Poisoning due to an over-the-counter hypnotic, Sleep-Qik (hyoscine, cyproheptadine, valerian)

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Summary

The clinical features and risk of hepatotoxicity of 'Sleep-Qik' (valerian dry extract 75 mg, hyoscine hydrobromide 0.25 mg, cyproheptadine hydrochloride 2 mg) were determined in 23 patients treated in our hospital between 1988 and 1991. The main clinical problems were central nervous system depression and anticholinergic poisoning. There was no clinical evidence of acute hepatitis in the 23 patients after taking an average of 2.5 g of valerian (range 0.5 to 12 g). There was no evidence of subclinical liver damage in 12 patients who had routine liver function tests performed approximately 6–12 hours after ingestion. Delayed onset of severe liver damage was excluded in 10 patients in whom a telephone follow-up was possible. However, subclinical liver dysfunction in the acute stage (onset after 12–24 hours) and in the intervening period after discharge from hospital could not be excluded. To establish the risk of hepatotoxicity in long-term users and in those taking an overdosage of valerian, a much larger study of longer duration with serial liver function tests is clearly needed.

Keywords: poisoning, hypnotic, Sleep-Qik

Introduction

In Hong Kong, self-medication with both Western drugs and Chinese herbal medicines is a very common practice.¹ This may be reflected to some extent by the particular choice of agents used for self-poisoning. From 1988 to 1991,² over-the-counter hypnotics and Chinese herbal medicines and medicinal oils accounted for approximately 12% of the main agents involved in self-poisoning.

In view of the lack of clinical data on combined cyproheptadine/hyoscine poisoning in adults, and recent concern about valerian's hepatotoxicity,³ we reviewed 23 cases of self-poisoning with 'Sleep-Qik' (hyoscine hydrobromide 0.25 mg, cyproheptadine hydrochloride 2 mg, valerian dry extract 75 mg).

Patients and methods

The Prince of Wales Hospital is the sole general teaching hospital in the New Territories East of

Hong Kong, serving a population of 1.1 million in 1994.

These 23 patients, who were identified from the admission books in four general medical wards, were admitted during a four-year period between 1988–91. Their hospital records were reviewed and the following information noted: demographic data, past history of chronic liver diseases, other agents taken, and the outcome.

Wherever possible, these subjects were contacted by telephone during October 1993 to confirm that they remained well after discharge from hospital.

Results

Nine men and 14 women, with a mean age of 23.8 years (range 15 to 37) took 'Sleep-Qik' mostly after some emotional upset or social crisis. Six patients also took alcohol (n = 2), other drugs (n = 3), a pesticide (n = 1) or 'Pansedan' (n = 1) (*Passiflora* extract, *Viscum album* extract, *Uncaria rhynchophylla* extract, *Humulus lupulus*). Apart from two patients with a past history of psychiatric illnesses, all were previously healthy. Four of the 23 patients had previous admissions with self-poisoning.

The alleged mean number of 'Sleep-Qik' tablets ingested was 33, range 6–166. The average time between ingestion and admission to an accident and emergency department was 2.8 hours. Four patients were asymptomatic. The signs and symptoms in the remaining 19 patients included drowsiness (n = 11), dilated pupils (n = 11), tachycardia (n = 6), nausea (n = 4), confusion (n = 3), urinary retention (n = 3), visual hallucination (n = 2), flushing (n = 2), dry mouth (n = 1) and dizziness (n = 1). Two patients who were drowsy or confused at presentation had also taken 'Pansedan' or alcohol, respectively.

Fifteen patients received gastric lavage (n = 14) or syrup of ipecac (n = 1). One patient who had taken 60 tablets of 'Sleep-Qik' alone required overnight admission to the intensive care unit for ventilatory support.

One set of routine liver function tests was ordered on admission in 12 patients and these were all within normal limits. Patients who were drowsy or confused at presentation became well within 24 hours. All 23 patients had completely recovered when discharged from the medical wards after an average of 1.7 days (range 1–6 days). Two patients were transferred to psychiatric wards for further management.

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Telephone contact was possible in 10 patients (including five without liver function tests measured as an in-patient), at an average of 43 months after the overdosage (range 27 to 65). These patients had remained well after discharge and none had continued taking 'Sleep-Qik'.

Discussion

Hyoscine hydrobromide, an antimuscarinic drug, is primarily used in the control of motion sickness and as a premedication to dry bronchial and salivary secretions. In acute overdosage, the main clinical problem is central nervous system (CNS) depression.

Cyproheptadine hydrochloride is a histamine H_1 -receptor antagonist and serotonin antagonist which also has antimuscarinic effects. It is primarily used for the symptomatic relief of urticaria, angioedema, rhinitis, and pruritic skin conditions. Other indications include migraine, anorexia, pituitary-dependent Cushing's syndrome and Nelson's syndrome, and carcinoid syndrome. Deaths following overdose are seen mainly in infants or young children. Fatal dosages are quoted as ranging between 25 and 250 mg/kg. Other toxic effects mainly relate to its antimuscarinic actions.

Valerian, derived from the underground parts of *Valeriana officinalis* L, has long been used in north-western Europe as a sedative.⁵ In the UK, it is commercially available in 85 herbal preparations including 'Kalms' and 'Neurelax'.⁶ The main constituents of valerian are volatile oils and the iridoids (valepotriates).⁵ The herb also contains small amounts of other alkaloids.

The clinical features of 'Sleep-Qik' poisoning seen in our patients can be attributed to the peripheral and central actions of its three constituents. However, during concurrent ingestion of hyoscine, cyproheptadine and valerian, such as in 'Sleep-Qik' poisoning, both the CNS depressant and anticholinergic effects are enhanced.

The cytotoxicity^{5,6} and hepatotoxicity³ of valerian are causing concern, particularly when long-term use is involved. Some valepotriates have been shown to be highly cytotoxic in experiments using cultured rat hepatoma cells.⁷ A time- and dose-related inhibition of incorporation of [¹⁴C]thymidine into the DNA of Ehrlich ascites carcinoma cells has been found, suggesting covalent binding of valepotriates to these cells.⁸ However, no significant effect could be observed in *in vivo* experiments when

Side-effects

Hyoscine:

- antimuscarinic drug
- drowsiness, confusion, coma
- bradycardia, tachycardia, hypotension
- blurred vision, dry mouth, urinary retention

Cyproheptadine hydrochloride:

- anti-histamine, -serotonin and -muscarinic effects
- CNS depression
- hallucinations, ataxia, convulsions

Valerian:

- ? acute hepatitis
- hypersensitivity

the valepotriates (valtrate 8a) were given orally or intraperitoneally.⁵

There is a lack of toxicology data regarding valerian in man. Four cases of liver damage and acute hepatitis were recently reported, following the use 'Neurelax' or 'Kalms', both of which contain skullcap (*Scutellaria gavericulata*) as well as valerian.³ Liver damage in these patients occurred days to months after taking these herbs, and was thought to be due to hypersensitivity reactions. Skullcap was present in a preparation containing mistletoe⁹ and in another herbal preparation 'BFC' that caused hepatitis.¹⁰

In this study, there was no clinical evidence of acute hepatitis in 23 patients after taking an average of 2.5 g of valerian (range 0.5 to 12 g). The amount actually absorbed was likely to be smaller in those subjects who developed vomiting or had gastric lavage. There was no evidence of subclinical liver damage in 12 patients who had routine liver function tests performed approximately 6 to 12 hours after ingestion. Delayed onset of severe liver damage was excluded in 10 patients in whom a telephone follow-up was possible. However, subclinical liver dysfunction developing acutely after 12 to 24 hours and in the intervening period after discharge from hospital could not be excluded.

The main clinical problems following overdosage of 'Sleep-Qik' are CNS depression and anticholinergic poisoning. To establish the risk of hepatotoxicity in long-term users and in those taking an overdose of valerian, a much larger study of longer duration with serial liver function tests is clearly needed.

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