Characteristics and outcomes of paracetamol poisoning cases at a general hospital in Northern Malaysia

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ABSTRACT

Introduction: Paracetamol is available as an over-the-counter medication in many countries including Malaysia. This drug has been implicated in many poisoning cases admitted to hospitals throughout the country.

Methods: We conducted a three-year retrospective review of 165 medical records of patients admitted to the Penang General Hospital for acute paracetamol poisoning. Cases were identified according to the discharge diagnosis documented in their medical records.

Results: Acute paracetamol poisoning occurred in all major ethnic groups. About 70 percent of our patients were female. There was minimal involvement of children. Admissions were more likely to be due to deliberate ingestions rather than accidental poisoning. In most cases, serum concentrations data plotted on the Rumack-Matthew nomogram predicted the majority of cases to be unlikely to be hepatotoxic, which were consistent with their mild clinical courses. Patients who acutely ingested more than 140 mg/kg or predicted to be hepatotoxic, based on their serum concentrations, had a significantly longer hospital stay.

Conclusion: Although acute paracetamol poisoning was common, the outcome was generally good.

Keywords: acute poisoning, drug ingestion, paracetamol, poisoning

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INTRODUCTION

In many countries, paracetamol ranks at the top of all known poisoning agents implicated in accidental or intentional poisoning[1-5]. In neighbouring Singapore, this drug is responsible for one-half of all deliberate self-poisoning among young people[6] and almost one-quarter of childhood poisonings[7]. In Malaysia, paracetamol is easily and widely available as an over-the-counter medication in several different formulations and strengths. Preliminary data showed a high prevalence of paracetamol poisoning among patients admitted for drug and chemical exposures to the Penang General Hospital. Penang is an island located in northwest Malaysia. It has a population of approximately 1.3 million people constituting three ethnic groups; Chinese (46.5%), Malay (42.5%) and Indians (10.6%)[8]. The Penang General Hospital received about 46.9% of total hospital admissions among five government hospitals in the state of Penang[9] with an estimated catchment population of about 600,000 people. This article reports the magnitude of acute paracetamol poisoning at this hospital, and the characteristics and outcomes of this type of poisoning over a three-year period.

METHODS

The present work is a retrospective case review of all patients with acute paracetamol poisoning admitted to the Penang General Hospital during the period from January 2000 to November 2002. Starting with a computer-generated list obtained from the hospital record office, all drug and chemical poisoning patients were identified according to the T-codes of the International Classification of Diseases, 10th revision (ICD-10). Patients' records were traced according to their identification card numbers and hospital registration numbers. Acute paracetamol poisoning cases were identified according to the discharge diagnosis documented in their medical records. Only records available at the time of the study were reviewed.

Data concerning demographical parameters of patients, doses and dosage forms ingested, treatment given during the hospital course and final patients' outcomes, were collected. Data on serum paracetamol concentration measurements were obtained from the hospital's therapeutic drug monitoring (TDM)

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Table I. Characteristics of paracetamol poisoning cases (n=165).

	Variable	N (%)
Age (in years)	0 - 15	17 (10.3)
	16 - 30	118 (71.5)
	31 - 45	23 (13.9)
	46 - 60	5 (3.0)
	>60	2 (1.2)
Ethnic group	Chinese	71 (43.0)
	Malay	48 (29.1)
	Indian	39 (23.6)
	Other	7 (4.2)
Gender	Female	118 (71.5)
	Male	47 (28.5)
Reported dose ingested (g)*	<5	41 (25.2)
	5 - 10	60 (36.8)
	10 - 15	32 (19.6)
	>15	30 (18.4)

*N = 163, dose not reported for 2 patients.

Table II. Relationship between ingested dose and nomogram prediction with duration of hospitalisation.

	Mean duration of hospitalisation (in hours)
Dose	
≤140 mg/kg	36.0*
>140 mg/kg	71.8
Nomogram prediction	
Unlikely hepatotoxic	38.7**
Possible/probable hepatotoxic	78.4

* N = 116, t-test, $p<0.05$

** N = 137, t-test, $p<0.05$

laboratory service. Prediction of likelihood of hepatotoxicity was based on the serum paracetamol concentration when plotted on the Rumack-Matthew nomogram. Latency time was calculated from the time of ingestion to the time patient was presented at the hospital. Descriptive statistics were used and presented as percentages. Comparison between groups were analysed by independent t-test. Results were considered statistically significant when $p<0.05$.

RESULTS

There were 165 cases of acute paracetamol poisoning during the study period. This constituted about 29% of all drug and chemical agents implicated in poisoning incidents. Females constituted 71.5% of cases versus 28.5% males, giving a sex ratio of 2.5:1. The majority of patients (73.3%) fell in the 16-30 year age group and the involvement of children below the age of 15 years old was minimal (Table I).

In 99 cases (60%), the drug was ingested intentionally. 55 cases (33.3%) involved accidental ingestions, while 11 cases (6.7%) were undetermined. Paracetamol was implicated alone in 132 cases (80%), and co-ingested with other agents in 33 (20%). Latency times could be determined in 153 patients. The mean latency time was found to be 10.73 hours (range 0.17 to 192 hours). 59.5% of paracetamol victims presented within eight hours, and 81.7% presented within 15 hours.

Tablets were the predominant (98.8%) dosage form ingested, while liquid form constituted only 1.2% of all cases. There were two cases where the amount ingested could not be determined. Of the remaining 163 patients, 30 of them (18.4%) ingested more than 15 g. Not all medical records documented the patients' body weight. Reported ingested dose based on body weight (mg/kg) was available for 116 patients. A large proportion (72.5%) ingested more than 140 mg/kg, although only 26% ingested more than 280 mg/kg.

All patients who came or were referred to the Penang General Hospital for paracetamol poisoning were initially managed at the Accident and Emergency (A&E) Department before being admitted to the respective wards. Initial management included gastric lavage, which was performed in 118 cases (71.5%). Seven patients refused gastric lavage and in nine cases, it had been performed somewhere else before being referred to this hospital. Activated charcoal was given while patients were in the A&E Department. It was given as a single or multiple doses in 30 cases (18.2%).

145 requests of serum paracetamol monitoring were identified from the TDM laboratory documents. Paracetamol concentrations could not be interpreted in eight cases mostly due to late presentations. About 60% were considered as "unlikely" to be hepatotoxic, when plotted on the Rumack-Matthew nomogram. On the other hand, using 140 mg/kg as the cut-off dose, about 28% of patients would be considered to have ingested an "unlikely" hepatotoxic dose (≤140 mg/kg).

Overall, 25 patients (15.2%) were asymptomatic during their hospital course. 124 (75.2%) experienced some forms of gastrointestinal symptoms. Other more severe complications included coagulopathy,

hepatic failure, and renal failure (7.3%). Three patients (1.8%) were admitted to the intensive care unit but no patient died as a result of paracetamol poisoning. Intravenous N-acetylcysteine (NAC) was given in 90 cases (54.5%). Six patients developed side effects resulting from the use of NAC. These side effects were reported as itching and rash. In such cases, either the rate of infusion of NAC was reduced (n = 5) or the infusion was stopped (n = 1).

The mean hospital stay was found to be 56.3 hours (range 1 to 648 hours). Table II shows the relationships between dose group and prediction of hepatotoxicity with duration of hospitalisation. Patients who ingested a higher acute dose (>140 mg/kg) and those who were predicted to have higher likelihood of hepatotoxicity based on the nomogram had a significantly longer duration of hospitalisation.

DISCUSSION

Our study has shown that poisoning due to paracetamol is very common in our setting, placing it at the top of all poisons implicated in drug poisoning. This resembles the poisoning picture found in the USA[5], Europe[1,10,11] and many other countries[3,4,7,12]. The predominance of females among our patients in the present study resembles that in the USA[13] and Denmark[14]. It appears that all three ethnic groups are involved in this poisoning.

Our findings have shown that there are more intentional compared to accidental ingestions. However, the proportion of intentional ingestion in this study is lower than that demonstrated by another study in the USA[13]. Overdosing with paracetamol in deliberate self-poisoning is very common. In Singapore, paracetamol represented 55% of overdosing cases among patients admitted to the hospital for deliberate self-poisoning[6]. Although patients with deliberate self-poisoning choose this drug for different reasons, the most common was because it is readily available[15]. As a result, legislation limiting paracetamol packaging size, like in the UK, has shown beneficial outcomes[16].

The outcomes of paracetamol poisoning depend on several factors. Schmidt et al[14] found that the quantity of paracetamol ingested and chronic alcohol abuse had been identified as independent risk factors in the development of paracetamol-induced hepatotoxicity. The minimal toxic amount in adults is approximately 7.5 g and liver toxicity usually follows ingestion of more than 15 g or 280 mg/kg[17]. In Western countries, rate of deaths due to paracetamol poisoning is high[11,18-20]. It is the largest single cause of death from acute poisoning in a hospital in the UK[11]. Our study shows that only 18.4% of our patients have ingested more than 15 g, which is lower than the findings reported in the UK (89%)[21]. This may explain the higher rates of deaths and hepatotoxicity found in other studies[13,18,20].

The majority of our patients were initially managed by gastric lavage and only a small number were given activated charcoal. These procedures might have contributed to the favourable outcomes in our setting. Both gastric lavage and activated charcoal can help to significantly reduce serum paracetamol concentrations[24]. The mean time from exposure to treatment has been reported to significantly affect the prognosis and final outcome of paracetamol toxicity. Prescott et al[23] demonstrated that the critical ingestion-treatment interval for complete protection against severe liver damage was eight hours. Efficacy diminished progressively thereafter, and treatment after 15 hours was completely ineffective. Those with liver damage tend to present late to the hospital and consequently given NAC after a longer delay[23]. In our study, the majority of patients were presented within 15 hours, and only about 40% were classified as potentially toxic based on the paracetamol concentration plot. The timely administration of NAC to these patients might have resulted in the favourable clinical outcomes generally seen in our patients.

Our study found that more than 50% of our patients received NAC, although only about 40% were classified as potentially toxic based on the paracetamol concentration plot. It is therefore possible that patients who were classified as "unlikely to be hepatotoxic" were also given NAC. This issue probably needs to be addressed in order to ensure the cost-effective use of NAC as well as to keep patients from any unnecessary exposure to the antidote. The proportion of our patients who developed adverse reactions to NAC (6.6%) was comparable to that reported by Schmidt and Dalhoff[25].

About 70% of our patients allegedly ingested more than 140 mg/kg, a dose considered to be potentially toxic. On the other hand, assessment using the Rumack-Matthew nomogram identified only about 40% to be potentially hepatotoxic. Data on the clinical course, however, showed that about 90% of patients were either asymptomatic or experienced some form of gastrointestinal distress. This shows that the lower percentage of patients predicted to be hepatotoxic based on the

nomogram is more consistent with the patients' clinical course, compared to the prediction based on the ingested dose. Our study also finds that both the higher dose group (>140 mg/kg) and the potentially hepatotoxic group had significantly longer duration of hospital stay. This shows that both ingested dose and assessment using the nomogram are consistent with the expected duration of hospitalisation.

In our setting, paracetamol poisoning is more likely to occur intentionally. However, the outcomes are more favourable than reported elsewhere. Our study finds that the clinical courses of patients are more consistent with prediction of toxicity based on serum concentration plot rather than on reported ingested dose.

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