Hepatic injury caused by mianserin

Dr S K OTANI, S KANEKO, H TASAKI, and Y FUKUSHIMA (Department of Neuropsychiatry, Hirosaki University Hospital, Hirosaki 036, Japan) write: There have been only three reported cases of hepatic injury associated with mianserin.1

We have recently observed three more cases. The first patient was a 46 year old man with depression. On the 14th day of receiving 30 mg of mianserin he developed a fever of 39.1°C. Diclofenac (100 mg/day) was prescribed for three days but had no effect. A blood analysis was then performed and cholestatic jaundice was found (table). Mianserin was discontinued and after six weeks the liver function was completely normal. The second patient was a 48 year old woman who took 20 mg of mianserin for three weeks to treat her depression. On the 22nd day the dose was increased to 30 mg and her depression was cured. Blood analysis on the 28th day showed an asymptomatic hepatic injury (table). Mianserin was discontinued, but it took three weeks before the liver function returned to normal. The third patient was a 63 year old woman. Her treatment started with 2 mg of flunitrazepam and 30 mg of mianserin, with the latter increased to 50 mg on the fifth day of treatment. On the 12th day of treatment blood analysis showed a hepatic injury (table). Mianserin was reduced to 30 mg, and 4 mg of bromazepam was then introduced. From the 19th day mianserin was further reduced to 20 mg. The liver function had returned to normal by the 26th day. Her depressive symptoms disappeared on the 33rd day and mianserin was discontinued.

All patients had normal liver function before mianserin treatment. When their hepatic injury disappeared when mianserin was discontinued or the dose reduced. Investigations excluded other diseases such as viral hepatitis. It is therefore reasonable to consider that mianserin caused the hepatic injury. With mianserin and other antipsychotic drugs, toxic metabolites have been incriminated as the cause of hepatic injury, and monitoring concentrations of these metabolites may be useful to prevent hepatic injury. In fact, on the basis of hepatic injury study, Rihet et al suggested that desmethylmianserin, the major metabolite of mianserin, is cytotoxic. Plasma concentrations of mianserin and desmethylmianserin in our patients were, however, similar to those in 20 other patients with no liver dysfunction, whose mean plasma concentration of mianserin was 105 nmol/l (range 41-213) and of desmethylmianserin 55 nmol/l (10-219).2 These findings suggest that the occurrence of hepatic injury does not depend on plasma concentrations of mianserin or desmethylmianserin, although in certain cases (such as case 3) the liver function may improve on reducing the dose. Therefore monitoring these compounds concentrations down to the hepatic injury. The manufacturer (Organon) knew of 138 cases of liver or biliary system disorders associated with mianserin treatment. Of these cases, only 23 showed an asymptomatic amphoterafransfere or alamine amotransferase value ≥ 120 U/l. Considering the wide use of mianserin, the incidence of related hepatic injury is low, but our cases suggest that liver function be checked at an early stage of mianserin treatment.

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Corrections

Hypercalcaemia in malignancy

The names of Dr S J Gallagher, Dr U Patel, and Dr 1T Boyle were omitted from the letter by Dr Stuart H Ralston (15 July, p 181).

Enteropathy induced by non-steroidal anti-inflammatory drugs

An author's error occurred in this letter by Drs 1 Butterman and J M Gould (29 July, p 326). The second sentence in the third paragraph should have read "Differentiation from Crohn's disease is easy by scanning using leucocyes labelled with indium-111 as patients with Crohn's disease have becnoimal scan within four hours whereas the other patients show abnormal results 18 hours after the "In labelled leucocytes have been given."