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INFORMATIONAL CONTENT OF LABORATORY AND ENZYMATIC INDICATORS IN THE DIAGNOSIS OF IMPAIRED RENAL FUNCTION IN NEWBORNS AFTER HYPOXIA

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Abstract: In recent years, according to WHO, there has been a tendency towards an increase in the incidence of urinary system diseases in newborns. Renal pathology ranks second in the structure of general morbidity in children after respiratory diseases and ranges from 15 to 53%. Every year, up to 40% of children are born sick or become ill during the neonatal period. On average, every tenth baby is born premature and with low birth weight. The incidence of kidney damage among the pediatric population varies from 0.4 to 11.8%. According to various sources, the incidence of urinary tract infections ranges from 0.1% in full-term infants and up to 10% in premature infants. With modern ecology and the frequency of complicated births, almost every newborn experiences hypoxia of varying severity, and in children who have suffered severe hypoxia, have concomitant diseases and have received massive therapy, the frequency of kidney damage increases significantly. In newborns treated in intensive care units, kidney pathology develops in approximately 32% of cases.

The metabolic processes occurring in the renal tissue and the functional state of the newborn's kidneys are undoubtedly influenced by gestational age and the degree of morpho-functional maturity of the child's organs and tissues. Therefore, it is important to study the degree of damage to the structural and functional elements of the nephron after hypoxia, to assess the effect of intensive therapy on the glomerular and tubular apparatus of the kidneys in order to select treatment.

Purpose of the study: To identify the information content of biochemical parameters of blood and urine with the development of an examination algorithm for newborn children after hypoxia with the development of renal pathology.

Research objectives:

1. Investigate glomerular filtration disorders based on serum creatinine levels in newborns.
2. To identify the dependence of the state of the tubular epithelium on the activity of the enzymes gammaglutamine transferase and alkaline phosphatase.
3. Analyze the role of urine pseudocholinesterase to assess the condition of the glomerular filter.

Materials and methods of research. The total number of subjects examined was 135 newborns admitted to the hospital in the first week of life and 16 children in the control group. The main group included newborns being treated in the intensive care unit in the first week of life; their condition was assessed as extremely severe or very severe - 106 children. 16 children died at various times from the moment of admission. The comparison group consisted of newborns with an uncomplicated perinatal history who were admitted in a

state of moderate severity to the neonatal pathology department with ARVI and local purulent-inflammatory processes - 29 children. The control group included practically healthy children 4-5 days of life, located in the maternity hospital - 16 children.

The main group was divided into three subgroups according to gestational age: 38-42 weeks (full term) - 30 children; 32-37 weeks (premature) – 60 newborns; 31 weeks or less (very premature) – 16.

All children underwent biochemical studies in blood serum and urine according to a specific scheme: study of creatinine levels in urine and blood serum using the Jaffa kinetic method without preliminary deproteinization. At the same time, the activity of the following enzymes was studied in urine: pseudocholinesterase, gammaglutamyltransferase, alkaline phosphatase using kinetic methods. In urine, the content of enzymes was determined in a three-hour (from 6-00 to 9-00 am) portion of urine. Since not a daily, but a three-hour portion of urine was analyzed, and the secretion of enzymes is subject to a circadian rhythm, the activity was recalculated per milligram of creatinine excreted, since creatinine is excreted at a constant rate throughout the day.

The activity of the enzyme pseudocholinesterase (pseudoChE) in urine was used to assess glomerular filtration. PseudoChE is an enzyme that reflects damage to the glomerular apparatus of the kidneys, since it normally does not pass through the glomerular filter. Enzymes that characterize damage or increased permeability of the membranes of the renal tubules include gammaglutamyltransferase (GGT) and alkaline phosphate (ALP).

RESULTS AND DISCUSSION. At the same time, newborns have features of water metabolism and creatinine metabolism that may complicate the assessment of these indicators. In our study, daily diuresis of newborns was assessed over time. Children from the main group received more infusion therapy than children from the comparison and control groups, as well as medications that stimulate diuresis. Therefore, the study was carried out in the main group of newborns.

We obtained statistically significant data ($p < 0.05$) showing that diuresis in newborns who have suffered hypoxia gradually increases in the first two weeks of life, and then remains stable in the remaining periods. In full-term (38-42 weeks) and premature infants (32-37 weeks), the increase in urine output was more gradual than in extremely preterm infants (31 weeks or less).

In the group of newborns who suffered hypoxia, creatinine significantly increased compared to children from the comparison group (the indicators of the comparison group coincide with the literature data) during the first month of life. On days 1-3 of life – $t = 2.44$; $p=0.0161$; on days 4-7 – $t = 3.35$; $p=0.0014$; on days 15-28 – $t=4.11$; $p=0.0003$. It was noted that the level of creatinine significantly decreases starting from the second week of life, but slightly behind the increase in diuresis. The differences within the main group turned out to be quite pronounced (Kruskal-Wallis test = 18.4; $p = 0$), within the comparison group they were not so significant, but statistically significant (Kruskal-Wallis test = 7.92; $p = 0.0476$). It is obvious that with an increase in diuresis, the clearance of substances excreted by the kidneys also increases, and, consequently, their content in the blood decreases.

To analyze some of the patterns identified when studying the dynamics of daily diuresis, the level of serum creatinine was analyzed depending on the gestational age and the type of hypoxia suffered. It was revealed that in the first three days of life of newborns, the level of serum creatinine did not differ significantly in all three groups. More pronounced changes were observed in the second week of life (Kruskall-Wallis coefficient = 6.87; $p = 0.0322$). In full-term infants, there was a gradual decrease in the level of serum creatinine, and in extremely premature infants there was initially a tendency to increase.

The gradual decrease in serum creatinine levels over the course of a month in all three groups is statistically significant ($F=8.23$; $p=0.0001$; $F=7.07$; $p=0.0003$; $F=9.17$; $p=0$, respectively). At the same time, in

extremely premature newborns, the decrease in serum creatinine occurs more slowly. When studying the excretion of creatinine in the urine in children of the main and control groups in the first week of life, depending on the type of hypoxia suffered, it was found that the excretion rate in the main group was 8.13 ± 2.04 µmol/kg/hour, and in the control group 3. 68 ± 1.6 µmol/kg/hour. The differences between the groups are significant: t = 4.25; p = 0.0001.

The results obtained confirm that, starting from the second week of life, the kidneys of children who have suffered hypoxia must excrete more creatinine in order for its level in the blood to normalize.

When measuring GGT activity depending on the type of hypoxia suffered, it was revealed that there were no statistically significant differences between the groups (p> 0.05). In our studies, there was a tendency to increase activity values in acute asphyxia. In mixed asphyxia, GGT activity was also quite high, but a large scatter of the obtained values was noted. Apparently, in this case, the factors that cause chronic and acute hypoxia in each specific case and the intensity of their impact play an important role. In addition, it was noted that out of 30 children examined over time 2-3 times with an interval of 10-14 days, 21 had an increase in GGT levels, and in 3 of them by the end of the first month of life the results did not differ from the norm. Similar results were observed in children with both initially high and low values of enzyme activity.

The optimal marker of glomerular damage is the enzyme pseudocholinesterase (pseudoChE); an increase in its activity in urine indicates the permeability of the glomerular filter. When studying the influence of the type of hypoxia and gestational age on the state of the glomerular filter, it turned out that there was no statistically significant dependence of pseudoChE activity on these factors (p>0.05), and there was no decrease in the first month of life (p>0.05). At the same time, there is a tendency to increase pseudoChE activity in very premature infants - 4.12±1.36 kU/mg creatinine compared to 2.42±0.82 in full-term infants and 2.85±0.44 kU/mg creatinine in premature newborns.

CONCLUSIONS

1. Disorders of glomerular filtration are manifested mainly by a decrease in filtration rate and a corresponding increase in the level of creatinine in the blood serum.
2. The activity of GGT and alkaline phosphatase in the urine reliably reflects the state of the tubular epithelium against the background of hypoxia and prolonged drug load. An increase in the level of GGT in the urine also characterizes the toxic effect of the therapy.
3. Pseudocholinesterase (pseudoChE) is a marker of damage to the glomeruli of the kidneys. An increase in pseudoChE activity in urine indicates a violation of the permeability of the glomerular filter and hypoxic damage to the glomeruli.

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