Hyaline membrane disease as a factor in perinatal death

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Abstract: This article provides detailed information on perinatal death in hyaline membrane disease.

Keywords: bronchus, alveolus, mucous membrane, submucosa, epithelium

Introduction: Despite the measures of antenatal prophylaxis, modern methods of pregnancy prolongation, the number of preterm births does not decrease [1,4]. Given this fact, the World Health Organization in 1970 adopted new criteria for a live birth: the lower limit of a live birth is determined by the gestational age of 22 weeks, birth weight of 500 grams and body length of 25 cm [2-3]. As a result, a new contingent of newborns has appeared in neonatal intensive care units - children with extremely low birth weight (ELBW) at birth. The incidence of hyaline membrane disease (HMD) has increased, as there is a certain pattern in the development of the disease: the lower the gestational age, the higher the risk of developing HMD [5]. Much attention is paid to the study of BGM [6-10]. Measures for antenatal prevention of BGM development have been developed, however, morbidity, mortality and disability remain high [11-13].

In addition, the use of modern technologies: artificial lung ventilation (ALV), including high-frequency; the use of exogenous surfactants, on the one hand, reduced mortality from BGM, on the other hand, led to a change in the clinical signs of the disease. Currently, scientific works devoted to BGM cover the use of various modes of invasive and non-invasive high-frequency mechanical ventilation, the method of early application of constant positive airway pressure, and the prophylactic and therapeutic administration of endogenous surfactants [14-22]. At the same time, there are no works devoted to the morphological and morphometric study of the lungs of children who died from BGM.

The purpose of the study: was to identify the features of morphological changes in the lungs in premature newborns with BGM with the use of exogenous surfactants and artificial ventilation.

Materials and methods: An analysis of the protocols of pathoanatomical examination of 90 premature newborns who died from severe respiratory failure was carried out. For histological examination, lung pieces were taken from different segments of both lungs during post-mortem autopsy. Lung condition was assessed visually during autopsy. Lung pieces were fixed in 10% neutral formalin and

embedded in paraffin. Histological sections were stained with hematoxylin-eosin, according to Van Gieson.

Results and discussion: In the comparison group, the condition of all newborns at birth was extremely difficult, due to respiratory and heart failure against the background of deep morphofunctional immaturity. The structure of lung tissue corresponds to gestational age and is consistent with the data of a number of researchers. In some newborns, the alveolar epithelium is high, with rounded normochromic nuclei. At the same time, in many newborns, the alveolar epithelium with signs of damage is low, the nuclei of epithelial cells are deformed. Part of the alveoli is rounded with a flattened alveolar epithelium. There are also expanded, air alveoli, with cubic epithelium, in which dystrophic changes were recorded: vacuolization of the cytoplasm, deformation of the nuclei. Some of the alveoli are bizarre in shape, others look like they have thinned interalveolar septa. Small alveoli look like an hourglass. In the capillaries of the interalveolar septa, there is a large cuboidal epithelium with a homogeneous cytoplasm and a marginal arrangement of the nucleus. In aerated alveoli, the epithelium is significantly flattened, evenly located on the lamina propria. The alveolar passages are narrowed; in many fields of view they are not differentiated. The lumen of the bronchi is predominantly stellate in shape, many cystically dilated bronchioles pass into cystically dilated alveoli, forming bizarre-shaped cavities. In such formations, lamellar desquamation of the epithelium is noted. In dilated bronchioles, the epithelium is preserved and flattened. In this group of newborns, the interalveolar septa are thickened and loose. The dilated lymphatic vessels are randomly scattered over the septa, often merging into optically empty cavities. Arteries with a thickened wall, parietal arrangement of erythrocytes. In the vast majority of cases, aspiration of amniothelial scales, meconium bodies, is detected. Hyaline membranes were not registered in 100% of cases. The aggravating factors that influenced the course and outcome of the disease in all the studied groups of newborns were intranatal hypoxia, the development of intraventricular, intracerebral hemorrhages, cerebral edema.

The next group is premature newborns who developed BGM, but they did not receive exogenous surfactants in the complex therapy of the disease. In this group of very premature newborns with ELBW. Most of the children were transferred to mechanical ventilation immediately after birth, or in the first hours of life. During the first 6 hours of life, 2 children died, 12-24 hours after birth - 6 children, after 2 days and 3 days - 5 newborns, 2 children lived 4-5 days, 6 days - 3, more 2 children lived 6 days. In the lungs of 2 newborns who died within the first 12 hours after birth, large alveoli with homogeneous GM are visualized. The largest number of alveoli with membranes is located in the peribronchial areas, the smallest is subpleural. The membranes have a "discontinuous" appearance, fit snugly against the inner wall of

the alveoli. The alveolar passages are enlarged, most of them are filled with lumps of layered pink hyaline masses. Cellular reaction to membranes is not expressed. The alveoli contain amniothelial scales and meconium bodies, maternal erythrocytes. Around the respiratory bronchioles there are a large number of small plethoric vessels. In the wide interalveolar septa, plethora is expressed, a large number of anastomoses. Under the pleura, in the interalveolar septa, around the vessels and respiratory bronchioles - small focal hemorrhages. In premature newborns who died up to a day after birth, GM are visualized in all fields of vision, completely lining or filling small alveoli. The alveolar ducts are dilated and obturated with lumpy hyaline membranes of deep pink color. Hyaline membranes do not occur in collapsed alveoli. Cellular response to membranes is poor. Scales of amniothelium are visible in the alveoli. The lower the gestational age of the child, the more variable the shape of the alveoli. In newborns with ENMT, the alveoli have an angular, polygonal, stellate, elongated, process, rounded shape; in newborns with a gestation period of more than 29 weeks, the lumen of the alveoli is predominantly oval or rounded. In the lumen of the alveoli, amniothelial scales, fibrin-like masses, and segmented leukocytes are detected. Arterio-venular anastomoses and lymphatic vessels are dilated. Around vessels, bronchioles, under a pleura focal hemorrhages come to light. In newborns with ELBW who lived for 2-3 days, GM in the alveoli had a fragmentary character. Cellular reaction is not expressed. Single scales of amniothelium are revealed. There are peribronchial areas of small distelectasis, focal subpleural emphysema. The plethora of blood vessels is characteristic. There is interstitial edema and focal serous alveolar edema.

In newborns with ELMT who lived 4-5 or more days after birth, rare fragmented GMs are recorded in small and medium alveoli. The phenomena of resorption and cellular reaction are expressed. Edema of the stroma and expansion of the lymphatic vessels are also characteristic. A feature of the newborns of this group is the appearance of a cellular reaction to hyaline membranes 4-5 days after birth.

Morphological changes in the lungs of newborns who received Surfactant BL had their own characteristics. A few GMs were found in children who died 12 hours after birth. They are located fragmentarily along the inner wall of small alveoli in the form of thin homogeneous structures. Focal atelectasis, hemorrhages around the vessels, bronchi, in the interstitial space are revealed. The interalveolar septa are thickened. The pleura is swollen. Venules and arterioles are plethoric, endothelial edema is noted. The main localization of hyaline membranes is small alveoli and alveolar ducts. The alveolar epithelium is desquamated, represented by large alveolocytes with a homogeneous large nucleus and granular cytoplasm. In the alveoli, among the membranes, there are single segmented leukocytes, alveolar macrophages, amniothelial scales and erythrocytes are found. In the bronchioles,

abundant desquamation of the epithelium is noted. The lumens of the lymphatic vessels are different: from slit-like to dilated with the formation of cystic cavities. A large number of arteriovenous anastomoses are located peribronchially and subpleurally. Vascular endothelium swollen, with granular cytoplasm. All newborns do not have alveolar edema. In the lumen of individual large alveoli, there are single lipid drops. In half of the patients of this group, who lived for 1-2 days, hyaline membranes were found in large numbers in the form of wide strips up to 1/3 of the lumen of the alveoli and lumps that obturate medium, small alveoli, alveolar passages and respiratory bronchioles. In such alveoli, the epithelium is absent. Among the hyaline masses are amniothelial scales, erythrocytes and segmented leukocytes, fragments of nuclei. In some newborns, by the 17th hour of life, the disintegration of GM begins, by the 36th hour of postnatal age, their active lysis by leukocytes is noted. The plethora of venules and capillaries is characteristic, a large number of vessels of various calibers with a smoothed, almost flat endothelium are noted peribronchially. There is no alveolar edema. Interstitial edema was noted mainly in the pleura and peribronchially.

In 4 patients who lived for 3 days, there are large and medium-sized alveoli of oval and round shape, in addition, cavities of 2-3 alveoli with thinned interalveolar septa were formed. The main amount of GM is in these alveoli, as well as in collapsed alveoli and in the lumen of the respiratory bronchioles, medium-sized bronchi. Cellular response is minimal. Lipid drops were not found. Width, cellular composition and fibrosis interalveolar septa, the number of newly formed capillaries increase depending on the life expectancy of children. Interstitial edema, pleural edema in these newborns is moderately expressed. In a child who died after 7 days, single GM remained in the form of thin homogeneous eosinophilic structures located fragmentarily along the inner wall, predominantly small. Factors that influenced the course and outcome of the disease were acute intranatal hypoxia; development of intraventricular hemorrhages, cerebral edema. Cellular reaction to GM was noted in half of newborns. Cellular response to GM appears 12 hours after birth, reaching a maximum by 3 days. In the group of newborns who received Curosurf, three subgroups were distinguished depending on the severity of hyaline membranes (HM).

The first subgroup - 4 children with an average life expectancy of 12 hours. Histological examination revealed multiple GM in small alveoli and bronchial lumen. In medium-sized alveoli, GMs are found in the form of "bridges" between the walls. In large alveoli and alveolar ducts there are accumulations of hyaline masses. Desquamation of the alveolar epithelium, located in the thickness of the hyaline masses, is noted. Thin GM fragmentarily line the inner wall of the alveoli of different diameters. Single atelectases of various localization are visible: around the bronchi, under the pleura. Isolated cells of the alveolar epithelium with signs of karyolysis

were preserved. In the respiratory bronchioles, desquamated epithelium and hyaline masses are revealed. For all patients, circulatory disorders are characteristic: the lumens of aterioles, venules, capillaries are dilated, the endothelial lining is partially absent. Small hemorrhages are found around the vessels and bronchi, in the interalveolar septa.

The second subgroup - 9 premature newborns with a significant amount of GM. Life expectancy in this subgroup was 2-3 days. Alveoli of various shapes and sizes. Small alveoli contain homogeneous, sometimes lumpy hyaline masses that cover their lumen. In the alveoli of medium and large sizes, GM have a ribbon-like or strip-like appearance, spread fragmentarily along the inner wall of the alveoli. Such alveoli are airy, and the preserved alveolar epithelium swells into the lumen of the alveoli between membrane fragments. In places, GMs have a layered appearance, changing color from soft pink to deep blue. When stained according to Van Gieson, the membranes are stained in a bright crimson color. Amniothelial scales, meconium bodies, maternal erythrocytes, desquamated bronchiolar epithelium, lipid drops. When a fatal outcome occurs 1 day after birth, the epithelium of the bronchi is preserved; at a later date, desquamated epithelium and fibrin -like masses appear in the lumen of the bronchi. The bronchiolar epithelium is partially preserved. Expanded bronchi and alveoli form areas of broncho -alveolar emphysema. Around such formations in the thickened interalveolar septa, a vascular reaction and plethora of capillaries are expressed, a large number of arteriolo-venular anastomoses are determined. There is no alveolar edema.

The third subgroup - 7 premature newborns who lived from 5 to 14 days after birth. In the classical form of BGM, active resorption of the GM is recorded by this time. However, only in 3 children of this subgroup, single GM with resorption phenomena were found in the lungs. In other cases, homogeneous and layered GM fragments are visualized, among which there are desquamated alveolocytes, segmented leukocytes, fragments of their nuclei, bronchiolar epithelium, amniothelial scales, lymphocytes. Interalveolar septa of different thickness, dilated, proliferation of fibroblasts, many newly formed vessels. The thinned partitions are fibrosed, with lymphocytic infiltration, single segmented leukocytes. Often, the bronchial lumen is dilated, characterized by the formation of large cavities, partially lined with sharply flattened bronchiolar epithelium. These cavities often merge with areas of alveolar emphysema. All children have areas of alveolar emphysema of varying severity, hemorrhages in the interalveolar septa, under the pleura, around the vessels and bronchi. In the stroma there are a large number of small full-blooded vessels of the capillary type and arteriolo - venular anastomoses. Lymphatic vessels have a predominantly slit-like lumen.

Conclusion: One of the important factors contributing to damage to the alveolar epithelium and the development of BGM in premature newborns is intranatal hypoxia and aspiration of amniotic fluid, which is documented by the content of amniothelial scales, meconium bodies, and maternal erythrocytes in the lumen of the alveoli. Violations of hemomicrocirculation, oxygenating function of the lungs are facilitated by functioning arteriolo-venular anastomoses, through which blood is shunted in the lungs. In addition, a number of other factors affect the course and outcome of the disease: the development of intraventricular, intracerebral hemorrhages, cerebral edema, periventricular leukomalacia. With an increase in life expectancy, late complications may develop: necrotizing enterocolitis, acute perforated gastric ulcer. Without the use of exogenous surfactants, GM are detected as early as 4-6 hours after birth. Active formation of GM occurs up to 2-3 days of life, then the process of their resorption begins. The use of "Curosurf" delays the formation of GM and helps to increase the life expectancy of newborns. However, these newborns developed late complications like BGM itself - bronchopulmonary dysplasia.

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