Optimization of Therapeutic Measurements in Rotavirus Infection in Infants with Perinatal Exposure to HIV

Hryhoriy Trotsky

Abstract
The features of the clinical course of rotavirus infection in infants with perinatal exposure to HIV were studied. Serum level of procalcitonin as a marker of inflammatory activity and the need for antimicrobial therapy was determined. The efficiency of the proposed additions to basic treatment (low-lactose mixture for two months, antibiotic therapy in case of elevated procalcitonin level) was demonstrated.

Keywords
children; perinatal exposure to HIV; rotavirus infection; procalcitonin

Problem statement and analysis of the recent research
According to estimates, about 220,000 Ukrainians are HIV-positive. As of January 1, 2014, 3,287 HIV-infected children at the age of 0-18 years were registered by health care institutions of Ukraine: 3,129 (95.2%) children were born to HIV-infected mothers and 158 (4.8%) children were infected in other ways (through unprotected sex, injection drug use, other parenteral interventions). As of January 1, 2014, in addition to HIV-positive children with confirmed status, there were 6,915 children born to HIV-infected mothers with unconfirmed HIV status [4]. Children with perinatal HIV contact are very vulnerable to infectious diseases, have longer and severer recovery period, which can negatively affect their development [8].

Rotavirus infection is very common among young children. Approximately 50,000 children in Ukraine contract intestinal infections annually. 25-50% of all cases of gastroenteritis in children under the age of 5 years are caused by rotavirus infection (RVI). Rotavirus infection in children with perinatal HIV exposure may result in severe clinical course and complications. According to N. Kotova, HIV-negative children born to HIV-positive mothers contract intestinal infections significantly more often than children in the control group [2, 3]. Probiotics may correct this condition but biologic drugs are prohibited for treatment of children with undetermined HIV status [9, 10].

The objective of the research was to increase the effectiveness of treatment of rotavirus intestinal infection in infants with perinatal HIV exposure through the correction of the nutritional status as well as the expansion of the range of diagnostic and therapeutic measures considering specific clinical situation.

1. Materials and methods
There were examined 40 children with RVI at the age of 1-2 years (the average age was 18.2±3.5 months), born to HIV-infected mothers. The following laboratory tests were made: complete blood count, biochemical profile (determination of serum levels of K, Na, Cl, glucose, total bilirubin, fractions, urea, and creatinine), scatoscopy, stool culture to detect pathogenic bacteria, the fecal pH, PCR for HIV, rota test and PCR for rotavirus infection. Clinical stool samples were examined with Citotest Rota (Pharmasco) ELISA test-systems and AmpliSens® Rotavirus-EPh PCR kit, procalcitonin (PCT) plasma concentration was determined using immunoluminometric assay (B.R.A.H.M.S. Diagnostica, GmbH, Berlin, Germany).

Children with clinical signs of rotavirus infection born to HIV-infected mothers were divided into 2 groups of 20 persons; their age, sex and severity of condition were considered. Children of the main group received a low-lactose mixture, antibiotic therapy as well as Smekta enterosorbent in addition to basic therapy. The control group received only basic therapy according to the protocol of diagnosis and treatment of infectious secretory diarrhea in children [4]. According to the protocol, basic therapy for this category of children included rehydration therapy which was determined by the degree of dehydration (Rehydron at a dose of 10 ml/kg orally after each watery stool or vomiting; a 0.9% NaCl solution and a 5% glucose solution in the ratio 1:1 at a dose of 50-100 mL/kg intravenously), aluminosilicate sorbents for 5-7 days and a...
low-lactose diet [4].

2. Results and discussion

The study of clinical signs showed that 26 (65%) children had a moderate and 14 (35%) children had a severe clinical course of rotavirus infection. The mean duration of rotavirus infection clinical symptoms was as follows: vomiting – 2.9±0.77 days; diarrhea – 6.2±0.84 days. The increase in body temperature to 38°C was observed in 35 (87.5%) children with the average duration of 4.2±1.11 days. The signs of poisoning such as weakness and lethargy were noticed in 39 (97.5%) children; the signs of anhydration persisted 3.6±0.69 days. Accordingly, children needed long-term intensive therapy (3.2±0.71 days) and prolonged hospitalization (7.4±0.2 days).

The analysis of laboratory finding revealed that the level of total serum protein ranged from 66.8±3.75 g/l and corresponded to the lower limit of normal values; electrolyte levels (K, Na, Cl) corresponded to the indicators of the age norm, namely potassium level was 5.1±0.2 mmol/l (normal potassium level - 4.14-5.75 mmol/l), sodium level was 136.2±2 mmol/l (normal sodium level - 133-141 mmol/l), chloride level – 101.2±2.1 mmol/l (normal chloride level - 98-107 mmol/l). The average blood glucose level corresponded to normal values being 4.6±0.4 mmol/l. The levels of total bilirubin and its fractions were within the age norm: total bilirubin – 14.1±0.7 mmol/l (normal values of total bilirubin - 8.5-20 mmol/l), the levels of urea and creatinine corresponded to the normal range (3.3-5.6 mmol/l and 18-35 mmol/l, respectively).

A qualitative PCR test was used to detect HIV in children born to HIV-positive mothers to determine their status at the age of 18 months. The test was negative in all 40 children (inclusion criterion). The rota test was made as screening one, and its result (positive) was one of the inclusion criteria.

Rotavirus PCR was performed in both groups to confirm the presence of rotavirus RNA in the stools of children included in the study.

The level of plasma procalcitonin (PCT) was determined as an inflammatory marker. This indicator is important in the management of patients with acute intestinal infection since it helps determine the need for antibiotics. According to the protocol of treatment of secretory diarrhea in children [4], antibiotic therapy is indicated only for children with immunodeficiency conditions up to 1 year of age; HIV-infected children at the stage of AIDS. However, according to several studies, the optimal indication for antibiotic administration is procalcitonin level >0.4 ng/ml [1]. Similar (although not identical) thresholds are suggested by Schuetz et al. [1]. These researchers believe that when the biomarker concentration is less than 0.25 ng/ml there is no need for antibiotics. The use of antibiotics is recommended at PCT blood level of 0.25-0.5 ng/ml. PCT level in the study group was 0.21-0.98 ng/mL. Coprological examination of all children with RVI showed the characteristic signs of maldigestion and malabsorption manifested themselves as amylorhea, steatorrhea, creatorrorhoea which probably were associated with the feeding pattern. The stools were unformed, watery and mixed with mucus. Children with rotavirus infection developed signs of lactase deficiency — stool pH less than 5.5. Fecal cultures yielded no growth.

To improve the nutritional status of children with perinatal HIV exposure we suggested to supplement the diet of children in the main group with a low-lactose mixture. Since they were not nourished with mixtures and children of this age with RVI are recommended a lactose free or low lactose diet we used a feeding system for younger children. To improve the nutrition as well as to decrease the symptoms of secondary lactase deficiency, children in the main group received 200 ml of a low-lactose mixture twice a day for 2 months.

In addition to standard therapy (in PCT level above a threshold of 0.4 ng/ml) a broad-spectrum antibiotic was prescribed, namely third-generation cephalosporin – Ceftriaxone at a dose of 80 mg/kg parenterally twice a day for 7 days.

Smekta enterosorbent was prescribed orally, 1 sachet of 3g once a day for 7 days. This is an anti diarrheal agent; aluminosilicate of natural origin with a strong adsorption effect.

Within two months we examined the dynamics of anthropometric parameters, the indicators of blood and urine tests in children with perinatal HIV exposure in both groups depending on the feeding type. At the beginning and at the end of the study we examined anthropometric indices (body weight, body length, circumferences of chest, shoulder, and thigh) both in absolute numbers and according to the centile charts, as well as values of complete blood count (RBC, Hb, color index). The results are presented in Table 1.

All children of the main group had a normal period of adaptation to the new product, and its introduction to the diet did not cause any functional disorders of the digestive system or allergic reactions.

The comparison of anthropometric indicators of children in the main group before and after introduction of the low-lactose mixture showed a significant increase in both body weight and height, as well as chest, shoulder and thigh circumference. In children of the control group on the background of basic diet, the increase in anthropometric indicators such as body weight as well as chest, shoulder and thigh circumference was slower; it did not influence their height being lower than in the children of the main group. The evaluation of body weight and height according to the centile charts corresponded to P 25-50, while in the children of control group — within P 10-25.

Two months later there was no difference in such blood values as RBC, Hb and color index. No difference was found in urine specific gravity index which indicated normal renal function in both groups.

Thus, the supplementation of basic treatment with a mixture which is a source of proteins, polyunsaturated fatty acids and energy contributes to positive dynamics in the physical
Table 1. Anthropometric and laboratory parameters in infants with perinatal HIV exposure after two months of taking a low-lactose mixture, M±m

<table>
<thead>
<tr>
<th>Index</th>
<th>Main group (n=20)</th>
<th>Control group (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before the introduction of the product</td>
<td>After the introduction of the product</td>
</tr>
<tr>
<td>RBC</td>
<td>3.98±0.07</td>
<td>4.01±0.05</td>
</tr>
<tr>
<td>Hb, g/l</td>
<td>119.89±0.80</td>
<td>121.82±0.40</td>
</tr>
<tr>
<td>Color index</td>
<td>0.88±0.01</td>
<td>0.91±0.01</td>
</tr>
<tr>
<td>Urine specific gravity</td>
<td>1014.89±0.87</td>
<td>1015.9±0.87</td>
</tr>
<tr>
<td>Height, cm</td>
<td>78.33±1.26</td>
<td>82.03±0.97</td>
</tr>
<tr>
<td>Weight, g</td>
<td>10127.78±380.49</td>
<td>11927.78±182.1</td>
</tr>
<tr>
<td>Chest circumference, cm</td>
<td>41.83±0.27</td>
<td>43.23±0.21</td>
</tr>
<tr>
<td>Shoulder circumference, cm</td>
<td>13.38±0.31</td>
<td>15.28±0.11</td>
</tr>
<tr>
<td>Thigh circumference, cm</td>
<td>22.81±0.66</td>
<td>24.68±0.44</td>
</tr>
</tbody>
</table>

The data of comparative analysis of symptom duration in children of the main group who received a low-lactose mixture and antibiotics, and the patients of the control group who received basic therapy only are presented in Table 2.

In the main group of children with perinatal HIV contact, there were 8 children with PCT level above a threshold of 0.4 ng/ml (which could signify mixed infection - bacterial flora joining) and in the control group, there were 7 children with PCT level above a threshold of 0.4 ng/ml. The comparison of PCT data found that the clinical symptoms of acute intestinal infection reduced significantly faster in children who received antibiotic therapy.

The follow-up observation and study of the main complaints of children with RVI was conducted within two months from the onset of illness. In children of the main group a significant reduction in complaints was noticed by the end of the 1st month of the follow-up observation. The restoration of appetite in 92.3% of children was noticed within the 2nd month of the observation (p=0.02). Recurrent abdominal pain and its equivalent, as well as functional intestinal disorders in the form of unstable stool were recorded within the 2nd month of the observation. In children of the main group a significant reduction in complaints was noticed by the end of the 1st month of the follow-up observation. The restoration of appetite in 92.3% of children was noticed within the 2nd month of the observation (p=0.02). Recurrent abdominal pain and its equivalent, as well as functional intestinal disorders in the form of unstable stool were recorded within the 2nd month of the observation. In children of the main group a significant reduction in complaints was noticed by the end of the 1st month of the follow-up observation. The restoration of appetite in 92.3% of children was noticed within the 2nd month of the observation (p=0.02). Recurrent abdominal pain and its equivalent, as well as functional intestinal disorders in the form of unstable stool were recorded within the 2nd month of the observation.

3. Conclusions

- The prescription of the low-lactose mixture to young children with perinatal HIV exposure for 2 months can improve their physical development.

- PCT level above a threshold of 0.4 ng/ml as a marker of the process of bacterial inflammation in the body can be used as an indication for antibiotic therapy in young children with perinatal HIV exposure in rotavirus infection.

4. Prospects for further research

References


### Table 2. Comparative characteristics of clinical symptoms in children with rotavirus infection born to HIV-infected mothers depending on prescribed therapy (M±m), days

<table>
<thead>
<tr>
<th>Efficiency criteria</th>
<th>Main group, n= 20</th>
<th>Control group, n=20</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poisoning</td>
<td>4.1 ±0.51</td>
<td>6.2±0.63</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Fever</td>
<td>4.2±1.11</td>
<td>5.4±0.9</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2.9±0.77</td>
<td>3.4±0.4</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Normalization of appetite</td>
<td>5.5±1.34</td>
<td>6.1±0.9</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Exccicosis</td>
<td>3.6±0.69</td>
<td>4.2±0.41</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Diarrhea duration</td>
<td>6.2±0.84</td>
<td>8.4±1.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Intensive therapy duration</td>
<td>3.2±0.71</td>
<td>5.1±0.8</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Hospital stay</td>
<td>7.1 ±0.73</td>
<td>9.4±0.82</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>


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