

A study of the pulmonary complications of preterm infants after prenatal corticosteroids prophylaxis in a major Bulgarian hospital

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Abstract: An increasingly common problem in obstetrics and neonatology is premature birth. This problem is the cause of many health complications in premature neonates and is leading to neonatal mortality. These complications affect the whole body of premature babies, the respiratory system has the largest percentage due to lack of the period for intrauterine maturation of the lung. The purpose of this study is to analyze data on complications, and especially pulmonary complications that develop preterm infants, and to analyze the impact of premature corticosteroid prophylaxis.

A retrospective case-control study was carried out at the Clinic of Obstetrics and Gynecology, University Hospital "St. Georgi" Plovdiv, Bulgaria for the period 2015-2016 year. 167 preterm infants have been studied. They were divided into two main groups: a working group of 89 preterm infants with prenatal corticosteroid prophylaxis and a control group of 78 preterm infants without prenatal prophylaxis. Data on clinical outcomes, health status, background complications of prenatal corticosteroid prophylaxis have been analyzed. The summary, however, of the results that is: the 3.6% difference has been found between newborn children with RDS and those with all other disabilities; this shows that in preterm infants the priority is to damage the respiratory system. Over 60% of the prematurity develop Respiratory distress syndrome. The presence of respiratory complications is due to the earlier gestational week of birth and the older age of the mother and is somewhat limited by the prenatal administration of corticosteroids.

Key words: prenatal corticosteroid prophylaxis, preterm birth, pulmonary complications

Introduction

Premature birth is a leading medical, social and economic problem. It is the most common cause of neonatal mortality in developed countries.¹⁻⁴ Its consequences are multiple complications leading to a high neonatal mortality in the national and global world. Birth before the term does not provide the baby with enough time to develop. The earlier before the term a child is born, the more serious health problems can be caused by early or late complications.⁵ Among the most common complications in the prematurity are severe

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ventilation deficiency syndrome, apnea, respiratory distress, broncho-pulmonary dysplasia, pulmonary edema, cerebral haemorrhage, renal damage, heart damage, necrotizing enterocolitis, infections and many others.

The Bulgarian statistics produced data that 10-12% (2015) of all pregnancies terminated with a preterm birth. In spite of the series of surveys in this field and the efforts of specialists in Gynecology and Obstetrics preterm births, follow a continuous trend to increasing.⁶ According to data from the National Statistical Institute for 2015, 65 446 children were born in Bulgaria⁷. 6 413 children were born in Plovdiv and 2100 of them were born in the Clinic of Obstetrics and Gynecology at UMHAT "St. George "Plovdiv, Bulgaria where the present study was conducted. The rate of preterm infants for this clinic is 11% or approximately 231 newborns were born prematurely.

Complications of the respiratory system are numerous in premature babies due to lack of the period for intrauterine maturation of the lung.

One of the pathological syndromes of premature neonates is precisely related to the development of the lungs and is referred to as a Hyaline membrane disease (HMD) or neonatal Respiratory Distress Syndrome. It is caused by a deficiency in the synthesis of surfactant combined with structural immaturity of the lungs. It may also be a consequence of a neonatal infection.⁸⁻⁹ Hyaline membrane disease affects 1% of premature neonates in the world and is the leading cause of death in this group of patients.¹⁰ Complications of the respiratory system are numerous in premature babies due to lack of the period for intrauterine maturation of the lung.

Respiratory distress syndrome is the most common cause leading to death among premature neonates.¹¹ Even those who survive are at high risk of developing cerebral palsy, subsequent problems in the educational process and respiratory disorders.¹² Statistics show that in high-income countries the percentage of pre-natal births varies from 7% to 12%, while in low- and middle-income countries, such as those in Africa, it can reach 20%.

The premature babies are at risk of apnea (sudden breathing stoppage). It leads to a varying rate of change in heart rate, decrease in oxygen in the blood or hypotension. For this reason, it is necessary to monitor the occurrence of complications in preterm newborns.¹³

Pulmonary haemorrhage - this complication leads to death in a large percentage of the cases in which it occurs. Since etiology and pathogenesis have not yet been fully elucidated, there is insufficient adequate prophylaxis and treatment. The factors associated with it and the accompanying clinical picture continue to be clarified.¹⁴

In the long term, complications may reflect the overall development of surviving preterm infants. Premature babies more often suffer from chronic health problems, some of which may require hospital treatment.

Aim

The purpose of this study is to analyze data on complications, and especially pulmonary complications that develop preterm infants, and to analyze the impact of premature corticosteroid prophylaxis.

Materials and methods

The University Hospital St. Georgi, which has a 140-year history and is the largest hospital in southern Bulgaria, serving 1300 hospital beds. The Clinic for Obstetrics and Gynecology serves 131 hospital beds and has a Maternity ward, Neonatology ward, Ward of Pathological Pregnancy and Surgical Gynecology ward. A retrospective and prospective case-control study was conducted at the Clinic of Obstetrics and Gynecology, UMHAT "St. Georgi "Plovdiv, Bulgaria for the period of one and a half years. Documentary method is used, with primary data for pre-term infants recruited from "Case History", "Mother's Epicrisis" and "Newborn's Epicrisis." All mothers of newborns covered by the study signed an "Informed consent" document, consenting to the use of their data. An individual protocol was created and completed for each of cases. The data were processed with a statistical program SPSS Vol. 19.

The study involved 167 preterm infants and all of them were born in the Maternity ward at the Clinic of Obstetrics and Gynecology of St. George University Hospital in period March 2015 – September 2016. All of 167 participants in the survey were divided into two main groups: a working group of 89 preterm infants to whose mothers it was administered prenatal corticosteroid prophylaxis - "cases" and a control group of 78 preterm infants without prenatal prophylaxis "controls".

For the purposes of the study, additional intragroup regrouping is performed based on the next indicators: according to the gestational week when the birth occurred, the newborns are divided into: early premature born - up to 32 and gestational week lately prematurely born from 32 gestational week to 36 gestational week+ 6 days; whether or not a prophylactic corticosteroid course has been completed or missing; the weight of newborns; etc.

The workgroup of 89 preterm infants was divided into 43 infants with a full course of corticosteroid prophylaxis of two or three applications of dexamethasone administered prenatal of their mothers. 22 of their mothers were administered with 2 applications (12 mg) and 21 with 3 applications (18 mg) of dexamethasone. And 45 children with incomplete course of corticosteroid prophylaxis with administered one application of 1 amp. x 6 mg/ml of dexamethasone administered prenatal of their mothers. According to the practice in the clinic is accepted to be considered completed course of corticosteroid prophylaxis of both 2 and 3 applications of dexamethasone (2 ampoules x 6 mg/ml a total 12 mg and 3 amp. x 6 mg/ml, total 18 mg). Only one dexamethasone application is considered an incomplete course.

According to the postnatal complications, two groups were formed – 25 preterm infants with complication of neonatal RDS (HDM) and a group of 101 infants with complication of other forms of RDS. It was formed a group with a life-saving surfactant regimen of 37 children with single or multiple insufflated exogenous surfactant.

An individual research protocol is completed for each patient – a questionnaire has been specifically designed for the purpose of the study.

Criteria for including in the study: each live birth before 37 gestational week, according to the new standards of Obstetrics and Gynecology and Neonatology in Bulgaria from 2009, are in accordance with the European criteria for a live birth child. For the purpose of the study, all children with signs of life at birth, including those weighing less than 1000g, who died before the 168th hour, they hadn't been registered as live births till 2008, as well as those weighing less than 600g, who died before the third day after birth, they are recorded as aborted.

Criteria for exclusion from the study are newborns with severe malformations; newborns

with severe hereditary diseases; born after termination of pregnancy by medical check-up late; died in the first hours of their birth without intensive care.

Collection of primary data: After carefully checking the adequacy and completeness of the questionnaire completion, a corresponding code is placed and the primary data is entered into a statistical processing program. The data is entered and processed with the IBM SPSS Statistics Ver.19.0 statistical package. For a significance level where the zero hypothesis is accepted, $p < 0.05$ is taken.

Results and discussion

According the study 167 preterm infants, the mean gestational week of birth was 32.42 ± 3.38 gestational week. According to the study 89 (53.3%) were girls, and 78 (46.7%) were boys. The structural distribution, including the number and percentages of newborn children in each gestational week, is presented in Table. 1. Most children were born in 36 gestational week - 40 (24%), followed by children born in 35 gestational week - 26 (15.6%). The least born children were born in 25 gestational week. - 2 (1.2%), and in 29 gestational week - 4 (2.4%).

Table 1: Gestational Week of Birth

<i>Gestational Week</i>	<i>Number</i>	<i>Percentages</i>
25	2	1,2
26	13	7,8
27	6	3,6
28	8	4,8
29	4	2,4
30	16	9,6
31	16	9,6
32	10	6,0
33	6	3,6
34	20	12,0
35	26	15,6
36	40	24,0
Total	167	100,0

Table 2: Anthropometric characteristics of the newborn children studied

Anthropometric data	Number of children	Minimum	Maximum	Average	Deviation value
Child weight (gram)	167	700	2490	1687,19	521,240
Height (cm)	167	31	47	41,43	4,466

Table 3: Grade of prematurity according to the weight of the newborn child

Grade of prematurity	Number	Percentage
I –grade – from 2500g. to 2001g.	56	33,5
II –grade - from 2000g. to 1501g.	52	31,1
III - grade - from 1500g. to 1001g.	36	21,6
IV - grade - from 1000g. to 501g.	23	13,8
Total	167	100,0

Table 4: Number of applications with dexamethasone

Type of application	Number	Percentage
1 - multiple applications with dexamethasone 6 mg/ml	45	51,1
2 - multiple applications with dexamethasone 12 mg/ml	22	25,0
3 - multiple applications with dexamethasone 18 mg/ml	21	23,9
Total	88	100,0

Table 5: Premature newborns with HMD

Presence of HMD	Number	Percentage
No	142	85,0
Yes	25	15,0
Total	167	100,0

Table 6: Premature newborn children with others forms of RDS

Presence of RDS	Number	Percentage
No	66	39,5
Yes	101	60,5
Total	167	100,0

Table 2 shows the average weight and growth of preterm infants, respectively, showing the minimum and maximum values of the variables.

The average age of the surveyed mothers is $26,24 \pm 6,17$ years, the youngest is 15 years old and the oldest is 40. These who live in cities are 127 (76%) and these who live in villages are 40 (24%).

Table 3 presents the four stages of prematurity according to the weight of preterm infants, with 23 (13.8%) of newborn children are the fourth grade. Those with a third grade of prematurity are 36 (21.6%), and the most are newborn children with first grade of prematurity - 56 (33.5%).

89 (53.3%) from the 167 preterm newborn children that have been studied a prenatal prophylaxis with dexamethasone has been realised. The number and percent distribution, depends on the number of applications with dexamethasone, and is presented in table. 4. The highest is the percentage of cases with uncompleted corticosteroid prophylaxis, i.e. one application was applied - 45 (51.1%), and the cases with completed dexamethasone prophylaxis were the remaining sum of 2 and 3 applications - 43 (48.9%).

25 (15%) of premature newborns has developed neonatal Respiratory Distress Syndrome (nRDS) - Hyaline membrane disease (HMD) and at 101 (60.5%) have developed various other forms of Respiratory Distress Syndrome (RDS) (Table 5 and Table. 6). From the total registered premature infants with some (other) health complications, nearly 2/3 of the newborns are 107 (64.1%) of the cases (Table 7). There is a difference of 3.6% between newborns with Respiratory distress syndrome and those with other disabilities, all these shows that premature newborns priority damaging the respiratory system.

Table 8 shows the percentage distribution of preterm infants who have nRDS (HMD) and other forms of RDS. Approximately 1/4 - 25 (24.8%) of newborn children with RDS developed HMD.

Other established health complications in preterm infants are presented in Table 1. 9. The most common complications in newborn children are: transient tachypnea + hypoventilation + dyspnoea - 13 (12.4%). The following frequency indices (here they are as single complications) are pulmonary edema - 10 (9.5%) of cases and pulmonary hypoventilation, also in 10 (9.5%).

Table 7: Other health complications in preterm infants

Existence of other health complications	Number	Percentage
No	60	35,9
Yes	107	64,1
Total	167	100,0

Table 8: Structural distribution of preterm infants with HMD and other forms of RDS

Presence of RDS	Presence of HMD		Total
	No	Yes	
No	66	0	66
	100,0%	0,0%	100,0%
Yes	76	25	101
	75,2%	24,8%	100,0%
Total	142	25	167
	85,0%	15,0%	100,0%

Table 9: Other health complications in preterm infants

Healthy complications	№ Number.	%
exhaust-gas collections + intraventricular hemorrhage	2	1,9
pulmonary edema	10	9,5
pulmonary edema and intraventricular hemorrhage	2	1,9
acute bullous insufficiency	4	3,8
overlaid infection	8	7,6
bronchopulmonary dysplasia	4	3,8
pneumothorax	2	1,9
cardiovascular diseases	2	1,9
intraventricular haemorrhage + infection + bronchopulmonary dysplasia + pneumothorax + retinopathy + necrotizing enterocolitis	2	1,9
transient tachypnea	4	3,8
pulmonary hypoventilation	10	9,5
atelectasis	4	3,8
respiratory failure	2	1,9
transient tachypnea + hypoventilation + dyspnoea	13	12,4
transient tachypnea + atelectasis	2	1,9
hypoventilation + respiratory failure	2	1,9
dyspnoea + hypoventilation	6	5,7
atelectasis + respiratory insufficiency (DN)	2	1,9
transient tachypnea + cardiovascular complications	2	1,9
transient tachypnea + dyspnea + hypoventilation	4	3,8
transient tachypnea + dyspnea + atelectasis + hypoventilation	2	1,9
dyspnoea + transient tachypnea + respiratory failure	2	1,9
transient tachypnea + dyspnoea + pulmonary haemorrhage	2	1,9
respiratory failure + pulmonary edema	2	1,9
respiratory failure + hypoventilation + transient tachypnea	2	1,9
dyspnoea + transient tachypnea	2	1,9
transient tachypnea + hypoventilation	2	1,9
pulmonary edema + dyspnoea + hypoventilation	2	1,9
transient tachypnea + pulmonary edema	2	1,9
Total	105	100,0

The overlaid infection presents in 8 (7.6%) of newborn infants. In 6 newborn children, poly-systemic combined disorders were observed - apart from respiratory lesions there was also intraventricular hemorrhage, and in one case PDS was associated with cardiovascular damage. It should be noted that most of the newborn children have registered polypathology, which includes several respiratory tract damages. In summary, 94.3% of the pathology in preterm infants includes mainly single or combined respiratory disorders.

Those who have only extra-pulmonary pathology have a total of 6 cases: 4 (3.8%) acute kidney failure and 2 (1.9%) with cardiovascular disease. This relative share represents only 5.7% of all registered complications in preterm infants.

A surfactant has been administered to 37 (22.2%) children enrolled in the study. According to the premature born children survey -24 (14.4%) died.

Conclusions

The 3.6% difference between newborn children with RDS and those with all other disabilities shows that preterm infants have respiratory system damaged primary. Over 60% of premature infants developed respiratory distress syndrome.

The presence of respiratory complications is exacerbated by the higher rate of prematurity as well as by increasing maternal age and somewhat limited by prenatal corticosteroids.

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