

Paracetamol Ingestions at the Children's Emergency Department – A Three Year Series

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ABSTRACT

This is a three-year retrospective review of 96 cases of paracetamol ingestions seen by KK Children's Emergency Department. Paracetamol is the commonest substance (23%) involved in childhood poisonings. More than 60% occurred in children aged one to three years old with an equal gender distribution. Eighty-six percent were accidental ingestions and the intentional ones had a significant female bias, all occurring in children aged 12 and above. These older children ingested higher doses of paracetamol (average dose of 233 mg/kg) and had potentially serious serum paracetamol levels. There was no significant morbidity and no mortality in this series.

Keywords: Childhood poisonings, Paracetamol Ingestion, Intentional Ingestions, Teenage paracetamol poisoning

Singapore Med J 2003 Vol 44(2):079-083

INTRODUCTION

Paracetamol is one of the most commonly implicated substances for poisoning in both children and adults. Its ubiquitous presence in the household and easy availability makes it a substance with high potential for harm – both accidentally and non-accidentally.

This is a retrospective review profiling all cases of paracetamol ingestion seen at the Children's Emergency Department of KK Women's & Children's Hospital seen over a three-year period from 10 May 1997 to 9 May 2000.

METHOD OF STUDY

The data was culled from our in-house computer system based on ICD-9 Coding. The main ICD-9 codes used were 977/E858 and 977/E 980 ("Medicinal poisoning – Accidental in nature" and "Medicinal poisoning – Non-accidental in nature" respectively).

This was followed by a review of the patient records. In addition to basic demographic data, we looked at the incidence of accidental and non-accidental ingestions and clinical symptoms (if any)

at presentation. Accidental ingestion included cases where parents had unwittingly administered high non-therapeutic doses of paracetamol, or where the child had ingested the non-therapeutic doses without the parents' or caregiver's knowledge.

We calculated the time of presentation after acute ingestions (time at presentation to Children's Emergency minus time paracetamol was acutely ingested) and the reported doses of ingested adjusted to per kilogram body weight.

We also looked at the correlation between reported acute ingested doses to the final serum paracetamol levels obtained to see if the reported ingested doses was a sensitive and specific parameter in determining whether the exposure was potentially toxic to the child.

Finally, we looked at the various treatment instituted. These include use of activated charcoal, gastric lavage and use of intravenous N-acetyl cysteine. Complications from these treatments were noted.

The eventual disposition and outcome of these cases were charted (viz, whether the cases were admitted, discharged or absconded). Reported doses ingested were considered significant if 150 mg/kg or more was taken. Acute paracetamol ingestion was defined as a single dose ingestion. All serum paracetamol levels done were matched by time of ingestion against the standard Matthew-Rumack chart.

Children were divided into two main age groups – those aged 12 years and above and those below 12 years old, after preliminary analysis of data showed a distinct preponderance of significant non-accidental ingestions, higher reported ingested doses and serum paracetamol levels in those aged 12 years and above.

Hepatocellular damage was defined as transaminase levels two-times above the normal and severe damage was defined as raised transaminases above 1000 UI/L.

All data were entered into a Microsoft Excel programme and basic statistical analysis included simple chi-square testing.

RESULTS

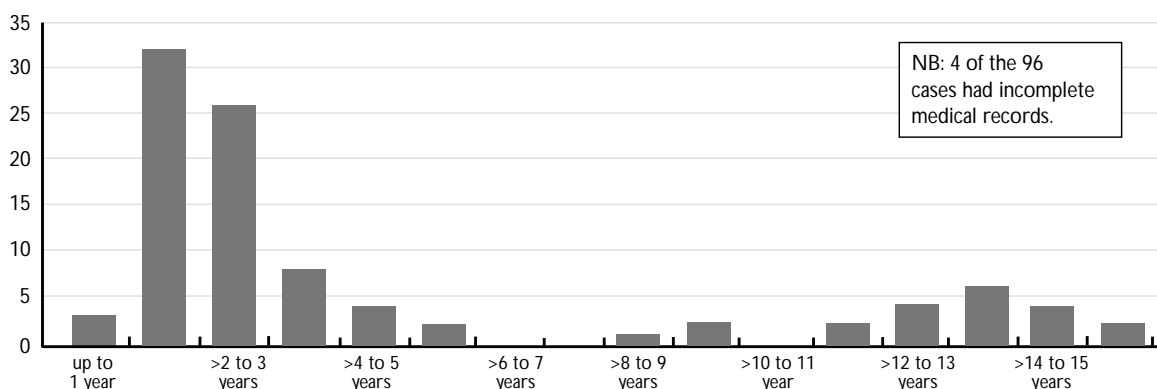
Of the 96 cases, six patients had incomplete records. Paracetamol accounted for 23% of all cases of

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Fig. 1 Age distribution (n=92).



poisonings seen during this three-year period. There was an equal gender mix (47 males and 49 females) and almost two-thirds (60.8%) were in children aged one to three years old (Fig. 1). Acute paracetamol ingestions accounted for 77.7% of the cohort (77/90).

Symptoms at Initial Presentation

Ninety-two patients (95.8%) were asymptomatic at presentation. The four symptomatic patients were aged 12 years and above and were cases of acute intentional ingestion. Three were drowsy and one had significant vomiting at presentation.

Of the patients who were drowsy, two had ingested more than 300 mg/kg while the third had ingested an unknown quantity. The teenager who vomited had ingested 164 mg/kg of paracetamol. None of the symptomatic cases had significant serum levels and they had not ingested any other substances.

Time of Presentation and Reported Doses for Acute Paracetamol Ingestions

Ninety-two percent (70/76) presented within six hours of an acute ingestion (Table I). The average reported dose of paracetamol ingested was 130 mg/kg (Table II). Seventy-one percent (54/76) were for ingestions of less than 150 mg/kg. Eighty percent of those with ingestions of more than 150 mg/kg tended to present after six hours compared to only 29% of those who had ingested less than 150 mg/kg. ($p < 0.05$).

Correlation of Reported Ingested Doses to Serum Paracetamol levels

There were 65 patients with acute paracetamol ingestions that had serum paracetamol levels done. There were six patients with significant serum levels and they were all teenagers that had ingested paracetamol intentionally. All were asymptomatic at presentation.

Table I. Time of presentation for acute ingestions.

Time of presentation for acute ingestions (n=76)	Number
Within 1 hour	16
Within 2 hours	20
Within 3 hours	10
Within 4 hours	12
Within 5 hours	3
Within 6 hours	8
Within 7 hours	2
Within 14 hours	1
After 24 hours	1
Unknown	3

Table II. Reported Doses Ingested.

Reported acute doses ingested (n=76)	Number
Less than 100 mg/kg	36
101-150 mg/kg	18
151-200 mg/kg	8
201-300 mg/kg	9
301-400 mg/kg	2
>400 mg/kg	3

Using reported acute ingestions of 150 mg/kg as a cut-off, we correlated these patients with the actual probable and possible toxic serum paracetamol levels done based on the Matthew-Rumack chart. Sensitivity of the reported acute ingestions in predicting toxic serum paracetamol level was 100% whilst the specificity was 72.9%.

Intentional Paracetamol Ingestions and Older Children

Fourteen percent of the ingestions (13/92) were non-accidental and of these, 12 were acute ingestions. Intentional ingestion was much more likely to occur in the female, aged 12 years and above ($p < 0.01$).

The average acute dose ingested intentionally was 233 mg/kg compared to the cohort average dose of 130 mg/kg. Almost all of these intentional acute ingestions (11/12) presented within six hours.

Table III. Nature of co-ingestants.

Nature of co-ingestants with paracetamol
Rhinothiol
Promethazine
Zenmolin
Cold special
Amoxil
Mefenamic acid
Chlorpheniramine
Caffeine
Ibuprofen
Fedac

There were proportionally more children aged 12 years and above who presented with paracetamol doses of 150 mg/kg and above (69% or 9/13) compared to the younger children (19% or 12/63) ($p < 0.05$). However, these older children did not present to the emergency department any later compared to the rest.

Treatment

Gastric lavage was done for 39 patients. In 16 of the cases gastric lavage was done more than one hour after ingestion and two were for non-acute ingestions. Oral charcoal (1 g/kg) was given for 37 cases. Fifteen cases were for acute ingestions that had occurred more than one hour later, while one was for a non-acute ingestion. Thirty-one cases were given intravenous N-acetyl-cysteine. There were no adverse complications in those who had these treatment modalities.

Co-ingestions with paracetamol (Table III)

Thirteen percent (12/92) were associated with co-ingestion with one or more largely toxicologically inert substances.

Outcome

Seventy-nine of our cases were admitted (82.3%), while 15 cases were discharged without follow-up and two cases absconded. Of the 79 admitted, 46 (58.8%) had doses below 150 mg/kg.

Fourteen cases, all aged 12 years and above and all intentional ingestions were referred to the psychiatrist for follow up as inpatients.

Morbidity and Mortality

None of our cases had significant hepatocellular injury. All biochemical derangement were mild and resolved on follow-up. There were no deaths.

DISCUSSION

Paracetamol remains the most frequent substance implicated in childhood poisonings⁽¹⁾. There is very

little morbidity and mortality in young children where it has been estimated that only three out of 417 patients will develop hepatotoxicity⁽²⁻⁶⁾.

Younger children tend to be more "resilient" to paracetamol ingestion⁽⁷⁾. In our series, more than 60% were children between one to three years old and 86% were accidental ingestions. There was no gender predisposition and 92% presented to us within six hours following an acute ingestion. Some authors suggest nine to 10 years old as the cut-off protective age limit. Animal studies have shown that younger mice have a four-fold greater glutathione turnover and increased activity of the glutathione system compared to older mice^(8,9). Younger children usually ingest liquid preparations⁽¹⁰⁻¹³⁾ and the frequent occurrence of spontaneous vomiting in children might also be protective^(2,4).

Acute ingestions of 150 mg/kg and above are considered potentially toxic. The actual validity of the reported ingested doses when correlated with measured serum paracetamol levels showed a better negative predictive value (1.00) versus a positive predictive value of 0.72, suggesting when reported ingested doses are within normal, there is low probability of the actual serum level being potentially toxic.

Recent studies⁽¹⁴⁻¹⁶⁾ have questioned whether the cut-off of 150 mg/kg is clinically valid, since this was largely extrapolated from adult metabolic models. In Bond et al's⁽¹⁴⁾ study, it was found that by raising the threshold to 200 mg/kg, 82% of referrals for children aged one to six years old could be eliminated without missing any of the "probable risk" patients. Mohler et al⁽¹⁵⁾ found that for asymptomatic children aged seven years and below, acute ingestions of below 200 mg/kg could be safely monitored at home. Since none of our younger children in our series developed any morbidity, we were unable to shed any light on this issue.

Younger children tend to take paracetamol accidentally while older children and adults present more with intentional ingestions. With accidental ingestions, doses could be overestimated and present earlier to the hospitals while more wilful attempts at intentional ingestions are possibly more accurate and present later. We saw this trend in our series, where children aged 12 years and older and predominantly females were more likely to have ingested paracetamol intentionally; they ingested more than 150 mg/kg and were the ones with potentially high serum levels. More children with higher reported levels of paracetamol ingestion presented after six

hours – 80% of those who presented after six hours had reported levels of >150 mg/kg versus only 9% presenting before six hours with levels of >150 mg/kg.

Alander et al⁽¹⁷⁾ concluded that hepatocellular damage (where liver transaminases are raised two-times above the normal values) was associated with presentation longer than 24 hours, aged 10 to 17 years, intentional overdose, amongst others. In our series, we did see some correlation with significant serum paracetamol levels in children aged 12 years and above and with intentional ingestion, though we had no cases of significant hepatic injury.

Simulation studies from Anderson et al^(18,19) have suggested that serum paracetamol levels peak at two hours in young children (aged one to five years old) with ingestions of >250 mg/kg of liquid preparations rather than at four hours, which was based on adult studies with tablets or capsules. Liquid paracetamol preparations are more rapidly absorbed and an earlier serum assessment might be equally feasible.

Treatment of significant paracetamol ingestion consists of removal of unabsorbed paracetamol through gastric lavage or by binding it to activated charcoal (1 g/kg). Recent consensus has determined that gastric lavage and oral charcoal is only efficacious if done within one hour following an acute ingestion^(20,21). Their role in nonacute ingestions remains controversial. In our series, 43% of cases had gastric lavage or were given oral charcoal more than one hour following acute ingestions (16/37 and 15/36 cases respectively). With better awareness, such unnecessary measures with no clinical benefits could be reduced.

The antidote for significant paracetamol ingestion is intravenous (IV) or oral N-acetyl-cysteine (NAC). In our series, 32% of the cases (31/91) were given IV NAC. These were cases with reported ingestions of more than 150 mg/kg or significant serum paracetamol levels. Some cases of paracetamol ingestions of more than 150 mg/kg were not given IV NAC because the serum levels when co-related with the Matthew-Rumack chart was not in the toxic range. There were no side-effects from administration of IV NAC.

A high proportion of cases admitted (58.8%) were asymptomatic with the reported levels ingested below 150 mg/kg. With better awareness both on the part of the clinician and parents, these cases could in future be managed as outpatients. However, this is contingent on the fact that the reported ingested levels are accurately observed

and reliable. The ultimate standard must be serum paracetamol levels measured, singly or serially.

All intentional overdoses should be referred to the child psychiatrist before being discharged home. Since the majority of paracetamol ingestions occur in the young accidentally, parents should be educated on the proper administration of paracetamol and on how to avoid such “medicinal accidents”.

Some of these measures include^(22,23):

- a) Childproofing the home. This involves keeping medicines and various toxic household chemicals away from the reach of younger exploring hands and mouths. They should be locked up, and be well-secured. Medicines should not be kept side-by-side with edible stuff and should also not be stored in innocent-looking used food containers lest children assume they are edible and unintentionally consume them.
- b) Child-resistant containers should be used to store various medicines, either meant for the child or for other family members. The main limitation of this review was its retrospective nature, thereby limiting the type of data we attempted to capture. For example, we could not properly differentiate between the various forms of “accidents” that had occurred. In addition, some data were lost or not available.

CONCLUSION

Paracetamol is the most common substance involved in childhood poisonings locally with an equal number of males and females affected. Ingestions in children aged 12 years and below were all accidental in nature and those aged one to three years old made up nearly two-thirds of all cases.

Reported doses in acute ingestions were highly sensitive but less specific. In our series, where caregivers reported ingested doses as below potentially toxic doses (viz less than 150 mg/kg), the corresponding serum paracetamol done concurred with this.

Clinicians managing paracetamol ingestions in older children (aged 12 years and above) should be aware that these are usually intentional ingestions associated with high doses of paracetamol and are more likely to be associated with potentially serious serum paracetamol levels. There was no significant morbidity and mortality in this series.

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