

Letter to the Editor

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Sir,

We are very grateful to Prof. Dr. Ralf Stahlmann and Prof. Dr. Dr. h.c. Kurt G. Naber for their interest in the clinical case that we have reported. We also thank the Editorial board for the opportunity to have a written discussion concerning the case. Canephron H containing extracts from Centaurium (*Centaurium umbellatum*), Lovage (*Levisticum officinale*) and Rosmarinus (*Rosmarinus officinale*) was registered and used in Russian Federation since 1994. During all that period there have been no cases of hepatic injury related to the drug reported by Russian doctors. However, it must be taken into account that the drug safety spontaneous reporting system exists only for four years. Therefore, a possibility of such cases missed still exists. Below we answer the questions of the letter's authors.

1. It is true that risperidon and clomipramine might cause hepatic injury [1, 2]. But, as we have reported, the patient was taking these two drugs regularly for two years before hepatitis occurred and there was no signs of hepatic impairment for all that time [3]. With the onset of hepatitis risperidone and clomipramine have not been withdrawn, there was no change in dose, and recovery from hepatitis occurred while the patient was still taking these two drugs. At the present time the patient is continuing the treatment with these two drugs in the same doses, and no sign of hepatic injury is marked. Remembering the role of CYP2D6 genetic polymorphism in adverse reactions to antipsychotics and antidepressants [4, 5], the patient was genotyped for CYP2D6 polymorphism. Genotype revealed was CYP2D6*1/*1, which means absence of genetic predisposition to adverse reactions to antipsychotics and antidepressants.
2. Ursodesoxicholic acid was not used because of fast improvement of cholestasis with common detoxication treatment.
3. We agree with the letter's authors concerning the Naranjo scale count being inadequate because of confusion with the names of medicinal plants. Still, answering *No* to one of the questions in Naranjo scale will lead to a total amount of «5», which corresponds to probable cause-effect relation [6].

We must notice that Canephron H was in use in Russian Federation for the prophylaxis of urinary tract infections' relapse but at the moment of writing this letter the drug has not been re-registered and is not being used. We also remind that evidence base for Canephron H remains weak: no large multicenter randomized trial was conducted to prove the efficacy and safety of the drug, therefore its use is not mentioned in American neither European expert guidelines [7], no systematic review on Canephron H is

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available at the Cochrane library. More information, including data from randomized clinical trials and spontaneous reports, is required to assess the risk of Canephron H related hepatic injury.

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