Deferasirox Induced Liver Injury in Haemochromatosis

Sir,

We read with interest the paper titled “Deferasirox Induced Liver Injury in Haemochromatosis” - a case report of severe liver dysfunction attributed to Deferasirox in a 63 years old female with hereditary Hemochromatosis. The initial dose of Deferasirox was 500 mg orally three times a day or about 18-25 mg/kg/day assuming a body weight of 60-80 kg (the patient’s weight was not reported). The Deferasirox product label suggests an initial dose of 20 mg/kg/day for treating transfusional hemosiderosis.1 However, the same dosing guidelines might not be applicable to patients with hereditary forms of iron overload who are not receiving regular transfusions.

In a recent phase 1/2, open label, multi-center, dose-escalation trial, a total of 49 patients with hereditary Haemochromatosis were enrolled with the primary objective to assess the safety profile of Deferasirox.2 A higher frequency of adverse effects, including renal and liver dysfunction, were reported in the cohort receiving 15 mg/kg/day. A lower starting dose of 10 mg/kg/day while maintaining adequate efficacy, had a more favourable adverse effect profile in this population of patients. It was also noted that patients with lower initial levels of body iron as measured by serum Ferritin levels, as well as those who underwent rapid reductions in serum Ferritin levels had a higher incidence of hepatic and renal adverse events. The overall incidence of adverse events in these patients was also higher than that observed in patients with transfusional iron overload.3

Since Deferasirox induced liver injury seems to be related to several factors including the dose of the medicine used, the baseline serum Ferritin level and the rate at which iron overload reduction takes place, one could postulate that the reported toxicity in this patient may have been due to the relatively large dose used. Larger studies are needed to further define the role of Deferasirox in non-transfusional iron overload syndromes. In the meantime, a lower starting dose is recommended as well as routine monitoring of hepatic and renal function tests while on therapy, especially during the initial weeks but also as iron stores are depleted.

The use of Deferasirox seems reasonable in appropriately chosen patients with iron overload given its favourable properties compared to the historic standard parenteral iron chelator Deferoxamine, including easy administration, cost-effectiveness, favourable safety profile and improved patient compliance.4

REFERENCES


Author’s Reply:

It is appropriate to use this medicine in a proper clinical setting and to follow approved guidelines for its use. Judicious and careful use of the agent is still an accepted practice. There are several initial trials in progress about the use and efficacy of this medicine and the commenter has mentioned a few of them. Currently FDA has a black box warning on the use of this medicine. The warning suggests that doctors closely monitor patients taking Exjade in particular, they should watch for changes in creatinine levels, as well as changes in the levels of transaminases and bilirubin. Reduction in weight based dosage of medicine can be an option to reduce the side effects of medicine but more studies are needed before it can be used as a standard of practice.