EPIDEMIOLOGICAL CHARACTERISTICS OF VIRAL DIARRHEA AMONG CHILDREN IN UZBEKISTAN

With the purpose of an estimation of the contribution of virus agents in the etiological structure of acute intestinal infections in children during the rise of prevalence of acute intestinal infections from 2009 to 2011 there were studied 1050 children admitted to the hospital with diarrheal diseases. It is established, that acute intestinal infections have a viral nature in 56.67% of cases. Thus the leading role belongs to rotaviruses and adenoviruses. Infectious agents of diarrheal diseases are rotaviruses in 28.1% of cases, adenoviruses - in 17.05%, and astroviruses - in 11.43%. The viral monoinfections occur more often, than mixed-infections. The rise of sporadic diseases of viral diarrhea was characterized by seasonal prevalence. For intestinal infections of viral etiology the seasonal rise in a cold season with peak of the rate of diseases of rotavirus infection in April, adenoviral infection in November, and astrovirus infection in December is characteristic.

Keywords: Acute intestinal infection, viral diarrhea, epidemiology, rotavirus, adenovirus, astrovirus, children, seasonal prevalence.

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Introduction

The acute intestinal infections are one of the current significant problems of the public health service both in developing, and advanced countries. Despite of the achieved successes in epidemiology, diagnostics, clinical pictures, pathogenic features, and medical tactics, the acute intestinal infections (AII) remain to be widespread diseases (Zhirakovskaya, Nikiforova, Korsakova, Yun, Tikunova, 2007; Gorelov, 2009). Last year’s there was noted clear change of etiological significance of pathogens, inducing acute diarrheal diseases in children (Gorelov et al., 2011; Atmar and Estes, 2006). The domination of the viral agents in occurrence of AII (about 50-70% of cases of AII in children are caused by viruses) was noted everywhere. According to WHO data each child practically has viral diarrhea irrespective of race and social-economic status within the first 5 years of life and this has the great economic burden for the system of public health services and all society (Masankova et al., 2009; Bulanova et al., 2009). It is well-known, that children of early age are the most vulnerable contingent for viral diarrhea (Gorelov et al., 2011; Parashar, 2003).

The results of large foreign researches testify to existence of significant geographical distinctions in prevalence of viral diarrhea. It is necessary to note, that now the questions of prevalence of roto-, adeno-, and astrovirus infection with children and features of their seasonal distribution remains to be insufficiently studied. However, the study of etiological structure of viral diarrhea represents the large practical importance for development of measures for their prevention, monitoring and treatment.

The purpose of this study was to find out a place of rotaviruses, adenoviruses, and astroviruses in the etiological structure of acute intestinal infections in children depending on a season of year.

Materials and methods

In order to evaluate the contribution of viral diarrhea into etiological structure of acute intestinal infections, as well as to elucidate some questions of this pathology we studied 1050 children at the age from 6 months till 5 years with acute intestinal infection who
underwent inpatient treatment in the clinic of Research Institute of Virology of the Ministry of Health of the Republic of Uzbekistan during the period from February 1, 2009 to January 31, 2011.

All patients, who was under supervision, were performed common clinical, biochemical investigations, coproscopy, bacteriological investigations of faeces for identification of Shigella, Salmonella and opportunistic pathogenic agents of microflora. The bacteriological study of washing water from the stomach and study of feces for identification of Yersinia and Campylobacter was performed according to indications. The patients with negative results of bacteriological investigations were carried out additionally direct haemoagglutination test analysis for identification of antibodies to Shigella Flexner and Zonne, microorganisms of Salmonella (diagnosticums of the Russian Academy of Science “Biopreparation” St. Petersburg of Research Institute of Vaccines and Sera and G.N.Gabrichevskiy enterprise on manufacturing of bacterial preparations, Moscow).

The collection of clinical material was carried out during the first days of the patient staying in the hospital, but not later than the third day from the beginning of disease. The feces of the patients were collected in single plastic containers with transport medium containing cryoprotector and preservative. The samples were frozen at - 20°C and were stored till test. For possible performance of the repeated analysis the studied material was stored at - 70°C. The collected samples of faces were tested with using of ELISA method for presence of rotaviruses, adenoviruses, and astroviruses with use of test-system Aquaplast (St. Petersburg).

For performance of PCR analysis the samples of faces were collected in first 48 hours after admission to the hospital. The isolation of the nucleic acids from faces was performed with using of test-kits “Ribo-sorb” and “DNA-sorb B’ (CSRI of epidemiology, Moscow) with the method of affine sorption of nucleic acids on the silicate gel. The complete set of reagents “Reverta-L” was used for obtaining of complementary DNA. To detection of bacteria and viruses there was applied the test of system AmplySence ® (Moscow): “Shigella species, EIEC”, “Salmonella species”, “Campylobacter species”, “Rotavirus-290”, “Adenovirus-462”, “Astrovirus-165”.

The selection of the patients was performed by a method of randomized selection during all seasons of year. The selection of the samples was required for bacteriological cultivation as well as examination with EIA and PCR (in 95 patients) at the first day of admission to the hospital before the onset of etiotropic therapy.

Criteria of diagnostics for viral diarrhea in children were anamnesis data including acute onset of disease from symptoms of gastroenteritis, short incubational period, family contact or cases of disease in children’s collective, seasonal prevalence and results of laboratory examinations showing absence of bacteria in the faeces of the patients, and detection of an antigen (virus) at IEA and PCR-diagnostics.

The statistical analysis of the data received was performed according to the standard methods of variation statistics with use of the program Statistica 6.0 for Windows. The differences were considered statistically significant at p<0.05. Written informed consent was obtained from parents of each enrolled patient.

Results and discussion

The results of our investigations show rather high level of morbidity rate with viral diarrhea in the region: from 1050 samples with diarrheal diseases the virus antigens were are revealed in 595 samples, which in average accounted for 56.67%. Etiology of AII for the period of investigation was identified in 64.67 % of children. Among identified viral infections the most often infectious agents were rotaviruses in 295 patients (28.1%), adenoviruses - in 179 (17.05%) patients and astrovirus in 121 (11.43%). Bacterial infection was revealed only in 8.0% of cases (84 patients), that was reliably rare in relation to rotaviruses, adenoviruses, astrovirus and intestinal infection of unknown etiology (p<0.001). From them salmonella were found out in 5.1% (53 patients), and Shigella in
2.9% (31 patients). Etiological agent was not identified by the used diagnostic methods in 35.33% of cases at presence of a clinical picture of AII. Probably, reason of disease in these cases were others microorganisms, not identified in this research.

In the overwhelming majority of cases the viral infections in children were developing as mono-infection (in 473 from 595 patients) and rarely as mixed-infection (in 122 patients). Bacterial mono-infections were found in 57 patients (5.43%). The results of studying mono- and mixed infections in the patients with AII are presented in table 1. As it is visible in the table 1 during study period in the etiological structure of AII among identified mono-infections rotaviruses prevailed (21.0%) in comparison with other pathogens, that was statistically reliable in relation to astroviruses, salmonella and Shigella (p<0.001). Adenoviruses occupied the second place on frequency of detection (14.0%). Astrovirus were the third significant etiological pathogens in comparison with salmonella and shigella (p<0.001). The fourth was salmonella 31 (2.95%). The fifth etiological agent was shigella which was identified in 2.48% cases, that was reliably less often in comparison with rotaviruses, adenoviruses and astroviruses (p<0.001).

Table 1. Frequency of mono- and mixed-infections identification in children with AII

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Mono-infection</th>
<th>Mixed-infection</th>
<th>Total frequency of identification</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Abs.</td>
<td>%</td>
<td>Abs.</td>
</tr>
<tr>
<td>Rotaviruses</td>
<td>221</td>
<td>21</td>
<td>74</td>
</tr>
<tr>
<td>Adenoviruses</td>
<td>147</td>
<td>14</td>
<td>32</td>
</tr>
<tr>
<td>Astroviruses</td>
<td>105</td>
<td>10</td>
<td>16</td>
</tr>
<tr>
<td>Salmonella</td>
<td>31</td>
<td>2.95</td>
<td>22</td>
</tr>
<tr>
<td>Shigella</td>
<td>26</td>
<td>2.48</td>
<td>5</td>
</tr>
<tr>
<td>Intestinal infections of unknown etiology</td>
<td>-</td>
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</tr>
</tbody>
</table>

We analyzed frequency of identification of mono-viral diarrhea during the all period of study on months, in different seasons of year, peak of morbidity with rotavirus, adenovirus and astrovirus diarrhea was noted in 2009, 2010, and 2011. In different seasons during one year there was change of dominant viral diarrheal diseases. So in the winter – spring seasonal period (January-May) there was observed the peak rotavirus infections, the greatest growth of number of cases of adenoviral infections was found from September till February (autumn-winter) and the astrovirus were identified in the sick children during the year, however the rise of morbidity rate was noted from October to December. The comparative analysis of their frequency of identification during all months of study it is established, that frequency rotaviruses identification fluctuated from 0.5% to 22.6%, adenoviruses - 0.7% to 22.4% and astrovirus from 0.95% to 26.7%.

Rotavirus infection had the expressed seasonal prevalence with rise of frequency in the winter period and further increase in a spring season. In spite of the fact that rotavirus infection was found out mainly in time of cold weather, in some sporadic cases it was revealed also in summer (Figure 1). The rise morbidity rate began in January and achieved the maximal meaning in March and April. The peak of morbidity rate was noted in April. The lowest frequency of detection of rotavirus infection at children was revealed from June to October.

For adenoviral infection the seasonal prevalence was also characteristic. The rise of frequency of identification was revealed from September to February, with the maximal peak in November.

The quantity of the revealed positive tests of astrovirus changed within all the year. In September the share of the revealed astrovirus was 0.95%. Rise of astrovirus diarrhea observed in October and November, and peak of disease was noted in December, that
accounted for 26.7%, leaving behind more widespread rotavirus and adenovirus infections.

The results of our investigations show that the frequency of viral agent identification in different seasons is various (Figure 2).

**Figure 1. Frequency of identification of pathogens of viral diarrhea by months over the whole period of observation**

**Figure 2. Frequency of mono-viral diarrhea in various seasons (% of number of specimens collected over the period of observation)**

In winter among identified mono-infections the astrovirus prevailed (49.5%). The second place was occupied by adenoviruses (45.6%) and third place was given to rotaviruses (28.5%).
In spring there was observed domination of rotaviruses (59.3%), then astrovirus (13.3%) and adenoviruses (7.5%), respectively.

In summer there was observed single cases of viral diarrhea in children, but among them the astrovirus infection (7.6%) was more often revealed in this period.

In autumn there were leading adenoviruses (42.8%) in comparison with rotavirus and astrovirus (against 7.3% and 29.5%, respectively), with the maximal frequency in December.

Thus, the results of investigations performed show that viral diarrhoeas are one of considerable etiological causes in development of diarrheal diseases in children. And viral diarrhea meets more often as mono-infections.

For viral diarrhoeas the seasonal prevalence is characteristic and they are revealed mainly in cold season. The change of leading viral diarrheal diseases occurs in various seasons during a year.

Discussion

Early diagnosis of diarrheal diseases promotes a choice of correct tactics of treatment, elimination of complications and prevention of the large economic burden in system of public health services. Therapeutic tactics at viral diarrhoeas differs strongly from tactics of treatment of AII of bacterial nature. At the establishment of bacterial nature of AII with heavy clinical course the etiotropic therapy with antibiotics is prescribed. In cases of viral AII antibacterial therapy had no positive therapeutic effect and, on the contrary, can extend regres of clinical symptoms of disease, worsen a condition of the patients and promote development of complications. Last years it has been proved that the duration of disease and its outcome in viral diarrhoeas depends on time and adequacy of treatment. Above stated emphasizes necessity of early diagnostics and specifications of etiological factor clinic-laboratory and epidemiological features of viral diarrhea in children.

Conclusion

The results of the studies performed indicated about wide prevalence of viral diarrhea in children in region and their etiological significance in the structure of acute intestinal infection. Diarrheal diseases in 56.67 % of cases have a viral nature. The high viral prevalence in etiology of diarrheal diseases were confirmed in another data published in in Europe, America and Asia, including neighbor Tajikistan and Russia Federation. Thus, the leading role belongs to rotaviruses and adenoviruses. Infectious agents of diarrheal diseases were rotaviruses in 28.1% of cases, adenoviruses in 17.05%, and astroviruses in 11.43%. The proportion of rotavirus infection observed in our study corresponds to sentinel surveillance data performed in Uzbekistan in 2005-2009 (Latipov et al., 2011). The viral mono-infections are identified more often than mixed infections. According to published data the prevalence rate of astroviruses and adenoviruses varying between 5% and 16% worldwide (Palombo and Bishop, 1996; Gaggero et al., 1998; Walter and Mitchell, 2000; Langley, 2005) that corresponds to our findings.

Bacterial infections are took much smaller role in causing of gastroenteritis, and did not exceed 8%. However, this corresponds to the data on the prevalence of these pathogens in the world (Niyogi, 2005; Haimovich and Venkatesan 2006; Navaneethan and Giannella 2011).

For intestinal infections of viral etiology the seasonal rise in a cold weather with peak of cases of rotavirus infections in April, adenovirus infection in November, and astrovirus infection - December is characteristic. Our results of seasonal trend of rotavirus infection are differing from data received during sentinel surveillance in 2005-2009 (Latipov et al., 2011), then the main distribution was detected in autumn and winter season with peak in October. Such differences could be explained by limitation of our study. We have included just one hospital in urban area that could not fully represent situation in whole
country, including rural area. Also in our study we are used more sensitive and specific test (PCR) versus that used in surveillance data (ELISA).

References


