Aggravation of non-steroidal anti-inflammatory drug-induced hepatitis and acute renal failure by slimming drug containing anthraquinones

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Keywords: acute renal failure; anthraquinone; hepatitis; non-steroidal anti-inflammatory drugs; slimming

Introduction

The renal toxicities of non-steroid anti-inflammatory drugs (NSAIDs) have been well reported [1] and the mechanism of injury is thought to be mediated by haemodynamic perturbation which results in functional renal ischaemia. The typical histological abnormality is acute tubular necrosis, which is usually reversible.

Anthraquinone and its derivatives are frequently found in slimming agents and have been valued for their cathartic and presumed detoxifying action. Diarrhoea, vomiting and abdominal discomfort are common side-effects, and in severe cases, may result in dehydration. Renal and liver complications resulting from the combined use of NSAID and anthraquinone-containing slimming agent have not reported. The current report highlighted the potential risk of NSAIDs when given in a patient on weight reduction treatment. The popularity of proprietary slimming drugs obligates due precaution be taken when NSAID is prescribed.

Case

A 25-year-old lady was admitted after a 1 week history of fever, vomiting and diarrhoea. Two weeks prior to the admission, the patient consumed a proprietary oral slimming drug which was purchased over-the-counter from a drugstore. She noticed nausea, vomiting, diarrhoea and low-grade fever a few days after starting the drug. A private practitioner was consulted and she was given nimesulide and ampicillin–clavulanate. Nimesulide 100 mg b.i.d. was taken for 4 days but the patient defaulted taking the antibiotic after one single dose. The vomiting and diarrhoea persisted and she presented to the hospital for further treatment. On admission, she was afebrile but was prostrate-looking. The skin turgor was low, though the haemodynamic parameters were stable. Her renal and liver functions were impaired with serum creatinine at 431 μmol/l (normal range 82–126 μmol/l), calcium (adjusted for serum albumin level) 2.42 mmol/l (normal range 2.11–2.55 mmol/l), alanine aminotransferase (ALT) 72 U/l (normal range 6–53 U/l), aspartate aminotransferase (AST) 219 U/l (normal range 2.11–2.55 mmol/l), alanine phosphatase 206 U/l (normal range 49–138 U/l) and bilirubin 16 μmol/l (normal range 7–19 μmol/l). There was mild leucocytosis (15.4 × 109/l), predominantly neutrophilia, and the eosinophil count was not raised. Erythrocyte sedimentation rate was 35 mm/h. All serological markers were negative or normal. C-reactive protein was 26.2 mg/dl. Viral and bacteriological screenings were all negative. Liver and renal ultrasonogram was unremarkable. In the succeeding 3 days, the renal and liver function remained deranged. A renal biopsy was performed and histological examination showed features of acute tubular necrosis. It was believed that the tubular injury was related to the use of nimesulide superimposing on the volume depleted state induced by the cathartic slimming agent. Conservative treatment was resorted to. Her renal and liver function improved spontaneously and she remained haemodynamically stable. Two weeks after admission, her renal and liver function completely normalized.

Chemical analysis of the slimming drugs was performed using gas chromatography-mass spectrometry [2]. Emodin and related anthraquinone derivatives (chrysophenol, physcion, obtusin) were detected. The chemical profile of the drug was compatible with Cassia obtusifolia, one of the claimed constituents of

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the product. Aristolochic acid and related compounds were not detected.

Discussion

Non-steroidal anti-inflammatory drug (NSAID)-induced liver and renal toxicities have previously been reported [1,3]. The temporal proximity of NSAID intake and the clinical presentation of the patient was supportive of a causative relationship. The reported patient had also consumed a non-prescriptional slimming regime 1 week prior to her initial presentation. Chemical analysis of the drug showed the presence of emodin and related anthraquinone derivatives which were compatible with C. obtusifolia. Anthraquinones belong to a group of natural stimulant laxatives that are often present in plants in the form of glycosides. These compounds are found in rhubarb root, senna leaf and pod, cascara sagrada, buckhorn and aloe. In a local consumer products survey, it was found anthraquinone stimulant laxatives were detected in 22 formulae of detoxifying and slimming products, ranging from 0.0007 to 1.597% [4]. The presence of herbs containing anthraquinones is, unfortunately, usually not disclosed on the labels. Anthraquinones may cause nausea, vomiting, abdominal cramps and diarrhoea with both therapeutic dose and overdose. Metabolites of anthraquinones can be absorbed and enter the enterohepatic circulation. A considerable portion of the substance accumulates mainly in the kidneys and is only released and eliminated very slowly [5]. Incorrect, longer-term intake and daily use could result in interactions between laxatives and macromolecules in the kidney [6]. Oliguria and proteinuria may be seen in severe cases and large doses of anthraquinones may cause nephritis [7].

Cases of rare hepatic inflammation possibly induced by anthraquinone derivatives have also been reported [8,9] and may be dose related. It was suggested that the anthraquinones may be metabolized in the intestine to form a hepatotoxic compound that some people were sensitive to, which ultimately resulted in reversible liver damage.

In our patient, use of the anthraquinone-containing slimming drug is unlikely to be the sole cause of her acute renal and hepatic impairment. Alternatively, the dehydrated state as caused by the cathartic slimming drug, when superimposed upon by the administration of NSAID, might have compounded the toxicity on both the liver and the kidney. The histological feature of acute tubular necrosis and the prompt recovery were also supportive of a reversible toxic insult.

In conclusion, for patients commenced on slimming drug therapies, especially those with laxative action, careful monitoring of hydration status is imperative. Concomitant administration of NSAIDs may lead to catastrophic consequences.

Conflict of interest statement. None declared.

References

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Received for publication: 13.12.03
Accepted in revised form: 13.1.04