

URSODEOXYCHOLIC ACID AND ADEMETHIONINE AS AN EFFECTIVE COMBINATION FOR THE ANTHRACYCLINE-INDUCED LIVER INJURY TREATMENT

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INTRODUCTION: The primary method of leukemia acute treatment is the program polychemotherapy (PCT), including anthracycline antibiotics. The success of leukemia acute PCT depends on the adequate doses use and intervals of cytotoxic drugs assignment. Liver injuries on the PCT background are the limiting factor for the PCT in its entirety. The anthracycline antibiotics use is associated with the risk of the drug-induced liver injury (DILI) development.

AIMS & METHODS: The aim of study is to improve the effectiveness of treatment of the anthracycline-induced DILI through the development of new pharmacological complexes.

We examined 54 leukemia acute myeloid patients, who developed DILI in the PCT dynamics with doxorubicin during the remission induction and consolidation. All patients received ursodeoxycholic acid (UDCA) 20mg/kg 60 days in combination with ademetionine 1200 mg/day i.v. 10 days of the transition to 1200mg/day orally 50 days.

RESULTS: The increased alkaline phosphatase (ALP) activity in 2.7 times (209 ± 22.9 IU/l vs 77.4 ± 10.8 IU/l; $p < 0.05$), gamma-glutamyl transpeptidase (GGT) - in 4.3 times (94.5 ± 10.39 IU/l vs 21.9 ± 4.2 IU/l; $p < 0.05$), bilirubin - in 4.8 times (58.1 ± 8.71 IU/l vs 12.1 ± 1.33 IU/l; $p < 0.05$). ALT - in 2.1 time (54.8 ± 4.9 IU/l vs 26.1 ± 3.65 IU/l, $p < 0.05$). AST in 2.9 times (57.1 ± 6.86 IU/l vs 19.7 ± 2.36 IU/l; $p < 0.05$) was found on the PCT background compared with healthy. While the arginase blood activity decreased in 2.5 times and the concentration of the average weight molecules (AWM) increased in 1.9 times.

After 30 days of treatment the ALT and AST activity decreased in 1.9 and 2.1 times respectively; ALP, GGT, total bilirubin - in 1.4, 2.3, 2.8 times respectively. At the 36th - 60th days of treatment the cytolytic and cholestatic syndromes parameters were normalized in 44 (81.5%) pts. The correlation between the reduction of cholestasis clinical symptoms and ALP ($r = 0.76$), GGT ($r = 0.85$) activity was established. The arginase activity increased in 1.7 times on the background of decreased the AWM level in 1.5 times, reflecting the increased detoxication processes. This allows to conduct PCT in full compliance with the cytostatics administration regimen.

CONCLUSION: Thus, the combination of UDCA and ademetionine in high doses is the optimal approach to treatment and prevention of DILI, induced by anthracyclines. Disclosure of Interest: None Declared. *Gut* 2012; 61 (Suppl 3): A343