

Management of acute paracetamol poisoning in a tertiary care hospital

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(Index words: acute paracetamol poisoning, N-acetylcysteine, methionine)

Abstract

Objectives To compare the management of acute paracetamol poisoning with the best evidence available, and to determine the effect of plasma paracetamol level estimation on the management.

Design Descriptive study with an intervention.

Setting Medical wards of the National Hospital of Sri Lanka, Colombo.

Patients Patients admitted with a history of acute paracetamol poisoning.

Intervention Measurement of plasma paracetamol.

Methods Data were obtained from the patients, medical staff and medical records. Plasma paracetamol was estimated between 4-24 hours of paracetamol ingestion. The current management practices were compared with the best evidence on acute paracetamol poisoning management.

Results 157 patients were included. The mean ingested dose of paracetamol was 333 mg/kg body weight. Majority of the patients (84%) were transfers. Induced emesis and activated charcoal were given to 91% of patients. N-acetylcysteine was given to 66, methionine to 55, and both to 2. A clinically important delay in the administration of antidotes was noted; 68% of patients received antidotes after 8 hours of the acute ingestion. Only 31 (26%) had paracetamol levels above the Rumack-Matthew normogram. 74 patients received an antidote despite having a plasma paracetamol level below the toxic level according to the normogram.

Interpretation Management of acute paracetamol poisoning could be improved by following best available evidence and adapting cheaper methods for plasma paracetamol estimation.

Introduction

Paracetamol is a widely used over-the-counter analgesic and antipyretic in Sri Lanka. It is a common method of self-poisoning in the UK and North America [1], and an emerging problem in Sri Lanka. The admissions with acute paracetamol poisoning to the National Hospital of Sri Lanka (NHSL) have increased from 35 in 2003 to 515 in 2005. An increase in admissions to hospitals in the

North-Central Province has also been noted over the same period.

Patients with acute paracetamol poisoning rarely develop specific clinical features within 12 hours of acute ingestion that predict hepatotoxicity. In countries with a high prevalence of paracetamol poisoning plasma paracetamol concentrations are used to define the risk of hepatotoxicity and need for antidotes. As paracetamol assays are not available in the Government hospitals in Sri Lanka the decision to initiate treatment is based on ingested dose determined from the patients' history [2]. Management of paracetamol poisoning is costly. In USA, the average cost of managing a patient with paracetamol poisoning was US\$ 2172 in 1995 [3,4].

The primary objectives of the study were to describe the current management and the effect of plasma paracetamol level estimation in the management. The secondary objective was to compare the current management with the best evidence available.

Methods

Approval was obtained from Ethical Review Committees of the NHSL and the Faculty of Medicine, Colombo. Patients admitted to the NHSL with acute paracetamol poisoning over four months (May-August 2006) were prospectively studied. The NHSL receives both direct admissions and transfers from peripheral hospitals. Data were obtained from patients (after obtaining verbal consent), medical staff and medical records using a pre-tested structured questionnaire.

Plasma paracetamol was measured in patients who presented within 24 hours of acute ingestion at four hours from the time of ingestion or from presentation. Plasma paracetamol levels were estimated using two methods: High performance liquid chromatography (HPLC) [5,6] and a low cost colorimetric method [7,8]. HPLC was considered the reference method. The Rumack-Matthew (R-M) nomogram was used to determine the risk of hepatotoxicity and need for antidote [2]. The patient management was compared with the best available evidence.

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Results

A cohort of 157 patients was enrolled in our study. The male to female ratio was 1:3, and median age was 20 years. The mean body weight was 47 kg (SD 10.9, range 23-124) and the mean ingested dose of paracetamol was 333 mg/kg (SD 226, range 77-1351). Information on the source of purchase or access to paracetamol for self-poisoning was available for 116 patients; 99 purchased paracetamol from groceries, 6 from pharmacies, and 11 stated that it was from the stock at home. The median time between acute ingestion and admission to NHSL was 6 hours 37 minutes with 61% being admitted within 8 hours. The majority of patients were transfers (84 %, n=132). The reasons given for the transfer were unavailability of antidotes, and liver function tests, or for specialised care.

Management of patients is described under two headings; (i) current management and outcome, and (ii) potential effect of plasma paracetamol levels on the management

Current management and outcome

The majority (91%) of patients received both induced emesis and activated charcoal irrespective of the ingested dose of paracetamol. Emesis was typically induced by ingesting two tablespoons of NaHCO₃ dissolved in 200 ml of water. Activated charcoal was administered orally (50-100 g in 200 ml of water). Home remedies for gastric decontamination before admission were used by 9% of patients and included coconut milk, salt water, soup, curry leaves broth and lemon juice. Table 1 shows the decontamination procedures in relation to the time of administration; only 36 (29%) received activated charcoal within the recommended time of 2 hours [9, 10, 11].

The decision to treat and continue with an antidote was largely based on the history of an ingested dose greater than 150 mg/kg or a decision of the physician that there was a possibility of hepatic damage. Plasma paracetamol was not done as it was unavailable in the Government hospitals. The high cost of the test in the private sector (Sri Lankan Rupees 1800-2200), and the fact

that most transferred patients were admitted at night may also have contributed to the failure to estimate plasma paracetamol level.

Based on the ingested dose (>150mg/kg), an antidote was indicated in 140 patients but only 125 received it. In 8 patients antidote was not given as it was unavailable, and in 7 the reason was not clear. N-acetylcysteine (NAC) was the physician's first choice, but it was frequently out of stock. Methionine was used as the alternative antidote; 68 patients received NAC, 55 methionine and 2 received both. Of the 13 who ingested a dose less than 150 mg/kg, 9 were not given any antidote and 4 were given methionine. Four patients in whom the dose of paracetamol was unknown received methionine. Thirteen (19%) of the 70 patients developed hypersensitivity reactions to NAC; of whom 9 were treated with parenteral antihistamines and hydrocortisone.

The hospital bed days ranged from one to six, and 5 were transferred back immediately with a supply of methionine. No patient was admitted to intensive care and none died. Only one patient with a history of ingesting 400 mg/kg paracetamol developed minor hepatotoxicity. She received NAC at the base hospital before transfer on the second day. She had an INR = 1.22, AST of 900U/l and ALT of 650U/l on day 5.

Potential influence of plasma paracetamol levels in the management

Plasma paracetamol levels were done for 119 patients in our study; 31(26%) of these were above the R-M line. The current management of these 119 patients (based on ingested dose and physician's judgment) is compared to a strategy of using plasma paracetamol levels to the current management as shown in table 2. Based on the R-M nomogram, of the 31 patients who were at risk of toxicity, 2 were not given any antidote, 15 were given NAC, and 14 methionine. Of the 88 patients who were not at risk, 34 were given NAC, 38 methionine, two both, and 14 (16%) were not given any antidote. Hence in the absence of paracetamol levels, two were under-treated, and 74 were over-treated with antidote.

Table 1. Time of administration of gastric decontamination procedures (n=157)

Time of administration	Number of patients	
	Activated charcoal	Induced emesis
Within 1 h	11	19
Within 2 h	25	25
After 2 h	88	90
Not given	23	14
Time not available	10	9

Table 2. Number of patients who received antidote when history of ingested dose and plasma paracetamol levels are used as treatment thresholds

	<i>Management in reference to toxic dose</i>		<i>Management in reference to paracetamol level</i>	
	<i>History <150mg/kg (n = 9)</i>	<i>History >150mg/kg (n =110)</i>	<i>Toxic level (n = 31)</i>	<i>Below toxic level (n = 88)</i>
Methionine	3	43	14	38
NAC	0	55	15	34
NAC+ methionine	0	2	0	2
Antidotes not given	6*	10†	2†	14†

* Antidotes were not given as it was not indicated

†Antidotes were not given as they were not available

When the paracetamol level was determined using both analytical techniques (HPLC and the colorimetric method), the time taken for estimation and final report was 6 times faster and 10 times cheaper for the colorimetric technique (30min and Rupees 200 versus 180 min and Rupees 2000). The observed agreement between the toxic and non-toxic levels by the two methods was 83.5 %.

Discussion

The number of admissions for paracetamol poisoning to NHSL have increased over the years. The probable reasons include increased media coverage, local cultural acceptance and ready access. In this study the majority obtained paracetamol from the local groceries with no restrictions in pack size. In countries where the incidence of paracetamol poisoning is high there are restrictions on the pack size and the number of tablets issued during a single purchase [12].

Despite most patients presenting to a hospital within 8 hours of ingestion, they did not get the antidote in time. This is a clinically important delay as the effectiveness of both NAC and methionine is maximal when given within 8 hours of ingestion [13, 14]. Other than unavailability of antidotes, there were no medical indications for the transfer of uncomplicated paracetamol poisoning cases from a peripheral hospital.

Evidence does not support the use of gastric lavage, activated charcoal or induced emesis given later than two hours after ingestion in reducing the absorption of paracetamol [9, 10, 11], but 143 (91%) patients were exposed to the unpleasant experience of induced emesis despite lack of evidence.

NAC is an expensive antidote. The cost of NAC (Rupees 11000) is high in Sri Lanka compared to the UK, where the same amount of NAC costs about Rupees 3800 [15]. This shows the need for alternative procurement and

supply methods of NAC. NAC is not superior to methionine [11, 13], and the latter can be used when there is no clinical evidence of hepatotoxicity at the time of presentation.

Appropriate use of antidotes would be facilitated by prompt access to accurate estimations of paracetamol concentration within the Government hospital system. Presently the argument against this option is the cost of plasma paracetamol estimation which ranges from Rupees 1800 to 2200 in the private sector. Our preliminary findings show that the colorimetric technique we adopted is inexpensive, quick and reliable.

Conclusions

The current management of acute paracetamol poisoning in the NHSL is not aligned with the best available evidence, and it causes unnecessary expense to the public health care system. Minimising transfers by ensuring availability of antidotes at peripheral hospitals, promotion of evidence-based management related to decontamination and timing of antidote administration, and having an accurate, cheap and quick method for plasma paracetamol estimation in major hospitals, will improve the quality of patient care and reduce costs.

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Not waving but drowning

Nobody heard him, the dead man,
But still he lay moaning:
I was much further out than you thought
And not waving but drowning.

Poor chap, he always loved larking
And now he's dead
It must have been too cold for him his heart gave way,
They said.

Or, no no no, it was too cold always
(Still the dead one lay moaning)
I was much too far out all my life
And not waving but drowning.

Stevie Smith, English Poet (1902 - 1971)