



HEPTRAL IS USED IN LIVER DISEASES

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Running title: Pharmacology of heptral

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Abstract

Geptral (ademetionine) has a hepatoprotective, antidepressant, disintoxication, regenerating, antioxidant, and neuroprotective action. It compensates for the deficiency in ademetionine and stimulates its production in the organism, first of all in the liver and brain.

Heptral (Ademetionine) plays one of the main functions in the intermediate metabolism, takes part in the processes of methylation and transsulfuration and aminopropylation. The use of Heptral in patients with chronic liver diseases with accompanying cholestasis and encephalopathy of different degree, at depressions, related to alcohol and toxic liver disorders, is pathogenically reasoned for prevention of liver encephalopathy.

Heptral (S-adenosine-L-methionine) was given to 32 patients with chronic diffuse diseases of the liver and intrahepatic cholestasis. 16 of them had primary biliary cirrhosis (PBC). Phase I of the treatment lasted 16 days when the drug was injected intravenously in a dose 800 mg/day. It was followed by phase 2--1600 mg/day taken for 16 days. A response was registered in the majority of patients. They had relieved symptoms of asthenia, skin pruritus, jaundice. The patients with liver cirrhosis and chronic hepatitis exhibited a statistically significant fall in ALT, AST and GGTP. PBC patients showed insignificant lowering of cholesterol, bilirubin. No resistance was noted in repeated courses. Heptral tolerance was satisfactory.

The purpose of the work - to study disorders of the liver with pancreatic necrosis and try to reduce them by hepatoprotector ademetionine. Experiments were conducted on 29 inbred male rats. In animals, the study group and comparison group simulated pancreatic necrosis. Animal control group 5 minutes after the simulation pancreonecrosis ademetionine injected in a dose 11.4 mg/kg. The parameters of intensity of free radical oxidation, endotoxemia, cytolysis in the liver, pancreas and blood of the portal and hepatic veins. The study found that pancreatic necrosis accompanied by the development of liver failure, and hepatoprotector ademetionine not only protects the liver, but also the pancreas, reducing their functional and metabolic disorders.

The efficacy of Heptral® (ademethionine) was evaluated in the treatment of chemotherapy-induced hepatotoxicity in 19 patients with various malignancies. Four-week administration of oral Heptral® 400 mg twice daily was shown to reduce the level of transaminases to normal values in 10 of 12 patients with grade 1 toxicity.

Longer (2-to-4 month) use of Heptral® was required to normalize the level of transaminases in grade 2 hepatotoxicity. The chemotherapy regimen was not changed during the use of this drug.

In this study it was found out that Heptral has eliminated the main symptoms of cholestasis during the first 2-3 weeks, namely: skin itching, dyspeptic disorder, icteric coloring of skin and mucous membranes. It promotes to stop asthenia, insomnia, depression; decreases serum activity of total alkaline phosphates and concentration of bilirubin, cholesterol, lipoprotein; leads to norm the process of lipoprotein metabolism and decreases the liver size (according to the USI results). Heptral treatment results in positive effect which means decreasing frequency of complications, in particular gestosis, ChFPN, pre-term termination of pregnancy and perinatal mortality.

The aim of study was to evaluate effectiveness of heptral (S-Adenosylmethionine-Adomet) and folic acid during the acute toxic damage of the liver induced by carbon tetrachloride. Experiments have been carried out on pubertal rats. The carbon tetrachloride intoxication was performed by subcutaneous injection of CCL(4) 1 ml/kg dissolved in 1 ml of olive oil. The activity of aspartat- and alaninaminotransferases, alkaline phosphatase, the content of free and total bilirubine in the blood, as well as total oxidant and antioxidant activity of the blood, were measured by the spectrophotometric techniques. Oxidative stress, cytolyses of the hepatocytes and cholestasis were observed during CCL(4) intoxication. Heptral, and in less degree, folic acid improved liver function during the acute toxic damage, but complex therapy with heptral and folic acid revealed more expressive hepatoprotective effect. It is suggested that better positive effect of complex therapy with heptral and folic acid compared with monotherapy by each drug is probably associated with resynthesis of methionine from homocystein (toxic metabolite of adenosylmethionine) by folate. This combination allows reducing the side effects of heptral induced by homocysteine.

Aim

To assess benefit for children with malignant blood disease (MBD) of the hepatoprotector heptral.

Materials and methods

67 children with blood malignancy aged 3-14 years were examined (53 of them had acute lymphoblastic leukemia). 39 patients were in the study group (25 of them had hepatitis B or C), 28 were controls. Initially, heptral was injected intravenously (14

days) then orally (16-30 days). Activity of transaminases and number of violations of polychemotherapy protocols because of hepatic toxicity were registered.

Results

Heptral administration led to inhibited activity of AlAT and AsAT especially in non-infected patients. Protocol deviations became less frequent.

Conclusion

Heptral is a potent hepatoprotector in hepatic lesions of toxic, viral and mixed origin. Heptral is an effective drug for treating pregnant women suffering from ChG, having pathogenetic effect due to multi-sided corrective influence on excretive function of hepatic and biliary channels.

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