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INFORMATION TECHNOLOGIES IN CLINICAL AND PHARMACEUTICAL MANAGEMENT OF NEWBORN PATIENTS WITH ROTAVIRUS INFECTION: RETROSPECTIVE ANALYSIS

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Introduction

Viruses has one of the leading roles in human pathology, causing a large number of acute and chronic diseases. In the twentieth century, viral infections have caused far more deaths than all armed conflicts that took place during this period. For example, during the 80s of the past century, about 300 million people died from natural smallpox, and influenza virus caused about 100 million deaths, mostly during Spanish influenza pandemic of 1918-1919 and later pandemics [1-7]. Although the number of deaths caused by viral infections has decreased significantly, they continue to be a significant factor in reducing overall labor productivity. For example, in the United States, there are about 200,000 hospitalizations annually caused by influenza and about 30 million cases of acute gastroenteritis, resulting in 120,000 hospitalizations annually [8].

The problem of global spread of acute intestinal infections (AII) is currently relevant [9-11], since they constitute one of the leading places among human infectious diseases, concession only the rate of influenza and acute respiratory infections [12]. The spectrum of pathogens causing AII is diverse and includes pathogenic and opportunistic bacteria, protozoa, and also viruses [13-16]. Several studies have shown that this virus are causes of 25 to 60% incidences of AII, including rotaviruses a leading role in the structure of children's AII viral etiology [17-18]. More than 110 million cases of rotavirus infection (RVI), mostly among young children, are reported annually worldwide, of which about 25 million people are being admitted to hospital. [19]. In Ukraine, the rate of RVI varied from 0.93 to 3.18 per 100,000 of total population in different years, with a lot of acute intestinal infections, which is about 45%, remained etiologically non-deciphered [20]. Analysis of the incidence of RVI recently shown its tendency to increase, especially among young children, there is a real risk for population and relevance of RVI in Ukraine [21].

The diverse spectrum of viral action on the human body, spread of viral infections and severe complications determine the relevance of effective therapy use. Currently, several antiviral drugs are known and introduced into medical practice, which belong to different groups of substances, such as nucleosides analogues, interferons, immunoglobulins G etc [22]. Ongoing relevance of viral diseases stimulates the development of new therapys, and their implementation into medical practice will be accompanied by emerging issue of their effectiveness. Optimal decision of viral disease therapy leads to quick and complete recovery of patients.

Methods of complex therapy of rotavirus gastroenteritis in children, which include symptomatic, pathogenetic and diet therapy, are aimed primarily at rehydration, detoxification of the body and normalization of intestinal microbiocenosis. In view of the lack of etiotropic therapy for RVI at present, there is an urgent need to develop therapies aimed at suppressing certain stages of rotavirus reproduction [23, 24].

Therefore, the aim of our study was a retrospective analysis of the effectiveness of pharmacotherapy of newborn patients with rotavirus infection using the developed information technology.

Materials and Methods

In our study, we proposed to evaluate therapy outcome based on survival analysis approach [25]. Since cohort of patients has two available states: alive or dead, we proposed to use two states: hospitalized and discharged from hospital. Therefore, therapy effectiveness was associated with bed days. For a certain cohort such effectiveness could be displayed as probablity curve of stay in hospital, so a lower curve reflexes higher intervention effectiveness. This could be graphically described as transmission of patients in a cohort between two states: hospitalized and discharged (Fig. 1).

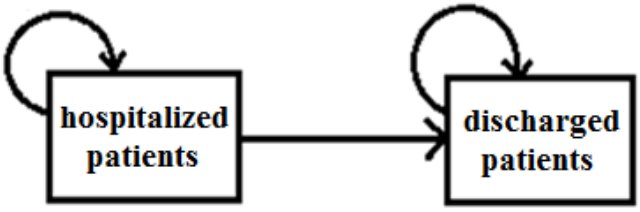

Figure 1. Transition of patients cohort between two states: hospitalized and discharged Formally, this can be described as following equations:

$$H_{t+1}=H_t-p_t\cdot H_t \quad (1)$$
$$D_{t+1}=D_t+p_t\cdot H_t$$

where H_t - proportion of hospitalized patients and D_t - proportion of discharged patients for a time t, p_t – probability of discharging in time t. Results of such modeling produced a hospitalization day probability curve (Figure 2).

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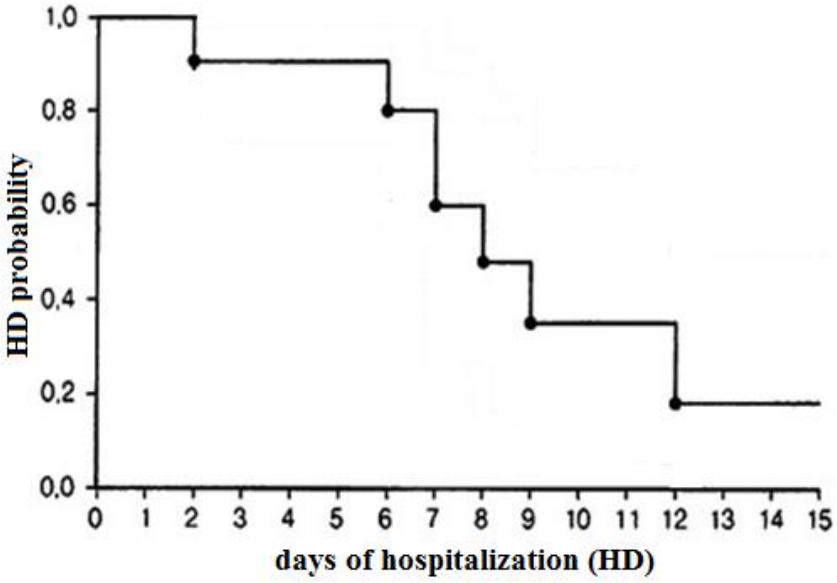

Figure 2. Hospitalization days probability

Results

This approach was based on the developed computer software "Clinical and Pharmaceutical Management of Viral Infections" and tested with the use of 85 medical cards for newborn babies from 5 to 60 days of life born in the period from 2001 to 2002, came from maternity hospitals to the intensive care unit of the NHSL "OKHMATDIT" mainly in a difficult conditions: with clinical manifestations of gastrointestinal disorders, hypoxic or hypoxic-hemorrhagic lesions of the central nervous system, hyperbaric ilirubinemia, respiratory distress syndrome, etc. The main demographic, clinical and pharmaceutical indicators of the studied patient's group are presented in software dialog box (Figure 3).

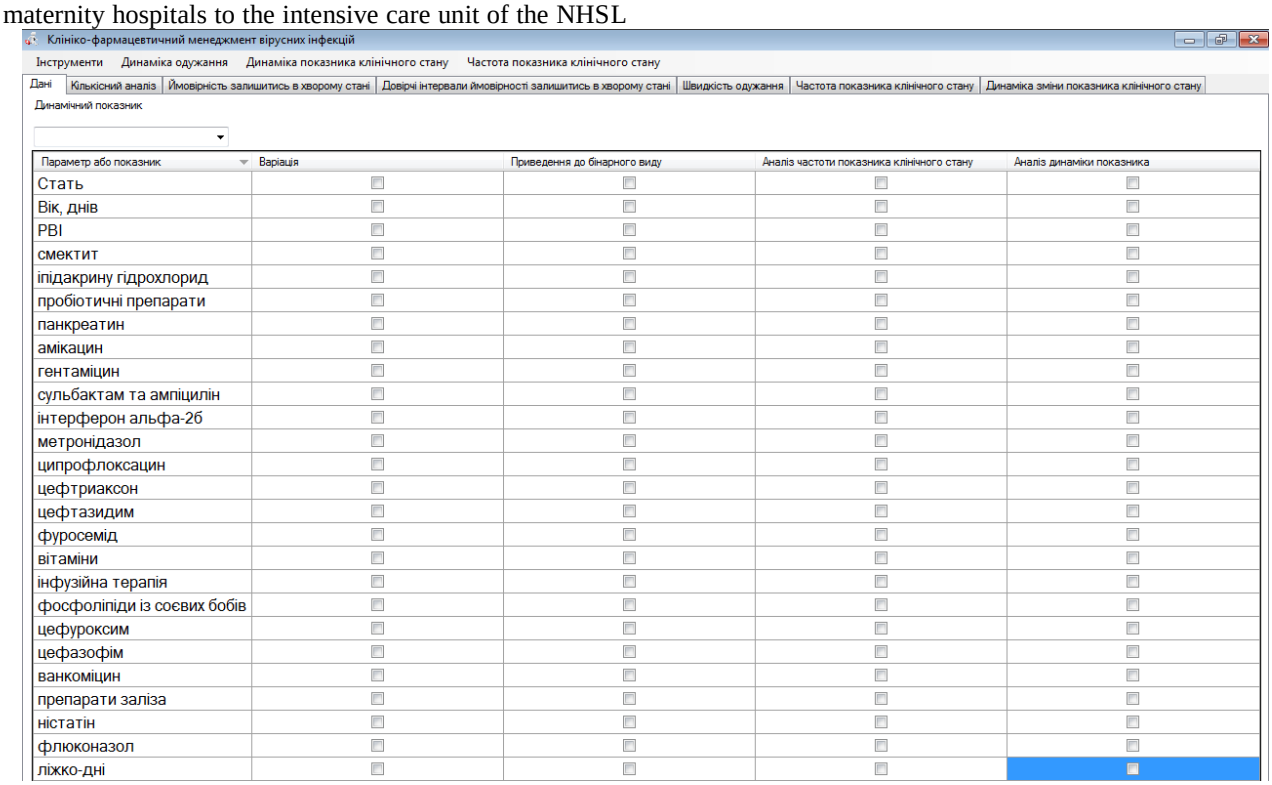

Figure 3. Computer program "Clinical and Pharmaceutical Management of Viral Infections"

Analysis of patient's medical records showed that all hospitalized patients were examined for RVI by the presence of rotavirus antigens in the clinical material (feces) by the indirect hemagglutination reaction method, the most accessible and widespread at that time in the laboratory practice. The principle of the method was that pretreated formalin or tannin erythrocytes (more often human or sheep), on the surface of which the specific

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antibodies are sorted, in the presence of a homologous antigen form aggregates, manifested by the phenomenon of agglutination [26]. Among the patients studied proved positive 60 persons (70.6%), 32 of whom received basic pathogenetic therapy.

The analysis showed that the onset of positive therapy outcomes for patients with RVI was longer, and therefore, it is more likely to remain in the hospital for the first 20 days of the disease (Fig. 4).

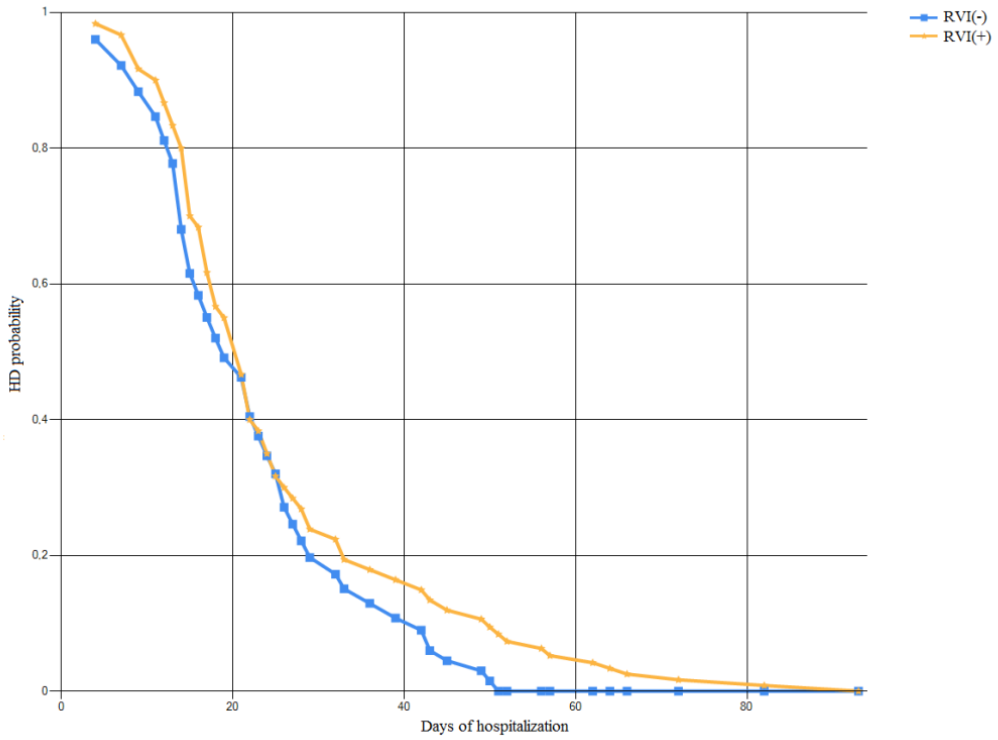

Figure 4. Hospitalization days probability (RVI presence or absence)

In a detailed analysis, both in all patients and only in patients with RVI, it was noted that the severity of the leading symptoms at the end of therapy was significantly reduced. However, the use of complex therapy with α2b-interferon was characterized by faster reverse development of clinical manifestations of the disease than in patients who did not receive interferon therapy (Fig. 5).

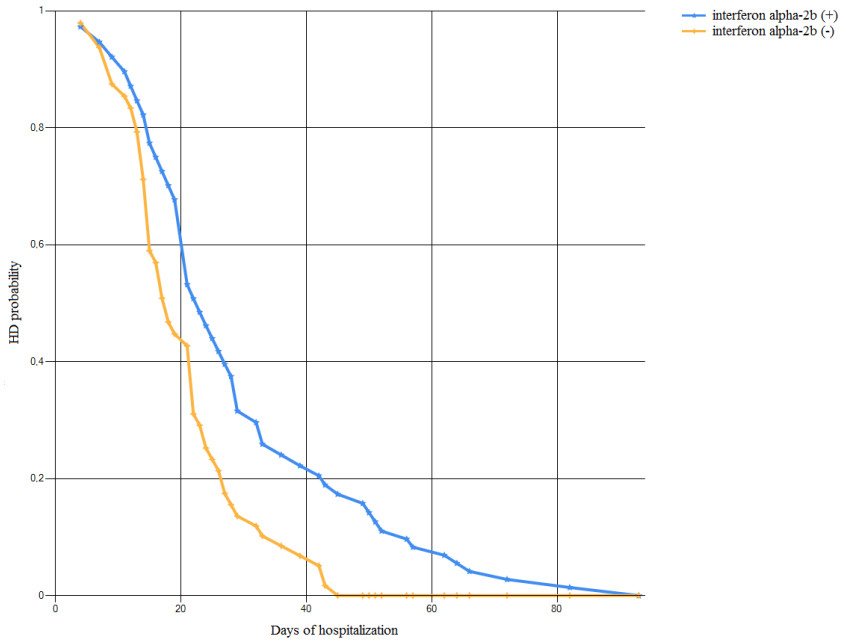

Figure 5. Hospitalization days probability (α_2b-interferon usage)

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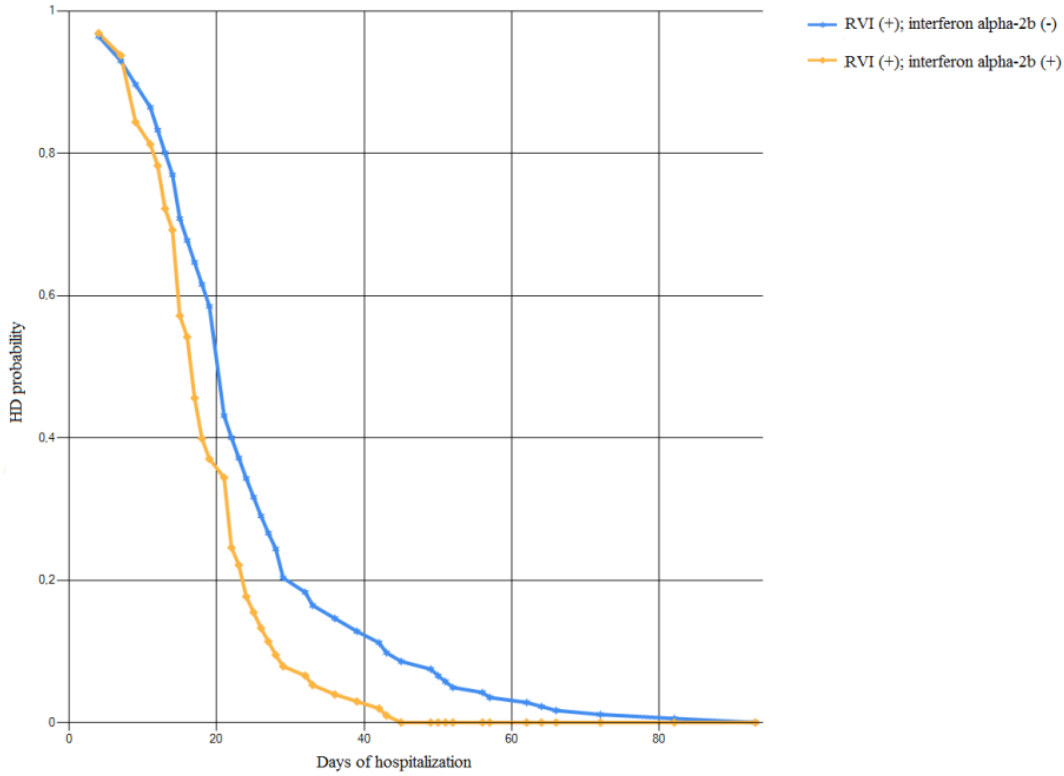

Figure 6. Hospitalization days probability (α_2b-interferon usage in RVI-positive newborn patients)

In comparison, it was also investigated the use of smectites - antidiarrheal agents of natural or synthetic origin with sorption properties. The obtained results gave a confident ability to indicate their effectiveness, which was determined by a significant decrease in the probability curve of hospitalization days, both in the analysis of patient's data (Fig. 7) and only in patients with RVI (Fig. 8).

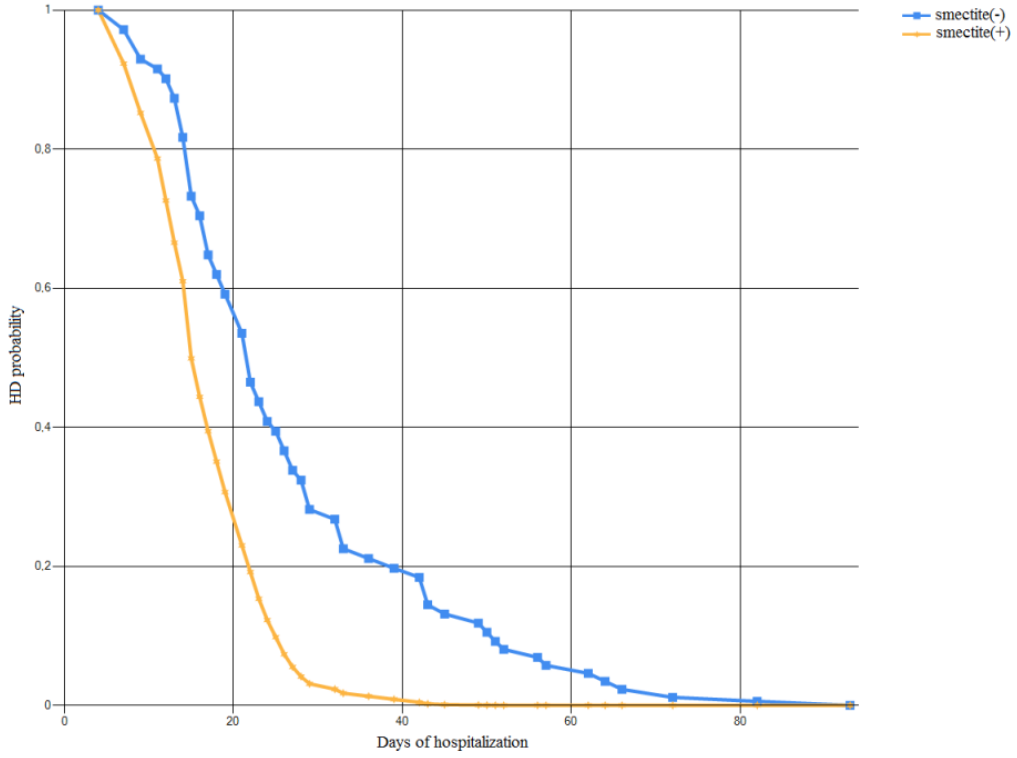

Figure 7. Hospitalization days probability (smectite usage)

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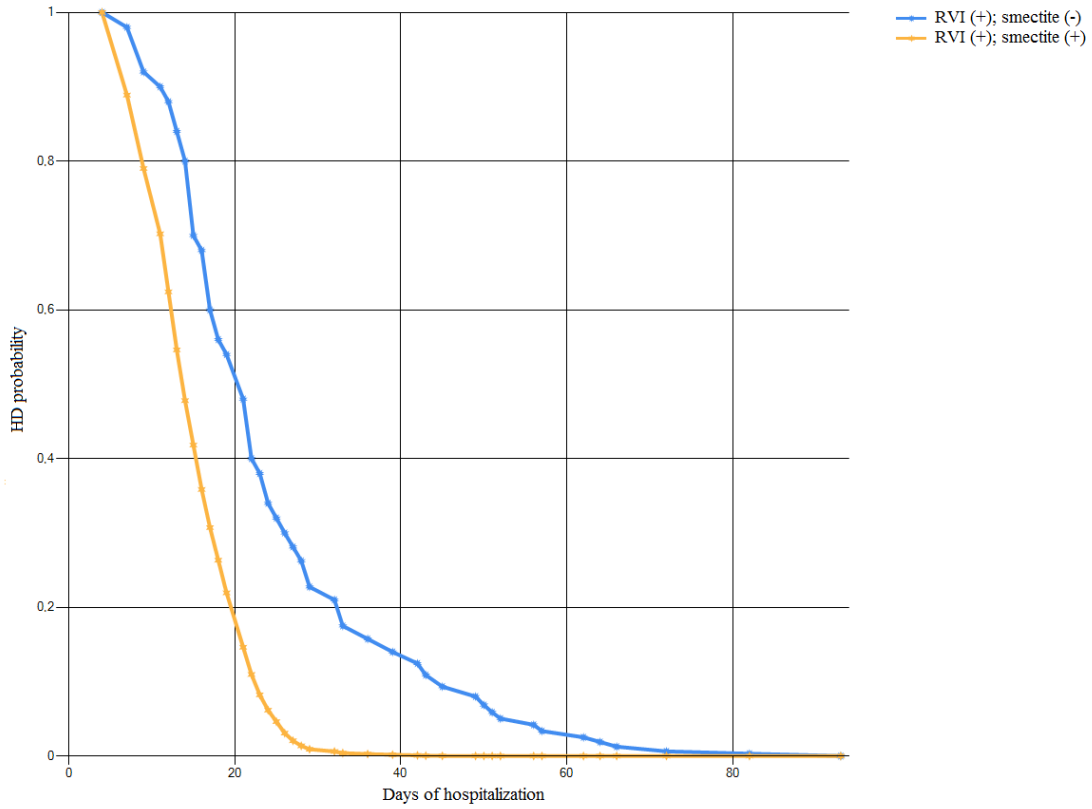

Figure 8. Hospitalization days probability (smectite usage in RVI-positive newborn patients)

Discussion

In our work, we studied the problem of optimal combined therapy for patients with RVI. In this vein, we tried to formalize this analysis and address the survival analysis technique, when the studied cohort move between two possible states [27]. This approach can be also addressed to Markov modeling in healthcare [28]. So our model is Markov, describing transition between two states, where one of which is absorbing (discharged, similar to dead in survival analysis). Markovian models are mostly used in description of chronic diseases course [29], but there are several papers, describing its use in assessment of cost-effectiveness of universal rotavirus immunization [30, 31]. The novelty of our research is that we proposed to use Markov model in evaluation of rotavirus therapy effectiveness.

The use of the proposed approach has been illustrated by analyzing the efficacy of the use of α2b-interferon and smectites with sorbitol effects in the combination therapy of newborns with RVI. The results of computer analysis confidently showed that the use of these drugs was characterized by a faster reverse development of clinical manifestations of the disease.

Definitely, our study has some limitations. In our research, we took into account only available full combinations of therapies. Nevertheless, it can be done easily for the evaluation of any single therapy of any combination of therapy effectiveness. From the other side, this is a huge analytical work, which is beyond the scope of this paper.

Conclusions

The retrospective analysis using the developed software showed that rectal application of recombinant α2b-interferon and smectites in the complex therapy of RVI in newborns can increase the clinical efficacy of therapy; namely, positively affect clinical manifestations of the disease through more rapid elimination of a number of symptoms.

The results of the study prove that ICT based on pharmacoeconomic modeling can become an effective tool for clinical and pharmaceutical management of patients in a hospital, and is a reliable source for assessing the recovery rate, which is necessary to support decision-making by the doctor in choosing the optimal patient pharmacotherapy in real time.

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Aim. A retrospective analysis of the effectiveness of pharmacotherapy of newborn patients with rotavirus infection using the developed information technology
Materials and Methods. We proposed to evaluate therapy outcome based on survival analysis approach. Since cohort of patients has two available states: alive or dead, we proposed to use two states: hospitalized and

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discharged from hospital. Therefore, therapy effectiveness was associated with durations os stay in hospotal. For a certain cohort such effectiveness could be displayed as probablity curve of stay in hospital, so a lower curve reflexes higher intervention effectiveness. This could be graphically described as transmission of patients in a cohort between two states: hospitalized and discharged patients. **Results.** This approach was based on the developed computer program "Clinical and Pharmaceutical Management of Viral Infections" and tested with the use of 85 medical records for newborn babies from 5 to 60 days of life born in the period from 2001 to 2002 and came from maternity hospitals to the 1st and 2nd outbreaks of newborns and the intensive care unit of the NHSL "OKHMATDIT" mainly in a difficult condition: with clinical manifestations of gastrointestinal disorders, hypoxic or hypoxic-hemorrhagic lesions of the central nervous system, hyperbaric ilirubinemia, respiratory distress syndrome, etc. Analysis of medical records showed that all hospitalized patients were examined for RVI by the presence of rotavirus antigens in the clinical material (feces) by the indirect hemagglutination reaction method, the most accessible and widespread at that time in the laboratory. The principle of the method was that pretreated formalin or tannin erythrocytes (more often human or sheep), on the surface of which the specific antibodies are sorted, in the presence of a homologous antigen form aggregates, manifested by the phenomenon of agglutination. Among the patients studied proved positive 60 persons (70.6%), 32 of whom received basic pathogenetic therapy. The analysis showed that the onset of positive therapy outcomes for patients with RVI was longer, and therefore, it is more likely to remain in the hospital for the first 1 to 20 days of the disease. In a detailed analysis, both in all patients and only in patients with RVI, it was noted that the severity of the leading symptoms at the end of therapy was significantly reduced. However, the use of complex therapy with α2b-interferon was characterized by faster reverse development of clinical manifestations of the disease than in patients who did not receive interferon. In comparison, it was also investigated the use of smectites - antidiarrheal agents of natural or synthetic origin with sorption properties. The obtained results gave a confident ability to indicate their effectiveness, which was determined by a significant decrease in the probability curve of hospitalization days, both in the analysis of data of all patients and only in patients with RVI. **Conclusion.** The retrospective analysis using the developed IT showed that rectal application of recombinant α2b-interferon and smectites in the complex therapy of RVI in newborns can increase the clinical efficacy of therapy, namely, positively affect clinical manifestations of the disease through more rapid elimination of a number of symptoms. The results of the study prove that ICT based on pharmacoeconomic modeling can become an effective tool for clinical and pharmaceutical management of patients in a hospital, and is a reliable source for assessing the recovery rate, which is necessary to support decision-making by the doctor in choosing the optimal patient pharmacotherapy in real time. **Keywords**: Information technologies, clinical and pharmaceutical management, newborn, rotavirus infection

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