To the Editors:

Fulminant heptic failure in a child following paracetamol overdosing

Paracetamol is viewed as a child-friendly drug, as children were thought to be less susceptible than adults to hepatotoxicity with an overdose (1). However, there are recent reports of hepatotoxicity in children, following the ingestion of multiple doses of paracetamol (2,3). We report such a case in a child who died of fulminant hepatic failure.

A previously well 6 year old boy weighing 18 kg was admitted to hospital with fever and vomiting of 6 days' and increasing drowsiness and haematemesis one days' duration. He had been treated with paracetamol, oral penicillin, promethazine, haloperidol, phenobarbitone, a brand of paracetamol at a dose of 750 mg three times a day for 3 days (125 mg/kg/day), and an another brand of paracetamol at a dose of 250 mg/kg/day from the day before admission.

He was afebrile and anicteric, with hepatomegaly and hepatic encephalopathy (grade 3). There was no skin bleeding. The serum alanine transaminase (ALT) was 4150 IU (ref 0-40), serum aspartate transaminase (AST) 9991 IU (ref 0-40), serum bilirubin 60.9 μmol/l, prothrombin time over 60 seconds (control 13) and random blood glucose 0.82 mmol/l. His blood urea and serum electrolytes were within normal. The plasma paracetamol level

done by immunoassay was 84 μg/ml. He was treated with N-acetylcysteine, a liver failure regime and fresh frozen plasma. He deteriorated and died. A post-mortem open biopsy of the liver showed massive confluent liver cell necrosis with sparing of only a few periportal hepatocytes showing microvesicular steatosis. The necrotic liver cells contained apoptotic bodies.

Fulminant hepatitis in children is associated with massive hepatocyte necrosis or hepatosteatosis (4). Severe liver damage following overdose of paracetamol over a short period of time is defined (2) as a peak plasma ALT or AST activity exceeding 1000 IU/l, and a high prothrombin time, with a typical centrilobular pattern of hepatic necrosis, as seen in this case. Microvesicular steatosis, prodromal illness high transaminase levels and coagulopathy could also be consistent with Reye's syndrome. Factors supporting paracetamol poisoning include a history of ingestion of high doses over several days, and a plasma paracetamol level of 84 μg/ml. A level over 3.5 μg/ml at 24 hours carries a serious risk of severe liver damage (5). The prodromal illness associated with fasting, and co-administration of phenobarbitone, an enzyme-inducing drug, would have contributed to the hepatotoxicity, as they are known potentiating factors (3).

It is important for physicians to consider the possibility of paracetamol poisoning in children presenting with a prodromal illness associated with fasting, regular ingestion of paracetamol over several days, and fulminant hepatic failure with high transaminase levels, coagulopathy and relatively low serum bilirubin. The early administration of N-acetylcysteine may be life saving.

References

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