Human & Experimental Toxicology (1995), 14, 187–189
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The clinical value of screening for paracetamol in patients with acute poisoning

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In this retrospective study, we determined the clinical value of screening for paracetamol in 294 Chinese patients with acute poisoning presenting to the general medical wards at the Prince of Wales Hospital between January 1992 and June 1993. Of the 86 patients suspected of having ingested paracetamol, eight had levels above the recommended 'treatment line'. Of the 208 patients with no suspected paracetamol ingestion, four were found to have elevated but non-toxic plasma levels. The incidence of missed, potentially serious paracetamol poisoning in our patients with no suspected paracetamol ingestion is extremely uncommon. Routine screening of all patients with acute poisoning for toxic plasma paracetamol concentrations is therefore not indicated and should never be a substitute for thorough history taking and physical examination.

Introduction

In overdosage, paracetamol (acetaminophen) causes liver and renal damage through the formation of a highly reactive metabolite that binds covalently to sulphydryl groups intracellular, once cellular glutathione has been depleted.[1,2] Fortunately, these complications can be prevented if intravenous N-acetylcysteine (NAC), which acts primarily by replenishment of cellular glutathione, is given within 10 h.[3] NAC is much less effective if given more than 15 h after overdose.[1,3]

Since paracetamol poisoning has no specific clinical manifestations in the early stage, diagnosis is often based on the history of ingestion and plasma paracetamol concentration measurement. However, history of ingestion is often unreliable.[4] Consequently, there may be a delay in recognition and treatment of the poisoning resulting in unnecessary morbidity or even mortality. Thus, many physicians routinely request plasma paracetamol measurement in all patients with acute poisoning.

In this retrospective study, we determined the clinical value of screening for paracetamol in 294 Chinese patients with acute poisoning presenting to the general medical wards at the Prince of Wales Hospital between January 1992 and June 1993. This is the sole general teaching hospital in the New Territories East of Hong Kong, serving a population of 1.1 million in 1993.

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(Received 15 March 1994; accepted 10 May 1994)

Subjects and methods

During the 18 month period, patients with acute poisoning in whom plasma paracetamol measurements had been performed were identified from the registry of requests in the Department of Chemical Pathology. They represented approximately 44% of the total number of patients admitted because of acute poisoning.

The hospital records of these patients were reviewed. Demographic data and information regarding diagnosis, reason for poisoning, agents involved, treatment given and the outcome were noted. The diagnosis of poisoning and identification of agents responsible were based on the history from the patient/witnesses, labelling on the bottles and/or the clinical features.

In our 24 h urgent laboratory, plasma paracetamol concentration is measured by the TDX method (Abbott Laboratories, USA). The detection limit of this method is 0.1 mmol l^{-1}.

Results

The patients were 77 men and 117 women, with a median age of 28 years (range 14–90). Poisoning was considered to be accidental in three patients. The majority of patients (99%) poisoned themselves after an emotional upset, social crisis, physical illness or alcohol/drug abuse. Routine instead of urgent requests for plasma paracetamol measurement was made in 13 patients (three in those suspected of having ingested paracetamol).

In 86 patients, ingestion of paracetamol or paracetamol-containing drugs with or without chemicals

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Table 1 Plasma paracetamol measurement in 294 Chinese patients with or without a history of paracetamol poisoning

	Plasma paracetamol concentrations (mmol l^{-1})		
	< 0.1	≥ 0.1 (but not toxic)	Toxic*
Paracetamol ingestion: suspected (n = 86)			
Drugs identified (n = 68)	25	35	8**
Nature of drugs known but not identified (n = 18)	12	6	0
Paracetamol ingestion: not suspected (n = 208)			
Drugs identified (n = 80)	77	3	0
Nature of drugs know but not identified (n - 66)	65	1	0
Unknown drugs	2	0	0
Drugs not involved (e.g. chemicals, town gas) (n = 60)	60	0	0

*Plasma paracetamol concentration above the 'treatment line' joining semilog plots of 1.32 mmol l^{-1} at 4 h and 0.2 mmol l^{-1} at 15 h after ingestion.
**Three patients developed liver damage.

was suspected (Table 1). Eighteen of these patients took unknown drugs for pain, fever or upper respiratory tract infections. Of the eight patients with plasma paracetamol levels above the recommended 'treatment line',[4] three developed liver damage but then recovered completely.

In 208 patients, ingestion of paracetamol was not suspected (Table 1). All the 60 patients who had not ingested drugs had no detectable plasma paracetamol (< 0.1 mmol l^{-1}l). In the remaining 148 patients, none were found to have toxic plasma paracetamol levels.

Discussion

In Hong Kong, paracetamol is commonly used for self-poisoning, and is widely available under several brand names as well as in combination with other drugs or herbal medicines. From 1988 to 1993, there were at least 210 adult cases treated in the Prince of Wales Hospital.[5] There are at present more than 700 adult and paediatric preparations containing paracetamol registered with the Government.

In Hong Kong, the management of patients with drug overdosage may be more difficult than elsewhere.[6] Over-the-counter (OTC) medicines are easily available and self-medication is a very common practice. Patients usually know the nature but not the exact names of their medications. Even if these are brought to the hospital, the containers, often plastic bags, may not be labelled. The same drug may be available in different colours and shapes making positive identification difficult. Diagnosis may be missed, particularly in patients taking mixed overdosage.

There are only a few major indications in clinical toxicology for the urgent measurement of plasma drug concentrations.[7] It should be requested only if the result can help to assess the severity of poisoning and hence the need for specific therapy or the prognosis. Paracetamol has no specific clinical features in the early stage of poisoning, but the risk of liver damage can be predicted from the plasma concentration. In those at risk, intravenous NAC should be given within 10–15 h.[1–3] Many physicians routinely request plasma paracetamol concentration measurement in all patients with acute poisoning, regardless of the history. The clinical value of this approach has, until recently, not been seriously questioned and evaluated.[8] It was particularly important in Hong Kong to find out the incidence of missed, potentially serious paracetamol poisoning.

In this study, we have shown that approximately one in 11 patients who presented with suspected paracetamol poisoning to our hospital will have a hepatotoxic level, and about one in 36 patients with no suspected paracetamol ingestion will have elevated, but non-toxic plasma level (Table 1). A previous study of all patients presenting to two emergency departments in the United States with drug overdose has shown that one in 70 patients will have unrecognised paracetamol poisoning, and one in 500 will have potentially hepatotoxic plasma concentrations.[8] Further studies are needed to establish selective criteria for plasma paracetamol measurements.

Intravenous NAC is remarkably effective in preventing even trivial liver damage if given within 8 h of ingestion, but will be much less effective if more than 15 h have elapsed.[1,3] It is important that plasma paracetamol concentrations are measured *urgently* in all patients with suspected paracetamol poisoning. Routine measurement of plasma paracetamol concentrations, as was the case in 13 of our patients, is hazardous and may result in late recognition and treatment of the poisoning.

Our laboratory at the Prince of Wales Hospital has been providing a 24 h service for measurement of plasma paracetamol concentrations since 1984. Results will normally be available within 1–2 h if requested urgently. Rapid plasma screening will

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allow patients at risk of liver damage to be identified early and given intravenous NAC. Those not at risk who might otherwise have been given NAC may be discharged earlier.

The incidence of missed, potentially serious paracetamol poisoning in our patients with no suspected paracetamol ingestion is extremely uncommon. Routine screening of all patients with acute poisoning for toxic plasma concentrations of paracetamol is therefore not indicated and should never be a substitute for thorough history taking and physical examination.

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