International Journal of Risk & Safety in Medicine 24 (2012) 121–122 DOI 10.3233/JRS-2012-0556 IOS Press

Letter to the Editor

Prof. Dr. Ralf Stahlmann^{a,*} and Prof. Dr. Dr. h.c. Kurt G. Naber^b

^aInstitute for Clinical Pharmacology and Toxicology, Charité – Universitätsmedizin Berlin, Luisenstr. 7, 10117 Berlin, Germany

^bKarl-Bickleder-Str. 44c, 94315 Straubing, Germany

Sir,

With great interest we read the report from Sychev and colleagues in the first 2011 issue of the *International Journal of Risk and Safety in Medicine* [2]. They describe the case of a 66-year-old woman who was admitted to internal medicine unit with jaundice of skin, mucosa, and sclera. The authors claim that the Centaurium extract in Canephron N, a herbal medicine, was most probably the cause for the severe hepatic reaction, because the drug was prescribed approximately one week before onset of symptoms which resolved after treatment with Canephron N was stopped. In Germany and other countries Canephron N is a widely used drug since 1975 for adjuvant treatment for example of urinary tract infections which consists of Centaurium herb, Lovage root, and Rosmarinus leaves powder, 18 mg of each. Hepatic reactions have not been described before in association with this medicine.

Although the case report is well written and most details are available, we miss some important information and for several reasons we doubt that the author's final conclusion is justified. Firstly, the schizophrenic patient received two other drugs which, in contrast to Canephron N, are known to cause drug-induced liver injury in rare cases (clomipramine and risperidon). Sychev and colleagues do not mention, how long these drugs had been given and if these drugs were stopped as well, when the suspicion of a drug induced hepatic failure was made. Secondly, it remains unclear why the patient was treated with ursodeoxycholic acid. A severe drug reaction - probably with an allergic background, as the authors discuss – would have justified a treatment with corticosteroids rather than treatment with a drug that is indicated for dissolution of cholesterol-rich gallstones. Thirdly, in an attempt to estimate the probability of a causal relationship between the drug and the adverse reaction the authors calculated a Naranjo score of 6. The first question in the list published by Naranjo and coworkers in 1981 is "Are there previous conclusive reports on this reaction?" In this context authors cite a paper published by Wurtz et al. in 2002. However, the gastroenterologists from Guadeloupe presented a case of a 49-year-old woman who developed jaundice in 1998 after use of Copaltra, a herbal preparation containing Coutarea latiflora and Centaurium erythreae, marketed by tropical herbs' laboratories. Wurtz and colleagues note that confusion between two plants should be considered: C. latiflora, a tropical Mexican plant from the Rubiaceae family,

0924-6479/12/\$27.50 © 2012 - IOS Press and the authors. All rights reserved

^{*}Address for correspondence: Prof. Dr. Ralf Stahlmann, Institute for Clinical Pharmacology and Toxicology, Charité – Universitätsmedizin Berlin, Luisenstr. 7, 10117 Berlin, Germany. E-mail: ralf.stahlmann@charite.de.

R. Stahlmann and K.G. Naber / Letter to the Editor

is called Copalchi in Mexico. The same name is also used to designate *Croton niveus*, which has been suggested to contain furanoterpenoids which might be hepatotoxic.

In summary, the case published by Sychev et al. cannot be used to support a suspected causal relationship between the use of Canephron N and the hepatic reaction as assumed by the authors. The two preparations, Canephron N and Copaltra, differ considerably. It is not possible to derive a score of "6" on the Naranjo scale by using the details described in the report.

References

- C.A. Naranjo, U. Busto, E.M. Sellers, P. Sandor, I. Ruiz, E.A. Roberts, E. Janecek, C. Domecq and D.J. Greenblatt, A method for estimating the probability of adverse drug reactions, *Clin Pharmacol Ther* 30 (1981), 239–245.
- [2] D.A. Sychev, A.V. Semenov and I.P. Polyakova, A case of hepatic injury suspected to be caused by Canephron N, A Centaurium Hill containing phytotherapeutics, *Int J Risk Saf Med* 23 (2011), 5–6.
- [3] A.S. Wurtz, T. Vial, B. Isoard and E. Saillard, Possible hepatotoxicity from Copaltra, an herbal medicine, *Ann Pharmacother* **36** (2002), 941–942.

122