The starting therapy of colibacillosis in children

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The colibacillosis are wildly spread all over the world and takes leading positions in etiological structure of acute intestinal infections in children. In our country, due to diagnostic difficulties, rate of registration of colibacillosis is low. The clinical epidemiological characteristics and issues of differentiated diagnostic of the given disease are studied insufficiently. Until nowadays, common approaches to therapy are lacking. The article presents evaluation of therapeutic activity of various methods of start therapy of colibacillosis in children. The clinical efficiency of various classes of antibacterial medications and enterosorbents are presented.

Keywords: colibacillosis, start therapy, enterosorbent, children.

Acute enteric infections (AEI) represent a problem of infectious disease both for the national health care and worldwide, taking a second spot in the structure of morbidity and mortality [1, 2].

AEI remains an urgent problem in pediatrics because of the incidence rate and severity, remaining one of the causes of infant mortality, ranking 2-3rd after respiratory diseases and HIV infection [3, 4].

According to WHO, annually more than 4 billion cases of AEI are recorded globally, 60% of patients are children of up to 3 years old.

In 2015, the Russian Federation saw increasing occurrences of AEI of established and non-established etiology, making up 750515 cases compared with the same period in 2014 – 740479. Among them, the share of children under 14 years old comprised 494970 cases, while in the same period of 2014 the number of cases stood at 490450 [5].

Difficulties in obtaining objective data about a factual etiological structure of AEI make practitioners resort to their own experience and regional data for guidelines [6].

Escherichia coli make a large contribution to the etiological structure of AEI in young children [7–9]. Colibacillosis is widely spread across the globe and takes leading positions in the structure of AEI, especially in children [10]. In our country, only 17-20 thousand cases of AEI cases are registered officially: these occurrences are caused by E. coli, 75% patients were children under 14 years old (G.G. Onischenko, 2012). Falling colibacillosis registration rate is due to diagnostic difficulties. The most
common routine method in medical practice for detecting *E. coli* diarrheagenic groups is the determination of the serogroup/serotype, followed by the indirect determination of isolate’s belonging to one of the known diarrheagenic *E. coli* groups. However, serologic examinations in children with colibacillosis do not represent any diagnostic value (A.V. Gorelov, 2003), while direct methods of specific virulence factors detection, carried out by bioassay tests, methods for detecting specific toxins, adhesion capacity for cell culture and identification of genes encoding virulence factors, by PCR, are rarely used [11-13].

Prescription of an optimal causal treatment is challenging for doctors, as a choice of antimicrobial preparation is essential, due to constant changeability of pathogen sensitivity to widely used antimicrobials and growth of antibiotic-resistant strains (L.N. Milyutina, 2005; E.P. Kadzhaeva, 2006). Up to 60% of *E. coli* are antibiotic-resistant strains (I.Yu. Melnikova, 2009).

An examination of 789 patients was carried out, aged from 1 month to 5 years old and treated in acute enteric infections departments of Children’s Infectious Diseases Hospital № 5 in Moscow from November 2009 to June 2011. Patients were randomly selected during all seasons of the year. A special record card designed by us was filled for every patient, and it was daily updated on the course of the disease, clinical and laboratory examination and data history was also recorded. Questionnaire survey of patients’ parents was conducted for further detailing of epidemiological anamnesis. The estimation of severity and clinical forms of AEI was performed on the basis of the manual for medical professionals “Clinical recommendations for diagnostics and treatment of acute enteric diseases in children” (A.V. Gorelov, L.N. Milyutina, D.V. Usenko, M. 2007) approved by the Ministry of Health and Social Development of the Russian Federation.

With the purpose of AEI trigger detection, all the patients were examined on the first day of admission by routine methods (bacterial swab test, Enzyme immunoassay (EIA) for rotavirus antigen detection) and by PCR. On the second week of the decease, serologic examinations of blood by treponema pallidum hemagglutination test with salmonella, shigellosis and Yersinia diagnostic agents were undertaken. The diagnosis of colibacillosis was made on the basis of AEI clinical picture and detection of diarrheal *E. coli* in PCR stool test. Test-systems AmpliSens Colibacillosis-F L (“Амплисенс Эшерихиозы-Ф Л”) (№ of the latest reregistration – FSR (ФСР) 2010/07977 18 November 2011) were used. Bacteriological examinations for colibacillosis were not undertaken due to a lack of diagnostic serums in the bacteriological laboratory of the hospital. The examination of 453 patients was performed in dynamics on the 1st and on the 4-5th day of hospital stay, with the aim of estimating elimination of diarrheal *E. coli*.

Taking into consideration the absence of unified approaches to colibacillosis therapy in children up until now, we retrospectively evaluated the starting therapy of the given deceases. We analyzed the efficacy of the starting therapy by antimicrobial preparations and enterosorbents combined with oral rehydration therapy in patients with moderate colibacillosis. The choice of the starting therapy is determined by admitting physicians. Enterosorbents (dioctahedral smectite and polymethylsiloxane polyhydrate) were used in age-specific dosage variances until stool normalization. Neosmektine and Enterosgel were used most frequently. Antimicrobial preparations were prescribed as a 5-7-day course intramuscularly or per os in age-specific dosage variances, nifuroxazide, aminoglycoside, cephalosporin of the 3rd generation and nalidixic acid were used. Most commonly administered were Enterofuryl, Amikacinum, Ceftriaxonum and Negram. On admission, all the patients received common basic therapy: diet, oral or if indicated intravenous rehydratation, ferments, antihistamines, pre- and probiotics, syndrome medications.
For evaluating the effectiveness of the performed treatment, 2 groups of patients were determined: the 1st group – 40 children administered antimicrobial preparations, the 2nd group – 36 children administered enterosorbsents. The groups were comparable in age, frequency of adverse premorbid background, admission dates and duration of hospital stay.

The effectiveness of the therapy was evaluated by the duration of fever symptoms, intoxication, vomiting, pathologic stool, deviation of leukocytes from the age norm in the general analysis of blood during early recovery. Table 1 shows data on the duration of AEI main symptoms in patients administered various starting therapy, including oral rehydration, antimicrobial treatment and enterosorbent therapy.

No fundamental differences in dynamics of clinical symptoms relief were detected in compared groups, though only fever was found to be more long-lasting on the background of antimicrobial treatment ($p<0.05$).

**Table 1. Duration of the main symptoms of AEI in patients administered various starting therapy including oral rehydration and antimicrobial preparations or enterosorbsents**

<table>
<thead>
<tr>
<th>Duration of symptoms, days</th>
<th>Antimicrobial preparations (n=40)</th>
<th>Enterosorbsents (n=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>4.36±0.4*</td>
<td>2.86±0.3</td>
</tr>
<tr>
<td>Intoxication</td>
<td>2.45±0.2</td>
<td>2.37±0.2</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2.36±0.4</td>
<td>2.58±0.3</td>
</tr>
<tr>
<td>Pathologic stool</td>
<td>5.9±0.8</td>
<td>4.29±0.5</td>
</tr>
</tbody>
</table>

* $p<0.05$

The results of comparing the leukocyte deviation from the age norm in the general analysis of blood in the period of early recovery of patients from the groups under consideration are presented in Table 2.

**Table 2. Leukocyte deviation from the age norm in the general analysis of blood in the period of early recovery of patients with AEI administered various starting therapy**

<table>
<thead>
<tr>
<th>Leukocyte deviation from the age norm in the general analysis of blood in the period of early recovery</th>
<th>Antimicrobial preparations (n=40), %</th>
<th>Enterosorbsents (n=36), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocytosis</td>
<td>16±5.8</td>
<td>5.9±3.9</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>40±7.7</td>
<td>23.5±7.1</td>
</tr>
<tr>
<td>Normocytosis</td>
<td>44±7.8</td>
<td>70.6±7.6*</td>
</tr>
</tbody>
</table>

* $p<0.05$

Patients administered enterosorbsents in the starting therapy demonstrated a relatively stable level of leukocytes, more often within age norm, compared to patients receiving antimicrobial preparations in the initial treatment ($70.6 \pm 7.6 \text{ и } 44 \pm 7.8\%$, $p<0.05$).

A comparative analysis of the effectiveness of various starting therapies of moderate colibacillosis in 2 comparable groups showed that duration of the main clinical symptoms did not differ fundamentally, though against a backdrop of enterosorbent treatment combined with oral rehydration, fever lasted less and leukocyte level in the general analysis of blood during early recovery was not subject to drastic changes, predominantly remaining within the limits of age norm.
Consequently, clinical effectiveness of enterosorbents is highly competitive with that of antimicrobial preparations.

To evaluate effectiveness of different classes of antimicrobial preparations, the 1st group of patients was divided into 4 subgroups. The 1st subgroup was comprised of 11 children, whose combined therapy included aminoglycosides; the 2nd subgroup consisted of 8 children that were subject to antimicrobial AEI therapy by nifuroxazide; the 3rd subgroup included 11 children administered efalosporines of the 3rd generation; and the 4th subgroup – 10 children receiving nalidixic acid. The groups under analysis were comparable in age, frequency of adverse premorbid background, admission dates.

Table 3 demonstrates duration of the main AEI symptoms and leukocyte deviation from age norm during early recovery, administered antimicrobial preparations of different classes for the starting therapy.

### Table 3. Duration of the main AEI symptoms and leukocyte deviation from age norm in the general analysis of blood during early recovery, administered antimicrobial preparations of different classes for the starting therapy.

<table>
<thead>
<tr>
<th>Studied parameters</th>
<th>Aminoglycosides n=11</th>
<th>Nifuroxazide n=8</th>
<th>Efalosporines n=11</th>
<th>Nalidixic acid n=10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>3.6±0.4*</td>
<td>2.2±0.3*</td>
<td>4.6±0.5*</td>
<td>2.5±0.4*</td>
</tr>
<tr>
<td>Intoxication</td>
<td>2.6±0.4</td>
<td>1.8±0.3</td>
<td>2.7±0.4</td>
<td>2.1±0.4</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1.8±0.3*</td>
<td>3.0±0.7</td>
<td>2.2±0.3</td>
<td>2.0±0.3*</td>
</tr>
<tr>
<td>Pathologic stool</td>
<td>9.1±1.2*</td>
<td>2.7±0.5</td>
<td>6.6±1.8</td>
<td>5.5±0.9*</td>
</tr>
<tr>
<td>Leukocytosis</td>
<td>5</td>
<td>2</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Normocytosis</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>7</td>
</tr>
</tbody>
</table>

*p<0.05

Nifuroxazide and nalidixic acid showed the greatest efficiency: in patients administered these medications duration of fever was significantly lower compared with patients treated with aminoglycosides and cephalosporins of the 3rd generation (2.2±0.3 days - patients administered nifuroxazide and 2.5±0.4 days - in patients treated with nalidixic acid against 3.6±0.4 and 4.6±0.5 days, respectively) (Fig. 1).

No significant differences were obtained regarding duration of intoxication syndrome in patients administered various antimicrobial medications.

Duration of vomiting in patients administered aminoglycosides (1.8±0.3 days) and nalidixic acid (2±0.3 days) was significantly less compared with that of patients treated with nifuroxazide (3±0.7 days) (p<0.05).

Duration of pathologic stool in patients administered nifuroxazide was less compared with those receiving aminoglycosides (2.7±0.5 and 9.1±1.2 days, p<0.05), while in patients administered nalidixic acid – less than in patients treated with cephalosporins (5.5±0.9 and 6.6 ±1.8 days, p<0.05). Figure 2 shows duration of pathologic stool in children with colibacillosis against a background of therapy with various antimicrobial medications.
Figure 1. Duration of fever in patients administered the starting therapy of various antibacterial medications

Figure 2. Duration of pathologic stool in children administered the starting therapy of various antibacterial medications

Evaluation of leukocyte deviation from age norm in the general analysis of blood during early recovery in patients from the analyzed groups did not show any significant differences.
Thus, the obtained data may attest to the fact that nifuroxazide and nalidixic acid as the starting antimicrobial therapy of moderate colibacillosis are the most efficient compared with other antimicrobial medications.

To evaluate effectiveness of different classes of enterosorbents, the 2nd group of patients was divided into 2 subgroups: the 1st subgroup comprised 18 children administered dioctahedral smectite, while the 2nd subgroup of 18 children – polymethylsiloxane polyhydrate. The groups were comparable in age, frequency of adverse premorbid background and admission dates.

Table 4 demonstrates duration of the AEI main clinical symptoms and leukocyte deviation from age norm in the general analysis of blood in children during early recovery, who were administered enterosorbents of various classes for the starting therapy.

No fundamental differences in dynamics of clinical symptoms relief were detected in the comparable groups. Only duration of pathologic stool was longer than that of patients receiving polymethylsiloxane polyhydrate (5.8±0.7 and 4±0.4 days, p<0.05). Leukocyte deviation from age norm in the general analysis of blood during early recovery in patients from the analyzed groups did not show any significant differences.

Consequently, duration of pathologic stool was less in children administered polymethylsiloxane polyhydrate.

Conclusions

1. Prescribing a 3-5-day course of enterosorbents (dioctahedral smectite and polymethylsiloxane polyhydrate) in combination with oral rehydration in the starting therapy of uncomplicated colibacillosis in age-specific dosage variances was found to have a remarkable clinical performance.
2. Antimicrobials (nifuroxazide and nalidixic acid) are the medications of choice for complicated course of colibacillosis in children.

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