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PREVENTION OF HYALINE MEMBRANE DISEASE (HMD) IN PRETERM INFANTS

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ABSTRACT

Premature birth is the most common cause of neonatal mortality in developed countries (5, 13, 15, 16). Over 80% of all cases of death in the world are result of neonatology premature birth (6, 29). The complications which are result of preterm birth are significant socioeconomic problem and the hyaline membrane disease (HMD) is in the leading place. In the field of prenatal medicine and neonatology are applied preventive treatments in order to reduce the risk of death of preterm newborns. We indicate general trends striving to achieve the optimal solution to the issues related to the reduction of complications in premature neonates in the countries around the world.

KEYWORDS: hyaline membrane disease (HMD), premature birth, corticosteroids, prevention, surfactant.

INTRODUCTION

In 2010, Blencowe H. et al. classify the 10 countries in the world having the highest number of preterm births. India takes the first place with 3519118 prematurely born infants, which is 13,0% of the born alive infants there. China takes the second place with about 1,2 million or 7,8% of the preterm infants worldwide. Nigeria, Pakistan and Indonesia are respectively on 3rd, 4th and 5th place in this classification with 5,2%, 5,0% and 4,5% of all cases of premature births. This classifications includes also the USA, Bangladesh, Philippines, Democratic Republic of Congo, taking respectively from 6th to 9th place. Brazil is on the last place with

279256 preterm infants, which is 9,2% of the total 3022823 born alive infants in the country. The authors summarize that from 74.8 million childbirths in the classified countries, 8,8 million (11,8%) are preterm.[3,5]

Statistical data prove that 8-10% of all pregnancies in Bulgaria end with preterm childbirth. Despite the search done in this direction and the efforts made by the obstetricians, during the last decade the tendency of increase of the number of preterm childbirths continues.[14]

The consequences of preterm childbirth include a number of medico-biological and socioeconomic negatives. The researches of Petrou S. et al. analyze the complex of negative aspects of preterm childbirth, respectively during the first 5 (2001), and 10 (2005) years of the life of premature infants.[22,23,24] The authors summarize that cerebral paralysis occurs with higher frequency in prematurely born infants compared to the ones born on the term. The first group is characterized with more frequent and durable complications of respiratory diseases and sensor deficiencies. The increased morbidity rate related to preterm childbirth affects the individual at later age too. This leads to considerable physical disorders of various degrees, emotionally and psychologically negative consequences and considerable socioeconomic expenditures both for the family and for the society as a whole.

Of great importance for reducing the frequency of preterm childbirths are the adequate and specialized prenatal cares. They have to be personalized and to take into account the complex of risk predispositions for each separate pregnancy.[17,18]

One of the pathological syndromes of the premature newborn infants is exactly related to the development of the lungs and it is denoted as hyaline membrane disease (HMD). It is caused by insufficiency in the synthesis of a surfactant in combination with the structural immaturity of the lungs. It could also be a consequence of a neonatal infection.[27,28] The hyaline membrane disease affects 1% of the preterm infants in the world and it is the main reason leading to the death of this group of patients.[26]

In medical literature sources the factors increasing, respectively reducing the risk of development of HMD, most often are systematized in two groups. The factors increasing the risk of development of HMD are: perinatal asphyxia, mother suffering from diabetes, multiple pregnancy; premature birth (before 28 g.w.). The factors reducing the risk of HMD are:

chronic fetal distress; amnionitis; application of corticosteroids and tocolytic therapy for the mother.

The clinical manifestation of the HMD occurs either immediately after birth or within 6 hours after that. The symptoms showing in the newborn infant with HMD are the following: expiratory moaning; epigastric and intercostal draw; nostril breathing; cyanosis - appearance of bluish or livid colour of the skin and mucosa which is due to the fact that the tissues located near the surface of the skin receive less oxygen saturation,[8,9] there is a possibility of development of apnea and/or hypothermia.[2]

The hyaline membrane disease often is accompanied by additional complications. Principally, they are divided into two groups, respectively – early and later complications. The early ones include: pulmonary edema; infection; intracranial hemorrhage, and periventricular leukomalacia; apnea; pulmonary hemorrhage; necrotizing enterocolitis and/or stomach and intestinal perforation. Later complications may include: bronchopulmonary dysplasia; retinopathy; neurological disorder.[4]

The hyaline membrane disease (HMD) is one of the most common complications of the preterm childbirth. HMD develops in preterm infants as a result of primary deficit of surfactant. This insufficiency is corrected by means of intratracheal application of exogenous surfactant. For maximum results, the medicine must be applied as soon as possible after the birth of the preterm infant.[11,25]

The surfactant insufficiency upsets the normal anatomy and physiology of the lungs of the preterm infants, increasing significantly the risk of developing hyaline membrane disease (HMD). This disease most often leads to death of the preterm infants.

The surfactant is applied for treatment and prophylaxis in neonatology, and its main properties are: reduction of the surface pressure at the boundary air-water in the alveoli intended to prevent the collapse of the alveoli and the distal bronchioles during exhaling; reduction of the pressure, required for the expansion of the lungs and improvement of their functioning; stabilization of the alveoli and the end bronchioles; prevention of pulmonary edema; improvement of the oxygenation; anti-infection protection; others.[25]

The application of surfactant replacement therapy in the respiratory syndrome of newborn infants is described for the first time by Fujiwara T. in 1980.[12] From that moment on the

medication is established as a revolutionary method in the intensive neonatal treatment and breathing reanimation.[20] In Bulgaria the application of exogenous surfactant starts in the beginning of the 90-ties of 20th century.[25]

The human surfactant contains phospholipids –Dipalmitoylphosphatidylcholine (DPPtdCho), unsaturated phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol and neutral lipids, as well as a surfactant binding proteins: SP-A, SP-B, SP-C и SP-D.[11] The main component is lecithin. Through monitoring its levels in the amniotic fluid during pregnancy the lungs maturity of the fetus is determined. If the ratio of lecithin and sphingomyelin is over 2, it is considered that the fetus maturation is adequate. If the value is less than 1, the risk of development hyaline membrane disease is defined as high.[25]

The main difference between the natural and synthetic surfactant is exactly that the first one has SP-B and SP-C proteins in concentration of 1-2%. This content of protein components makes it most alike to the human one, and it is accepted that its application leads to more efficient treatment.[11]

There is a wide variety of surfactant preparations which are reviewed mainly in two groups – synthetically produced and extracts from animal lungs (from bovines, pigs) The medication is used in the medical practice in a number of countries, and in the sales network it can be found under different names. Natural surfactant preparations are: Survanta® (USA), Infasurf® (USA), Surfacten® (Japan), Alveofact® (Germany), BLES® (Canada), Curosurf® (Italy).[11] In Bulgaria the most widely used animal surfactant is Curosurf®.[21]

The application of surfactant is adopted by a number of medical specialists for treatment of the hyaline membrane disease, however this therapy often is financially difficult to achieve. The high cost of the product is one of the reasons for seeking alternative substitute, but at a lower price, for example such as the financially more affordable betamethasone and dexamethasone. Other positive aspect of the corticosteroid application is the search of a prophylactic effect on the hyaline membrane disease, which from medical point of view is the most preferred preventive method.

In the beginning of the 70-ties, Liggins G. and Howie R., found out that if pregnant women threatened by preterm birth are prescribed with corticosteroids, then the probability their newborn infant to develop the syndrome of the respiratory distress or HMD is reduced

significantly. The applications adopted here are either with betamethasone phosphate or with betamethasone acetate. This search as well as the data resultant from it, change the method of treatment applied by the physicians in the risk cases of childbirth within the 24th and 36th gestational week, with the purpose of improving the quality of life of the preterm infants.[19]

Corticosteroids have been used in the medical practice for more than 40 years now in the cases of risk of preterm birth, with the purpose of allowing the fetus enough time its lungs to be developed to the required stage. Their use also reduces the incidence of Hyaline membrane disease in preterm infants, the neonatal morbidity and death rate with about 50 %.[10]

The standard corticosteroid prophylactic therapy in women with risk of premature birth is undertaken during 24 and 34 gestational weeks of the pregnancy. The therapy may include dexamethasone applied intramuscularly in 4 doses of 6 mg at interval of 12 hours[1,8] or betamethasone applied twice per 12 mg at interval of 24 hours.

Both corticosteroid products reduce the risk of perinatal death[7], as well as the risk of development of HMD. Dexamethasone is characterized with its greater affinity to the glucocorticoid receptors, but betamethasone has longer semi-life which gives it advantage and makes it preferred in the medical practice. From economic point of view the financially more affordable dexamethasone prophylaxis versus the surfactant treatment allows for its wider application.

The medical community is faced with many other issues as well, one of which is finding the most appropriate way to inform the families of preterm infants about the prophylaxis of HMD, the risks of development of other disease, and the complications related to it, the medications offered in the prenatal and neonatal period, and so on. Other issue is how to reduce the hospital stay of this group of patients, as the stay in the neonatal intensive wards is associated with increased stress for parents; it is supposed that the preterm infants also feel similar distress. It is possible exactly this stress during the neonatal period to be the reason for subsequent health and psychic complications or to cause delayed intellectual development. The widespread education of the medical professionals in the prophylactic methods aimed at achieving maximum risk reduction of development of hyaline membrane disease is one of the main goals of the contemporary neonatal medicine.

CONCLUSION

The opinion of the authors, on the basis of the analyzed data, supports the positive prophylactic and therapeutic effect of the corticosteroid therapy. Finding the answers to and solutions for the existing issues related to the prevention and treatment of HMD will reduce the risk of neonatal death rate and will prevent the occurrence and development of additional complications accompanying the HMD. The effective corticosteroid prophylaxis also would lead to reduced stay of the newborn infants in the neonatal and intensive hospital wards, and respectively better quality of life.

REFERENCES

1. ACOG Committee on Obstetric Practice. ACOG Opinion No. 475: antenatal corticosteroid therapy for fetal maturation. Obstet Gynecol, 2011; 177: 422- 424.
2. Agapitos E, Papadopoulou C, Kavantzas N, et al. The contribution of pathological examination of the placenta in the investigation of the causes of foetal mortality. Archives d'anatomie et de cytologie pathologiques 1996;44:5–11.
3. AiQun Huang, Xi Jin, XiaoHong Liu, SuHong Gao, Reproductive Health, 2015; 12: 1. matched case-control study of preterm birth in one hospital in Beijing, China", Publication date 5 January 2015,
4. Bladh M., Josefsson A., Carstensen J., Finnström O., Sydsjö G., Twin Research And Human Genetics: The Official Journal Of The International Society For Twin Studies, "Intergenerational Cohort Study of Preterm and Small-for-Gestational-Age Birth in Twins and Singletons", Oct, 2015; 18(5): 581-90.
5. Blencowe H, Cousens S, Oestergaard M, Chou D, Moller AB, et al. National, regional and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analyses and implications. Lancet, 2012; 379(9832): 2162–72.
6. Born too soon: The global action report on preterm birth. In C. P. Howson, M. V. Kinney, J. E. Lawn, (Eds.), Written report World Health Organization: Geneva.
7. Brownfoot FC, Crowther CA, Middleton P. Different corticosteroids and regimes for acceleration fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev., 2008; CD006764.
8. Crowther CA, McKinlay CJD, Middleton P, Harding JE. Repeat doses of prenatal corticosteroids for women at risk of prenatal birth for improving neonatal health outcomes. Cocrane Database Syst Rev., 2011; CD003935.

9. Culpepper L, Jack B. Psychosocial issues in pregnancy. Primary Care., 1993; 20: 599–619.
10. Danesh A, Janghorbani M, Khalatbari S. Effects of antenatal corticosteroids on maternal serum indicators of infection in women at risk for preterm delivery: A randomized trial comparing betamethasone and dexamethasone. J Res Med Sci., 2012; 17: 911–7.
11. Fox G., Sothinathan U., "The choice of surfactant for treatment of respiratory distress syndrome in preterm infants: A review of the evidence", R E S P I RATORY THE RA PY, 2 0 0 5, 8-12)
12. Fujiwara T, Adams FH. Surfactant in hyaline membrane disease. Pediatrics, 1980; 66(5): 795-98
13. Goldenberg RL, Culhane JF, Iams JD, Romero R. "Epidemiology and causes of preterm birth". The Lancet, 2008; 371(9606): 75–84.
14. Ivanov St. III part. Obstetrics: Textbook for medicine students, Sofia, Pathology of pregnancy. Preterm birth, 2014; 426: 195-198.
15. Heaman M., Blanchard J., Gupton A., Moffatt M., Currie R., Paediatric and Perinatal Epidemiology,19, Risk factors for spontaneous preterm birth among Aboriginal and non-Aboriginal women in Manitoba, 2005; 181–193.
16. Heron M. Deaths: leading causes for 2008. Natl Vital Stat Rep., 2012; 60(6): 1-94. http://humrep.oxfordjournals.org/content/14/11/2891.full
17. Iams JD, Romero R, Culhane JF, et al. Primary, secondary, and tertiary interventions to reduce the morbidity and mortality of preterm birth. Lancet, 2008; 371: 164–75
18. Krueger PM, Scholl TO. Adequacy of prenatal care and pregnancy outcome. Journal of the American Osteopathic Association, 2000; 100: 485–492.
19. Liggins, Graham Collingwood, and Ross Howie. "A Controlled Trial of Antepartum Glucocorticoid Treatment for Prevention of the Respiratory Distress Syndrome in Premature Infants." Pediatrics, 50(1972): 515–25. - See more at: https://embryo.asu.edu/pages/corticosteroids-effect-fetal-lung-maturation-1972-sir-graham-collingwood-liggins-and-ross#sthash.7jHcjq7u.dpuf
20. Liggins, Graham Collingwood, and Ross Howie. "A Controlled Trial of Antepartum Glucocorticoid Treatment for Prevention of the Respiratory Distress Syndrome in Premature Infants." Pediatrics 50(1972): 515–25. - See more at: https://embryo.asu.edu/pages/corticosteroids-effect-fetal-lung-maturation-1972-sir-graham-collingwood-liggins-and-ross#sthash.7jHcjq7u.dpuf

21. Mumdzhiev Hr., Cholakova M. Dobreva A., N. Stoyanova, Vangelov PM, Department of newborns - Stara Zagora, 2006-2008. Science Pulmonology 4/2008, "Application of surfactant in premature infants with respiratory distress", 165-169.
22. Petrou S, Mehta Z, Hockley C, Cook-Mozaffari P, Henderson J, Goldacre M. The impact of preterm birth on hospital inpatient admissions and costs during the first 5 years of life. Pediatrics, 2003; 112: 1290-7.
23. Petrou S, Sach T, Davidson L. The long-term costs of preterm birth and low birth weight: results of a systematic review. Child Care Health Dev, 2001; 27(2): 97–115.
24. Petrou S. The economic consequences of preterm birth during the first 10 years of life. BJOG, 2005; 112: 10-5.
25. Pramatarova T. NSA-Hospital,, Dr Ivan Seliminski " Sliven. Hyaline membrane disease in premature infants.
26. Rodriguez RJ, Martin RJ, and Fanaroff, AA. "Respiratory distress syndrome and its management". In Fanaroff, Avroy A; Martin, Richard J. Neonatal-perinatal medicine: diseases of the fetus and infant. St. Louis: Mosby, 2002; 1001–1011. ISBN 978-0-323-00929-4.
27. Santosham, Mathuram; Chan, Grace J.; Lee, Anne CC; Baqui, Abdullah H.; Tan, Jingwen; Black, Robert E. "Risk of Early-Onset Neonatal Infection with Maternal Infection or Colonization: A Global Systematic Review and Meta-Analysis". PLoS Medicine, 2013; 10(8): 1001502. doi:10.1371/journal.pmed.1001502. ISSN 1549-1676
28. Sinha, Sunil. Essential neonatal medicine. Chichester, West Sussex: John Wiley & Sons. ISBN 9780470670408; Access provided by the University of Pittsburgh, 2012.
29. Steer P "The epidemiology of preterm labour". British Journal of Obstetrics & Gynaecology, 2005; 112(1): 1–3.