrapulmonary one, the first treated was the pulmonary cyst. None of the patients required lobectomy or pneumectomy and the remaining cavity resorbed in a period of 4 to 6 months.

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Correspondance to:
Sebastian Ionescu
City: Bucarest, Country: Romania
Postal code: 041451
Institution: MS Curie Children Hospital
Phone, Fax,0040 21 4601040, 0040 21 4601260
E-mail: nsionescu@yahoo.com

ABDOMINOSCROTAL HYDROCELE, AN UNDERESTIMATED ENTITY

Radu-Iulian Spataru[1], Dan-Alexandru Iozsa[1], Cristina-Ioana Nisipasu[2]

Abstract
    Abdominoscrotal hydrocele (ASH) is a very unusual variety of hydrocele in childhood. The incompletely elucidated etiology and its possible serious complications make ASH a moreover debated topic of pediatric urology. Although, underestimated intraoperative difficulties or incomplete preoperative evaluation constitute ASH as a complex entity and misjudging as a simple hydrocele should be avoided.
Key words: Abdominoscrotal hydrocele

Introduction
Abdominoscrotal hydrocele (ASH) is an hourglass-shaped hydrocele consisting in two pouches (an inguinoscrotal component and an abdominal part) who communicate through the internal inguinal ring [1]. This type of hydrocele is very uncommon in adults and even more unusual in the pediatric population. It's reported incidence is about 0.17-3.1% of all hydroceles [2,3]. Etiology and pathogenesis of ASH is not clear. Association with other severe genital or urinary abnormalities makes ASH a challenge for the surgeon. We report our experience with this particular type of hydrocele (3 cases) trying to point out particular elements in their management.

Case #1
    A 14 month old boy referred to our department for a bilateral impressive scrotal tense enlargement, noted since birth. The ultrasonography revealed bilateral intra-abdominal extension as a cystic mass above the both internal inguinal rings. The patient was operated on the both sides using inguinal approach. We noted the important compression of both testes and their lax, fusiform aspect. We also observed the congestion of the tunica vaginalis, the dissection being very difficult in matter of hemostasis. The patient suffered an immediate postoperative acute haemorrhagic anemia (Hb: 6 g/dL). Intravenous iron was supplemented and the patient was reoperated in order to perform hemostasis. Bilateral drainage tubes were inserted and maintained for 5 days. Persistent bilateral inguinal swelling was noted after the surgery.

Case #2
    A 10 month old infant presented to our clinic for an important congenital right scrotal tense swelling. The US revealed the cystic intra-abdominal extension of the hydrocele. The patient was operated through an inguinal incision, after an initial evacuation of the hydrocele fluid. The intraabdominal component of the tunica vaginalis could be dissected and removed together with its inguinoscrotal part. We noted that the testes were compressed and stretched, having a dysmorphic aspect. Postoperative, an important inguinoscrotal hematoma has developed an haemorrhagic anemia was confirmed by the lab tests (Hb: 8,3 g/dL). Finally, the evolution was favourable with conservative management.

Case #3
    A 8 month old infant was admitted in our clinic for an impressive right scrotal tense swelling (Fig. 1). On anamnesis, we found that the swelling was known since birth and it increased progressively in size. The US suggested concomitant presence of a cystic image above the right internal inguinal ring. The MRI confirmed the diagnosis of ASH, showing the hourglass-shaped hydrocele (Fig. 2). Also, the right testicle couldn't be detected on the MRI.
    We performed the hydrocelectomy via a inferior inguinal crease incision after the transscrotal punction and evacuation of the serous clear fluid (220 ml). Intraoperative, no PPV was found. We managed the blunt dissection of the hydrocele, extracting its intraabdominal pouch through the widened transected internal inguinal ring (Fig. 3). The testis was compressed and elongated, having a fusiform aspect (Fig. 4). We removed the thickend tunica vaginalis as much as possible preserving the spermatic cord elements. Right orchidopexy was also performed. A inguinoscrotal drainage tube was inserted and maintained for 3 days. Postoperative, despite the careful hemostasis a significant inguinoscrotal swelling was noted for 14 days. Finally, the evolution was satisfying.

[1]"Marie Sklodowska Curie" Emergency Clinical Hospital for Children, Bucharest
[2]INMAS, Bucharest
E-mail: radu_spataru@yahoo.com, dan.iozsa@yahoo.com, cris.nisipasu@gmail.com

Fig. 1 Preoperatory aspect of the ASH. The intraabdominal component is marked after bimanual palpation.

Fig. 2 MRI image of the hourglass-shaped right hydrocele.

Fig. 3 Intraoperative image of the ASH showing the two exteriorized components of the tunica vaginalas: intraabdominal and inguinoscrotal.

Fig. 4 Dysmorphic right testis with the characteristic elongated aspect.

Discussions

Depending on the obliteration pattern of the processus vaginalis, various types of hydroceles are described: congenital or intermittent hydrocele, scrotal hydrocele, spermatic cord hydrocele, inguinal-scrotal hydrocele or abdomino-scrotal hydrocele. ASH is considered a large scrotal hydrocele that protrudes through the deep inguinal ring into the abdominal cavity,

determining the hourglass or dumbbell shape. [4] The intra-abdominal component usually lays properitoneal, but retroperitoneal position of the intra-abdominal element has been reported [5,6].

Etiology of ASH is stated in different theories. A high obliteration of the processus vaginalis, near the internal inguinal ring associated with fluid accumulation in the tunica vaginalis ascending through the inexpansible musculofascial coverings of the inguinal canal and consecutive protrusion in the abdominal cavity is the most agreed theory. Other assumptions include the existence of a valve-like mechanism in the patent processus vaginalis at the level of internal inguinal ring, a peritoneal diverticulum in the deep inguinal area, or distal expansion of an abdominal hydrocele in the inguinoscrotal space. [6] Existence of a patent processus vaginalis (PPV) should be evident in most of the cases reported, but only a few authors report the existence of this communication, so mentioning of PPV in ASH description is considered an element of misdiagnosis. Confusion between PPV and the slim part of the ASH which passes the internal inguinal ring is usually made [6, 10].

Careful examination can bring important clues over the nature of hydrocele. Bimanual (scrotal and abdominal) palpation of a large, tense hydrocele identifying one component's enlargement when compressing the other is a maneuver which can presume the existence of an ASH. Also, manual reduction of the hydrocele can result in a temporary diminishing of its size [9]. ASH's most obvious differential diagnosis is inguinal hernia [6]. Diagnosis can be easily confirmed by ultrasound examination, but use of CT or MRI for supplementary evaluation is reported and indicated in the presence of large scrotal hydrocele [3, 6, 9]. Estevao-Costa, et al. reported acute haemorrhagic ASH [7], Velasco AL, et al. mentioned a paratesticular malignant mesothelioma of the tunica vaginalis [8], or Gentile DP, et al. mentioned ASH as a cause of ureterohidronephrosis in infancy [5].

Testicular dysmorphism (TD), most probably because of the increased hydrocele pressure, has been reported in ASH cases. Vaos G, et al. study draws attention over cases of infantile ASH with normal testes, so it's difficult to enounce TD a congenital gonad abnormality or a secondary effect of ASH in pediatric population. [11] Secondary ureterohydronephrosis, lymphedema, intralesional hemorrhage, infection, cryptorchidism, crossed testicular ectopia, or paratesticular malignant mesothelioma are associations of ASH summarized by Cuervo JL, et al. in its study. [6]

Periodic US evaluation of a large scrotal hydrocele is indicated in order to prevent apparition of ASH. Surgical treatment is the treatment of choice as soon as ASH is confirmed in order to prevent compression over local abdominal or inguinoscrotal structures and its presumed consequences [9]. In 2006, Upadhyay V, et al. report a case of spontaneous resolution of ASH [11]. In the same year, De Renzo CC et Barone JG underline the natural remission of the intraabdominal pouch in a case of infantile ASH [13].

Although paramedian laparotomies or scrotal approaches in surgical treatment of ASH have been reported, simple inguinal hydrocelectomy is considered the best choice [6, 9, 14]. Laparoscopic assistance is indicated to be reserved in cases with associated abnormalities like contralateral nonpalpable testes or recurrent hernia [3].

Surgery in ASH doesn't assume a simple procedure, summarizes Cuervo JL, et al. Large, tense, protruding, thickened wall hydrocele makes difficult the separation of surrounding structures (like spermatic cord elements). Transscrotal aspiration of the fluid before the hydrocele dissection starts makes the surgery easier. Transection of the vas deferens or difficult hemostasis with postoperative hematoma has been reported. As ASH is not a communicating hydrocele, confusion between PPV and intraabdominal extension can be made. Also, insufficient excision of the pathogenic tunica vaginalis can result into recurrent hydrocele [6, 9].

Conclusions

ASH remains an unclear topic in pediatric urology. We assume that a large scrotal hydrocele associated with fluid accumulation and consequent upward herniation through the internal inguinal ring is the etiology of ASH, on account of we found no PPV in our cases.

The MRI brings valuable information over the extension of the hydrocele and its effect over the underlying structures. Intraoeperative testis evaluation should always be performed since several cases of dysplasia have been reported. The thickened tunica vaginalis and its inflammatory aspect sometimes can result into important bleeding which can lead to large hematomas or even severe anemia. We recommend accurate hemostasis preferable using bipolar cautery and postoperative inguinoscrotal drainage. On the other hand, the hydrocele by its size can change the anatomy of the spermatic cord, scattering and compressing its elements, so their careful individualization and dissection can avoid serious complications, like transection of vas deferens or devitalisation of the testis. Our limited experience with bilateral ASH indicates that staged surgery may be safer.

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Correspondence to:

Dan-Alexandru Iozsa
Maria Sklodowska Curie" Children Hospital
Bd. C-tin Brancoveanu nr. 20 Sector 4 Bucuresti
Mobile phone: 0040723322106
E-mail: dan.iozsa@yahoo.com

TWIN TO TWIN TRANSFUSION SYNDROME
– CLINICAL CASE –

Daniela Iacob[1], Marius Craina[1], Cristina Dragomir[2], Cătălin Dumitru[1], Claudia Cojocaru[2], Mirabela Dima[1], Radu E Iacob[1]

Abstract
        The twin to twin transfusion syndrome is a rare condition caused by intrauterine blood transfusion, from one fetus (donor) to another child (acceptor), through placental vascular anastomoses.
        The clinical case described is a rare perinatal pathology suspected in a woman with a multiple pregnancy monochorionic the fundal height increases rapidly (within 2-3 weeks), due to increased amount of amniotic fluid.
        Twin-to-twin transfusion syndrome is a rare perinatal affecting monozygotic twins (twins,, true ") that come from a twin pregnancy monochorionic; twins present has only one survivor, a male child, eutrophic, gestational age of 37 weeks. The twin II (female) is dead in utero and upon extraction by cesarean advanced signs of maceration.

The difference in weight extraction caesarean design of products is high (W1 = 3230 g, W2 = 1100g).

Key words: twin to twin transfusion syndrome, monochorionic, eutrophic

Introduction
        The twin to twin transfusion syndrome, also called the feto-fetal transfusion syndrome is a rare condition caused by intrauterine blood transfusion, from one fetus (donor) to another child (acceptor), through placental vascular anastomoses (figure 1).
        This syndrome is, along with the birth of conjoined twins, one of two twin pregnancy powerful complications; appears monochorionic monozygotic twin pregnancies (twins „true"), the communication between placental blood vessels common placental vascular anastomoses exist.
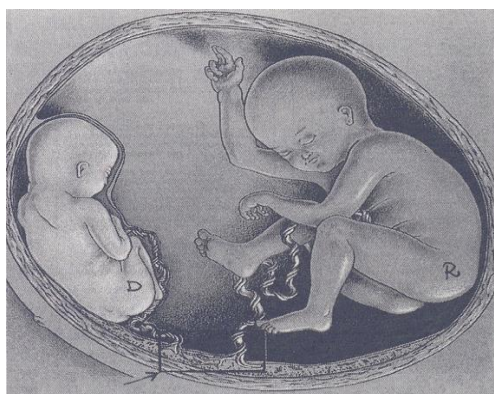

Figure 1. Twin-to-twin transfusion syndrome (Copy from tttsfoundation.org).

Purpose
        The clinical case described is a rare perinatal pathology suspected in a woman with a multiple pregnancy monochorionic the fundal height increases rapidly (within 2-3 weeks), due to increased amount of amniotic fluid.

Material and method
        ML, aged 42 years, a woman in the town of S., Timiş county, is hospitalized urgently on University Clinic of Obstetrics and Gynecology "Bega", being immediately sent emergency a Specialty Outpatient Obstetrics and Gynecology.
        The diagnosis on admission: Gesta V Para V, twin pregnancy, 37 weeks.
        A living child, the second child stopped evolving (antepartum stillbirth).
        The first fetus in breech (live), the second in alignment cross (dead).

[1]University of Medicine and Pharmacy "Victor Babeş" Timişoara, România
[2]Emergency Clinical County Hospital Timişoara - „Bega" Maternity, Department of Neonatology and Premature
E-mail: danielariacob@yahoo.com, mariuscraina@hotmail.com, dr.cristinadragomir@yahoo.com, florinatim@yahoo.com, dima_mirabela@yahoo.com, radueiacob@yahoo.com

Outdoor eutocic. The pregnant with high obstetrical risk by:

1.The twin to twin transfusion-transfusion syndrome with an antepartum stillbirth;

2. The great multiparous.

From history remember: household lives in rural areas, do not drink alcohol, coffee, tobacco; submit exercise, working in agriculture.

From history and obstetric: patient has 4 birth naturally (1 girl and 3 boys: 1993, 1997, 2003, 2009), no abortion, no other clinical or surgical pathology.

Load current was tracked in the Ambulatory Specialty Obstetrics and Gynecology and the doctor.

The task was taken out at 8 weeks of gestation, fetal movements appear first 14 weeks of gestation, and BCF (heartbeat) were rhythmic, regular.

Conducted analysis of the Resin load current: IO Rh + blood group, normotensive intrapartum added 15 Kg weight without bleeding during pregnancy, vitamin therapy and prophylaxis performed anemia and rickets Deficiency.

The remaining laboratory parameters within normal limits.

Note the appearance gemelarității: monochorionic diamniotic task.

The pregnancy has not conducted regular checks of pregnancy; last control before hospital admission was 30 weeks gestational age. At that time, clinical and obstetrical ultrasound pregnancy was evolving

2

with both live fetuses, the normal amount of amniotic fluid, fetal active movements present ultrasound both fetuses weighing 1160 ± 350 g, 1250 ± 365 g.

It presents the gestational age of 37 weeks at a routine ultrasound when laying off the development of one of the fetuses.

Note, that the patient could not relate subjective perception of loss of fetal active movements of one of the fetuses.

After consultation (24/03/2014), the patient is sent to the emergency and is admitted to Maternity "Bega" of Timisoara.

Laboratory investigations were within normal parameters, normotensive patients with metrorrhagia absent, with the onset of labor.

The route fetal cardiotocography live normal parameters with an index CTG note 9 (nine) (figure 2), fetus stopped Indices CTG note 0 (zero).
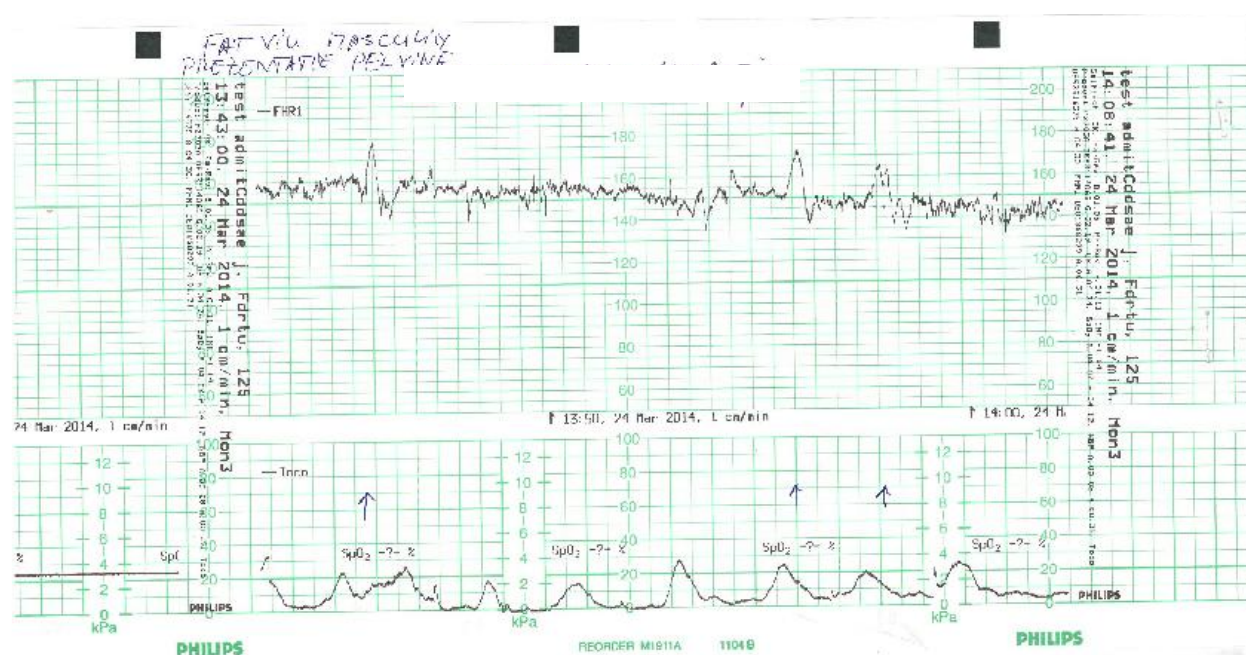

Figure 2. CTG child alive.

The obstetric ultrasound showed the following data:

The prince living in alignment one longitudinal breech decomplete how buttocks, back right fetal, amniotic fluid in normal amounts (BPD = 89.1 mm corresponding to 37 weeks. + 2 days, LF = 68.9 mm corresponding to 37 weeks. 6 days, AC = 154 mm corresponding to 36 weeks. + 5 days = 3122 ± 377 g estimates g;

The prince 2 stopped evolving (died antepartum) in transverse alignment with the left flank maternal fetal pelvis, atonic, absent fetal movements ultrasound, ultrasound

absent fetal breathing movements (Manning Score = 0), the minimum amount of amniotic fluid, blood flow absent vessels of the umbilical cord with a weight estimated at 1250 ± 355 g = g.

Deciding termination of pregnancy by cesarean protective purpose for living fetus and to avoid the possibility of obstetrical trauma in breech birth. Born lead in the same day (03/24/2014), the first live fetus in breech male, 3230 g, IA = 9:01 of the second fetus female, 1100 g, IA = 0 extracted from transverse alignment. Note the single

placenta - twin pregnancy diamniotic monochorionic - not identified retroplacentar hematoma or placenta praevia or accretion / wrinkle (figure 3).

Histopathology reveals the placenta: placental disc 20/15 / 3.5 cm, showing the two bags separated by September 1 amniotic common umbilical cords and two lengths of 11, 5 cm, 16.5 cm, respectively, both have three lumens vascular (figure 4).

Umbilical cords and fetal membranes are no pathological changes; placental fragments with mature villi with edema and extravasated hematic intervilozitar space; present seals of fibrinoid alteration and dystrophic microcalcifications.

Figure 3. Single placenta.

Figure 4. Unique placenta (one of the umbilical cords).

Dead antepartum fetal necropsy revealed: stillborn female in advanced maceration with skin sfacelate who blistered the large flaps (figure 5); G = 1100 g, L = 47 cm, PC = 27 cm, PT = 26 cm.

No visible defects in the external examination. The internal organs are in an advanced stage of maceration and autolysis.

The dimensions of the internal organs are: heart = 3/3 / 1.5 cm; liver = 6/3 / 1.5 cm; Spleen = 2/2 / 0.5 cm; kidney and adrenal = 4 / 1.5 / 1.2 cm; thymus = 2/2 / 0.3 cm; semiliquid consistency brain.

Figure 5. Female twin died in utero (twin II, donor).

At birth, the first newborn male presented good general condition, acrocyanosis, APGAR = 9-1 minutes for 10-5 minutes, breathing spontaneously (figure 6); desobstruction upper respiratory tract; cardiopulmonary stetacustic: heart sounds clear, well beaten, HR = 120 b / m, with superimposed cardiac murmurs, respiratory ampliations symmetric, normal vesicular murmur present bilaterally, FR = 50 b / m; the cord thick, white, shiny, pearly.

The normal tone and the reactivity are present spontaneously. W = 3230g, L = 50cm, HC = TC = 35cm and 34cm. Twin II: fetal death in utero (in the womb death is defined as a task „stop development after 12 weeks of amenorrhea"), antepartum late death, around week 35 of gestation.

The duration of fetal retention range is 2 weeks.

The evolution of neonatology department: During hospitalization, the infant (survivor) had moderately icteric skin discretion of pale background. We have carried out

laboratory. Phototherapy has been carried out. The evolution was favorable (figure 7).

Figure 6. Alive newborn (recipient twin).

Figure7. Newborn- fourth day of life.

Laboratory investigations:

Laboratory tests: blood count at 24 h of life indicates the presence of neonatal anemia (Hb = 11.3 g / l, Ht = 33.1%), Rh positive blood group OI; Astrup: normal; Biochemistry: hyperbilirubinemia (T B= 5.4 mg / l, DB = 0.7 mg / l), mild hypoalbuminemia, hypoproteinemia slight increased LDH. Blood culture is sterile; vernix culture: sterile

Ultrasound transfontanelar: mild hypoxic ischemic encephalopathy.

Echocardiography: Foramen ovale.

Exam objective: good general condition, skin moderate jaundice, balanced cardio-respiratory, oral cavity of normal appearance, abdomen elastic, soft, allow palpation, normal stool. Liver palpable 2 cm below the

costal margin. Spleen in physiological limits. Archaic reflexes normally present bilaterally symmetrical. Pulse oximetry: SO2 = 98-99% (under O2 free), HR = 137-140 b / min, AP = 59/33 mmHg, MAP = 41mmHg, Wa = 3200 g.

Conclusions

1. Twin-to-twin transfusion syndrome is a rare perinatal affecting monozygotic twins (twins,, true ") that come from a twin pregnancy monochorionic;
2. Twins present has only one survivor, a male child, eutrophic, gestational age of 37 weeks;
3. The twin II (female) is dead in utero and upon extraction by cesarean advanced signs of maceration;
4. The difference in weight extraction caesarean design of products is high (W = 3230 g, W = 1100g).

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Correspondence to:
Daniela Iacob
Transilvania Street 13, Sc. C, Ap. 7
Timisoara, Romania
E-mail: danielariacob@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.