METABOLIC STATUS IN PROLONGED NEONATAL HYPERBILIRUBINEMIA

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ABSTRACT

Prolonged neonatal hyperbilirubinemia is common in neonatal period. Neonatal hyperbilirubinemia acquires its relevance since this condition, in parallel with its frequent manifestation, is of great interest both in terms of occurrence time and its duration. According to numerous studies, the structure of prolonged neonatal hyperbilirubinemia is dominated by conjugational hyperbilirubinemia in newborns, where it is metabolically confirmed by metabolic changes such as hyperbilirubinemia in blood serum.

Keywords. Newborn, prolonged neonatal hyperbilirubinemia, metabolic status, procalcitonin, C-reactive protein

I. INTRODUCTION

Metabolic disorders in the form of hyperbilirubinemia are a frequently reported condition in neonatal period. In the structure of neonatal jaundice, according to the literature, prolonged neonatal hyperbilirubinemia is in the lead. Hyperbilirubinemia in newborns has been taking on a longer duration in recent decades. The reason for this phenomenon is not clear. [2,3,10].

Some degree of neonatal jaundice or hyperbilirubinemia is an unpredictable condition in 60–80% of newborns worldwide [1,8,13].

A certain part of these conditions is transient for the child and does not require special correction, but in some cases neonatal jaundice takes a protracted course, resulting in a high risk of complications caused by the neurotoxicity of indirect bilirubin [1,2,5]. Jaundice of newborns is of great significance in morbidity and mortality of newborns worldwide [1,2,10]. With respect to the data of numerous studies, the frequency of prolonged hyperbilirubinemia significantly ascends and amounts to 25–65% in term infants and 70–90% in premature infants [12, 13].

"Prolonged" conjugated jaundice is a surge in indirect bilirubin that persists in term infants for more than two weeks of life [7]. However, prolonged neonatal hyperbilirubinemia requires exclusion of other possible causes of hyperbilirubinemia [1,11]. Newborns with "prolonged" conjugational jaundice tend to develop several pathological conditions due to the immaturity of various organs and systems [6,13].

The relevance of prolonged neonatal hyperbilirubinemia is due to the high incidence of this condition, the lack of clear diagnostic criteria and the possibility of predicting the development of metabolic status shifts in prolonged neonatal hyperbilirubinemia, the need to isolate inflammation markers in prolonged neonatal hyperbilirubinemia, and the identification of a correlation between indicators of metabolic status and markers of inflammation.

II. MATERIAL AND METHODS

The work was carried out at the Samarkand State Medical Institute. Clinical recruitment of material was held at the Samarkand Regional Children's Multidisciplinary Medical Center in the neonatology department. The subjects of study are investigated blood, serum for the determination of procalcitonin, C-reactive protein, and trace elements.
of blood serum (after parental consent). Clinical-anamnestic, hematological, biochemical, functional (ultrasound of the liver and biliary tract, neurosonography, echocardiography), and statistical research methods were used. The investigation examined 200 newborns, studied anamnestic, and assessed the health of their mothers. Among the newborns, there were 122 boys (53%) and 78 girls (47%). Depending on the gestational age and the maximum bilirubin level, depending on the duration of jaundice, children were divided into two groups: Group I - with moderately prolonged hyperbilirubinemia (bilirubin level no more than 250.0 μmol / l); Group II - with prolonged high-grade hyperbilirubinemia (bilirubin level 251.0-500.0 μmol / l, a protracted character with duration of more than 21 days). Statistical result processing was accomplished using the software package "Microsoft Excel" and "Statistica 7.0" for "Windows". Quantitative data are presented in the arithmetic mean (M), representativeness error (m), and relative frequencies. The significance of the mean values' differences was determined using the Student's t-test(t). In contrast with a qualitative binarycriterion, the χ2 criterion was applied, to compare the percentages, the angular Fisher transformation (φ-transformation) was used. Correlation dependence was determined using Spearman's nonparametric test (ρ).

III. RESULTS AND DISCUSSION

In the examined newborns, prolonged hyperbilirubinemia was the main indicator for hospitalization. The data obtained depicted that in newborns with prolonged hyperbilirubinemia, visual changes in the skin were characteristic, in the form of prolonged hyperbilirubinemia for which most groups of newborns were hospitalized. Subicterity of skin and mucous membranes in newborns with prolonged hyperbilirubinemia visually appeared more often on the 3-4th day, life: in 36.1% - on the third day, in 42.5% - on the fourth. In 9.9% of newborns, jaundice arised on the second day of life, in 10.3% - on the fifth day, and 1.2% - on the sixth day of life. With prolonged neonatal hyperbilirubinemia, the subictericity of the skin and mucous membranes had a wavy pattern of jaundice. This condition was explained by the fact that most of newborns of this study group had a burdened perinatal history. In this group of newborns, during childbirth, there were obstetric interventions, children were born with a Caesar section, where epidural anesthetics were taken, birth injuries in the form of cephalohematoma were noted. All of the above etiological conditions adversely affected the body of the newborn. When analyzing the somatic status of women in group I, it was revealed in 49 women preeclampsia (57.65%), influenza during pregnancy 44 (51.76%), hypertension 2 (2.35%), moderate and severe anemia 80 (94.12%), nephropathy 8 (9.41%), pyelonephritis 33 (38.82%), in the group of studied mothers during pregnancy were revealed chickenpox, viral hepatitis, herpes which was 67.06%, the threat of termination of pregnancy 57 (67.06%), oedema 1 (1.18%). In the second analyzing group II, it was revealed in 2 women hypotension (1.74%), in 80 women preeclampsia (69.57%), influenza during pregnancy 71 (61.74%), hypertension 2 (1.74%), moderate and severe anemia 112 (97.39%), pathological increase in amniotic fluid 1 (0.87%), nephropathy 6 (5.22%), pyelonephritis 44 (38.26%), in the group of studied mothers during pregnancy so the same were revealed cytomegalovirus, chickenpox, viral hepatitis, herpes which was in 10 women (8.7%), the threat of termination of pregnancy 72 (62.61%), oedema 1 (0.87%).

In group II (moderately prolonged hyperbilirubinemia), mothers were significantly more prone to have anemia (p <0.05), in group I preeclamsia (p <0.05), exacerbation of pyelonephritis (p <0.04); chronic pyelonephritis (p2 <0.04) (Table 1).

Table 1. The incidence of women in the studied groups

<table>
<thead>
<tr>
<th>Nosology</th>
<th>I group, n=85</th>
<th>pI</th>
<th>II group, n=115</th>
<th>pII</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>abs</td>
<td>%</td>
<td>abs</td>
<td>%</td>
</tr>
<tr>
<td>Hypotension</td>
<td>0</td>
<td>0.00</td>
<td>2</td>
<td>1.74</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>49</td>
<td>57.65</td>
<td>80</td>
<td>69.57</td>
</tr>
<tr>
<td>Flu</td>
<td>44</td>
<td>51.76</td>
<td>71</td>
<td>61.74</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2</td>
<td>2.35</td>
<td>2</td>
<td>1.74</td>
</tr>
<tr>
<td>Anemia</td>
<td>80</td>
<td>94.12</td>
<td>112</td>
<td>97.39</td>
</tr>
<tr>
<td>Pathological increase in amniotic fluid</td>
<td>0</td>
<td>0.00</td>
<td>1</td>
<td>0.87</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>8</td>
<td>9.41</td>
<td>6</td>
<td>5.22</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>33</td>
<td>38.82</td>
<td>44</td>
<td>38.26</td>
</tr>
</tbody>
</table>
In all surveyed groups of newborns, there was no increase in the activity of serum aminotransferases, which excludes the viral etiology of jaundice. In 96.9% of children with prolonged hyperbilirubinemia of the 1st surveyed group had a slight icteric tinge of the face and chest already on the 14-16th day of life, in newborns with prolonged neonatal hyperbilirubinemia of the second surveyed group this indicator was observed only by 20-23 days.

The newborns examined by us were admitted to the neonatology department in most cases in the autumn and spring seasons. The circulation rate of the first surveyed group of newborns in winter was 12.94%, in spring 48.24%, in summer 8.24%, in autumn 30.58%. The circulation rate of the II surveyed group of newborns in winter was 26.96%, in spring 38.78%, in summer 12.17%, in autumn 26.09%. The differences in accessibility during the year between the first and second groups differ both in frequency and quantity (diagram 1).

![Figure 1. The amount of total bilirubin in the blood serum](image)

Visually, the appearance of skin yellowness, depending on the day of life, was observed at 85 +/- 11.2 μmol / l of total serum bilirubin. In newborns with a poorly expressed subcutaneous fat layer, visually skin yellowness manifested itself at a total bilirubin level of 84 +/- 9.6 μmol / L, in large newborns with a well-expressed subcutaneous fat layer – at 78 +/- 7.4 μmol / L (p <0.4).

In the first study group, on the 11-15th day of life, the level of total bilirubin at a level of 100-150 μmol / l was 2.35%, while the level of total bilirubin set to become 151-200 μmol / 13.53%, 201-250 μmol / 14.71%, at 16 -20 days of life of the newborn. The level of total bilirubin at a level of 100-150 μmol / l amounted to 2.35%, with a level of total bilirubin 151-200 μmol / l registered 7.05%, at a level of 201-250 μmol / l turned to be 9.41%, on the 21-25th day of the newborn's life, the level of total bilirubin at a level of 151-200 μmol / recorded to be 4.71%, with a level of total bilirubin of 201-250 μmol / l 8.24%; at 26-31 days of life of a newborn, the level of total bilirubin is 151-200 μmol / l 12.94%, the level of total bilirubin is 201-250 31.76% (diagram2).
Figure 2. The amount of total bilirubin in the blood serum

In the second examined group, on the 11-15th day of life, the level of total bilirubin at a level of 251-300 μmol / L was 5.22%, the level of total bilirubin at a level of 301-350 μmol / L was 6.09%, the level of total bilirubin at a level of 351-500 μmol / L was 1.74%, on the 16-20th day of life, the level of total bilirubin at a level of 251-300 μmol / L was 6.96%, the level of total bilirubin at a level of 301-350 μmol / L was 7.83%, the level of total bilirubin at the level of 351-450 μmol / L was 1.74%, the level of total bilirubin at the level of 451-500 μmol / L was 0.87%; on the 21-25th day of life in the second study group, the level of total bilirubin at a level of 251-300 μmol / L was 6.09%, the level of total bilirubin at a level of 301-350 μmol / L was 5.22%, the level of total bilirubin at the level of 351-450 μmol / L was 3.48%, the level of total bilirubin at the level of 401-450 μmol / L was 0.87%, the level of total bilirubin at the level of 451-500 μmol / L was 1.74. Hyperbilirubinemia in the second study group was much greater due to indirect bilirubin and was more often detected with a high concentration of total bilirubin in the blood serum (diagramm3).
The results of clinical studies delineated that at baseline, patients had pronounced violations of the metabolic parameters of venous blood (hyperbilirubinemia more than 400-450 μmol / l, a decrease in the total amount of protein in the blood serum, glucose less than 2.2-1.9 mmol / l, hypomagnesiemia 0.70-0.60 mol / l and hypocalcemia 1.0-1.5 mmol / L). Some infectious pathology was one of the common causes of prolonged hyperbilirubinemia for differential diagnosis by etiology, procalcitonin and inflammatory markers were studied in all newborns. The observed increase in the parameters of C-reactive protein at normal values of procalcitonin indicates the beginning of the development of inflammation of non-infectious (adaptive) genesis [9,13]. Of the 100 newborns examined with prolonged neonatal hyperbilirubinemia, procalcitonin was increased, i.e. above 0.5 ng/ml, only in 3 patients from group 2. In other newborns, procalcitonin was not increased. This does not coincide with the literature data [10,13] on the high sensitivity of procalcitonin in the presence of inflammatory activity, while the level of C-reactive protein is increased and leukocytosis is observed.

**IV. CONCLUSION**

In patients with prolonged neonatal hyperbilirubinemia during infection, a high C-reactive protein and leukocytosis are more reliable markers of inflammation than procalcitonin. High-risk factors for the formation of prolonged neonatal hyperbilirubinemia have been established, which include factors of perinatal hypoxia asphyxia (threat of abortion, preeclampsia, maternal anemia during pregnancy, chronic fetal hypoxia, asphyxia at birth, use of resuscitation, and subsequent rehabilitation measures), leading to the formation of hypoxic damage to the liver and brain.

**Conflict of interests and contribution of authors**

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REFERENCES