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The efficacy of using Proteflazid in comprehensive therapy of children with chronic hepatitis B

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To date, chronic hepatitis in children represents a challenging issue of pediatrics conditioned by steady tendency towards the growth of morbidity rate. According to official figures of the Ministry of Healthcare of Ukraine, the prevalence of chronic hepatitis in children during the years 1997-2000 made 0.5%. For the period of 1992-1999 the chronic hepatitis morbidity rate increased by 68.8%.

According to data of the World Health Organization, near 50 mln persons infected with viral hepatitis B are registered annually in the world. Transmission of infection from mother to child is one of potential ways of support of natural circulation of hepatitis B virus. Among 100 newborns one infected with hepatitis B virus is registered annually in the world [1, 2].

The issues of therapy of viral hepatitis remain the most complex problems in hepatology. The aspects of viral hepatitis therapy may not be solved without taking into account pathogenetic mechanisms of the disease development. It is known that chronic hepatitis in children occurs due to insufficient macrophagal protection, disbalance and defects of a cellular component of immune system, decreasing functional activity of phagocytic system, lack of efficient specific antibodies formation, and inhibition of interferon induction, which encourages virus propagation from the infected hepatocytes into "healthy". It contributes to virus persistence and preservation of pathological process in liver with formation of clinical picture of chronic infection [3, 4].

The modern immunopathogenesis concept enables solving issues of treatment of chronic viral hepatitis on the basis of using antiviral and immunoregulatory drugs from another point. Proteflazid belongs to these drugs — a new domestic herbal drug possessing a joint action: active stimulation of production of endogenic α-, γ-interferons and interaction with viral thymidine kinase. Along with antiviral effect the drug has detoxicative and antioxidant activity [5].

The **objective** of our study consists in estimation of efficacy using Proteflazid in comprehensive therapy of children with chronic hepatitis of viral etiology.

Materials and study methods.

We observed 18 subjects with chronic hepatitis B (CHB) in the age of 7-15 years. CHB was diagnosed on the basis of anamnestic data on the presence of parenteral manipulations and clinical signs of liver impairments within not less than 6 months, as well as the data of clinico-biochemical, instrumental and serological examinations.

The complex of laboratory instrumental examinations enabled establishment of CHB diagnosis with indication of activity rate of pathological process and liver tissue fibrosis. The estimation of hepatitis activity was carried out according to recommendations of international group of experts of the World Health Organization (Desmet, 1994) by the rate of rise of organo-specific enzymes. The minimal, low, moderate and high activity was differentiated. The fibrosis rate (minimal, moderate, and pronounced) was determined on the basis of ultrasonic scanning [6, 7]. The period of CHB course followed by normalization of transaminase activity and the significant softening of the disease clinical manifestations was deemed as a remission.

Findings and discussion thereof.

The analysis of morbidity among children in Poltava region shown that boys were suffering from chronic hepatitis by 1.6 times more often than girls. Among the observed subjects 2 children were with innate viral hepatitis B. In early childhood (before 1 year) 3 children were infected. Only 4 children suffered from symptomatic form of acute viral hepatitis, where in a half of cases it was anicteric. In the rest of children the primary chronic hepatitis B was developing.

Clinically, CHB symptomatology was manifested with a moderate liver enlargement and induration (in 55% of subjects), frequent changes of size and thickness of spleen. Dyspeptic (16% of cases) and astheno-vegetative manifestations (11.3% of cases) were met quite rarely. 22.4% of children complained about belly-ache.

The data of ultrasonic scanning of children with CHB in the active phase of disease detected alterations in the form of echostructure's inhomogeneity, liver hyperechogenicity, thickening of vessels walls, gall ducts and bladder being the consequence of inflammatory process and hepatic fibrosis development — in later period. Biliary dyskinesias were encountered in 84.2% of cases, where in older children dyskinesias of hypodynamic, hypotonic type were more often observed. Intoxication phenomena (apathy, weakness, loss of appetite) were reported in 12% of subjects. Extrahepatic symptoms (palmar erythema, telangiectasia, capillaritis) were noted in 38% of children. Skin covers ochrodermia was registered in 12% of cases, icteric sclera — in 36.5% of children subjects.

The prevailing number of CHB subjects — 55.5% (10 children) transaminase activity was low and moderate. Minimal activity was reported in 33.3% (6 children), the pronounced — in 11.1% (2 children) (Table 1).

Fibrosis rate could be estimated in 12 children with CHB: low manifested in 50% (6 children), moderate — 33.3% (4 children) and pronounced — 16.6% (2 children). In 6 children no liver tissue fibrosis was noted.

For the purpose of estimation of efficacy of Proteflazid the subjects were divided in 2 groups. The groups were packaged according to the time of admission to hospital and comparable by sex, age and presence of concomitant disease.

Table 1

Average biochemical parameters values in exacerbation periods in children with CHB.

Biochemical parameters	Activity of process				Normal
	Minimal n=6	Low n=6	Moderate n=4	Pronounced n=2	
Total bilirubin, umol/l	16.2±1.9	20.4±2.1	22.6±2.6	34.7±3.8	11.5±2.2
Conjugated bilirubin, umol/l	4.8±0.3	5.3±0.5	8.7±1.1	14.4±2.3	4.4±0.7
ALT, umol/l hour	1.1±0.4	2.2±0.4	4.5±0.7	7.0±1.2	0.1-0.7
AST, umol/l hour	1.0±0.3	2.4±0.4	4.8±0.9	7.3±1.6	0.1-0.5
γ-globulins, %	16.7±1.3	18.1±1.1	24.1±1.4	27.4±5.2	14.2-1.0
Thymol test, un.	3.3±0.2	3.7±0.2	4.2±0.2	3.5±0.9	3-4
Prothrombin ratio, %	70.1±3.7	66.7±2.9	53.3±2.2	50.2±4.7	70-110

The first group consisted of children with CHB (12 children), which were taking Proteflazid in the scope of complex therapy in the period of exacerbation according to the following pattern: 4 drops in one hour after meal, three times a day for 2 days, then by 7 drops in one hour after meal for 2 months. The second group consisted of 6 children with CHB, who were taking a basic therapy only.

In the first subjects group during the first week of drug administration we observed rapid regression of clinical symptoms: weakness, fatigue, apathy. At the average, the improvements of clinical picture occurred within 11.3±1.4 days, and in second group — 16.2±1.7 days. 2 weeks later in the first group children we observed normalization or tendency to the decrease of aminotransferase activity, bilirubin level, which spoke for reduction of cytolysis processes and hepatocytes membranes permeability.

Normalization of biochemical parameters in second group children occurred for 18.4±1.2 days, at the average. The level of thymol test, which was increased, decreased significantly which could be deemed as a tendency to restoration of normal colloidal state of serum proteins [6].

Following the results of treatment with Proteflazid, the average duration of hyperbilirubinemia in first group children made 12.6±1.12 days, and the second — 18.3±2.12 days.

Simultaneously with laboratory data improvements starting from week 4 of drug administration, the significant decrease of liver and spleen size and disappearance of dyspeptic phenomena was observed.

Conclusions:

1. In the group of children, who were taking Proteflazid in complex therapy of chronic hepatitis B, the following was observed: clinical symptoms regression, normalization of biochemical parameters, the decrease of inflammatory phenomena in parenchyma, restoration of liver physiological structure in shorter periods of time than in control group.

2. Children with the torpid chronic hepatitis B course with the delayed clinical symptoms improvements, a repeated Proteflazid course was indicated, which could be carried out under the conditions of outpatient observation in a month after therapy course in hospital.

3. The obtained results enabled recommending more widespread use of Proteflazid in treatment protocols of children with chronic hepatitis B according to the following pattern: 4 drops in one hour after meal for 2 months, then 7 drops in one hour after meal for 2 months.

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In this article the effectiveness of Proteflazid application in therapy of chronic hepatitis B in children was prescribed by the following scheme: 4 drops after meals for 2 days, then 7 drops after meals for 2 months. In dynamics of treatment the clinical, biochemical and morphological changes in hepar were studied. Under the influence of Proteflazid we observed the regress of clinical symptoms, biochemical indicators and reduction of inflammatory changes in hepar parenchyma in shorter period.