Paracetamol recall: a natural experiment influencing analgesic poisoning

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ABSTRACT

Objectives: To determine whether the occurrence of paracetamol and non-paracetamol analgesic deliberate self-poisoning (DSP) and accidental paediatric poisoning was affected by two periods of recall of paracetamol products.

Design: Retrospective, observational audit of proportions of poisonings with tablet and capsule formulations of paracetamol, ibuprofen and aspirin products during two recall periods compared with the number of poisonings during the same periods of the previous three years.

Setting: A national poisons information centre and a regional toxicology service.

Main outcome measures: Rates of DSP and accidental paediatric poisoning with paracetamol, ibuprofen and aspirin.

Results: During the two recall periods, there was a significant increase in ibuprofen DSP calls to the poisons information centre (RR, 1.86; 95% CI, 1.41–2.44; $P = 0.001$). There was no significant change in paracetamol or aspirin DSP calls over the two recall periods. However, there was a non-significant reduction in DSP calls with paracetamol in the first recall period alone ($P = 0.057$). There was a significant increase in the proportion of aspirin DSP presentations for the toxicology service (RR, 3.33; 95% CI, 0.97–11.4; $P = 0.043$), but no significant changes in paracetamol and ibuprofen DSP presentations. For accidental paediatric ingestions there was a significant increase in the proportion of ibuprofen calls (RR, 2.35; 95% CI, 1.85–2.98; $P = 0.001$), but no significant change in paracetamol or aspirin calls.

Conclusions: Reduced paracetamol availability increased poisoning with alternative analgesics, but had little effect on the incidence of paracetamol poisoning. Restriction of paracetamol-containing products may inadvertently increase poisoning with potentially more toxic agents.

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PARACETAMOL IS ONE of the most commonly ingested substances in deliberate self-poisoning (DSP) worldwide.[1-3] Queries regarding paracetamol generate large numbers of calls to poisons centres, and paracetamol is the single most common reason for a call to the New South Wales Poisons Information Centre.[4] There has been considerable concern regarding the availability of paracetamol and its use for deliberate self-harm in many countries.[5]

Following extortion threats to two pharmaceutical companies in Australia, paracetamol-containing products were recalled in two periods during 2000. The threats involved the addition of strychnine to some paracetamol-containing capsules (unfortunately confirmed by a number of cases of strychnine poisoning that occurred in the first half of 2000). These recalls presented a unique opportunity to investigate the effect of reduced availability of paracetamol on the incidence of DSP and accidental paediatric poisoning with paracetamol and other over-the-counter (OTC) analgesics.

The impact of reduced availability of paracetamol on patterns of DSP with paracetamol has been investigated previously.[6-9] Some investigators have found a reduction in the severity and incidence of severe paracetamol hepatotoxicity,[6-8] but these studies were limited in their focus and generalisability.[10-13] Few studies have considered the effect of paracetamol availability on the incidence of non-paracetamol poisoning, such as with other OTC analgesics.[14] There has been concern that, because the total number of DSP events is unlikely to be affected by paracetamol availability, there will be an increase in DSP involving other agents.[15]

Accidental ingestions by children are an important public health issue. Although there have been studies on changes in incidence of childhood poisoning with the introduction of child-resistant containers and changes in prescribing habits,[16] there have been no studies on the effect of availability of a particular medication on accidental poisoning in children.

We conducted a retrospective observational study to analyse the impact of the reduced availability of paracetamol on the incidence of DSP with paracetamol and other OTC analgesics. We also investigated accidental ingestions by children during these periods.

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METHODS

Our study was a retrospective comparison of the incidence of accidental and deliberate self-poisoning in two periods

1: NSW Poisons Information Centre data: deliberate self-poisoning (DSP) calls for the periods when paracetamol was available and restricted*

	Paracetamol available (1997–1999)			Paracetamol restricted (2000)		Change in absolute number of DSPs	Percentage change	Relative risk (95% CI)	*P*
	No.	Average/ year	% of DSP	No.	% of DSP				
Paracetamol	1 269	423	8.6%	370	8.1%	−53	−5.4%	0.95 (0.85–1.06)	0.326
Aspirin	165	55	1.1%	53	1.2%	−2	4.2%	1.04 (0.77–1.42)	0.793
Ibuprofen (OTC)	138	46	0.9%	79	1.7%	24	85.7%	1.86 (1.41–2.44)	0.001
Total DSP	14 775	4925	100%	4554	100%	—	—	—	—

* Paracetamol was restricted from 16 March 2000 to 21 May 2000, and from 6 June 2000 to 23 August 2000. The same dates in the preceding three years were used as the "paracetamol available" period. OTC = over-the-counter formulation.

of differing paracetamol availability. The two recall periods in 2000 were considered together as a period of paracetamol restriction. The periods during 1997, 1998 and 1999 for the same dates as the recall periods were used as the comparison periods during which paracetamol was freely available. Recall 1 occurred from 16 March 2000 until 21 May 2000 and affected products made by Herron. Recall 2 occurred from 6 June 2000 until 23 August 2000 and affected products made by Smith-KlineBeecham. The recalls involved the return of all paracetamol-containing products made by the respective companies regardless of the date of purchase — no batch numbers were specified.

Cases of self-poisoning were identified from two sources: calls to the NSW Poisons Information Centre (NSW PIC) and presentations to the Hunter Area Toxicology Service (HATS). NSW PIC covers NSW and Tasmania 24 hours a day and the rest of Australia overnight. HATS provides a 24 hours/day toxicology inpatient service for a population of about 500 000.

Cases reported included deliberate and accidental poisoning with tablet and capsule formulations of paracetamol-only products, ibuprofen (OTC formulation only) and aspirin in the two periods of differing paracetamol availability. A database of calls to the NSW PIC was searched for all calls relating to DSP and paediatric accidental ingestions of these drugs. The HATS database (discussed in more detail elsewhere)[3] was searched to find admissions with DSP involving these analgesics.

The total number of poisonings with each drug was considered as a percentage of the total number of DSPs for those periods at each centre. Accidental ingestions were considered as a percentage of the total number of accidental poisonings for those periods at the NSW PIC.

Statistical analysis

The numbers of deliberate and accidental self-poisonings for each drug in the recall and comparison periods were compared using continuity-corrected χ^2 tests. Fisher's exact test was used when cell numbers were small. *P* values less than 0.05 were considered statistically significant. We also computed relative risk and its 95% confidence intervals. All analyses were undertaken using SAS and CIA software programs.

RESULTS

There were 4554 calls regarding DSP to the NSW PIC during the recall periods in 2000, and 14 775 calls (4925 per year) in the comparison periods (Box 1). During the recall periods, there was no significant change for paracetamol or aspirin DSP, but a significant increase in calls about ibuprofen DSP ($P = 0.001$). For recall period 1 alone, in the restricted period there were 156 calls about paracetamol DSPs out of 2067 DSP calls (7.6%), compared with 598 calls about paracetamol DSPs out of 6729 DSP calls (8.9%) in the comparison periods ($P = 0.057$).

There were 230 DSP presentations to HATS during the recall periods in 2000,

2: Hunter Area Toxicology Service data: deliberate self-poisoning (DSP) calls for the periods when paracetamol was available and restricted*

	Paracetamol available (1997–1999)			Paracetamol restricted (2000)		Change in absolute number of DSPs	Percentage change	Relative risk (95% CI)	*P*
	No.	Average/ Year	% of DSP	No.	% of DSP				
Paracetamol	107	36	14.0%	36	15.7%	0	11.9%	1.12 (0.79–1.58)	0.528
Aspirin	5	2	0.7%	5	2.2%	3	232.6%	3.33 (0.97–11.4)	0.043
Ibuprofen (OTC)	6	2	0.8%	2	0.9%	0	10.9%	1.11 (0.23–5.46)	0.899
Total DSP	765	255	100%	230	100%	—	—	—	—

* Paracetamol was restricted from 16 March 2000 to 21 May 2000, and from 6 June 2000 to 23 August 2000. The same dates in the preceding three years were used as the "paracetamol available" period. OTC = over-the-counter formulation.

3: NSW Poisons Information Centre data: paediatric accidental poisonings for the periods when paracetamol was available and restricted*

	Paracetamol available (1997–1999)			Paracetamol restricted (2000)		Change in absolute number of accidental poisonings	Percentage change	Relative risk (95% CI)	*P*
	No.	Average/ year	%	No.	%				
Paracetamol (tablets only)	476	159	0.6%	159	0.7%	0	12.3%	1.12 (0.94–1.34)	0.203
Aspirin	194	65	0.3%	44	0.2%	–21	–23.7%	0.76 (0.55–1.06)	0.103
Ibuprofen (tablets only)	166	55	0.2%	116	0.5%	61	135%	2.35 (1.85–2.98)	0.001
Total accidental	73 525	24 508	100%	21 864	100%	—	—	—	—

* Paracetamol was restricted from 16 March 2000 to 21 May 2000, and from 6 June 2000 to 23 August 2000. The same dates in the preceding three years were used as the "paracetamol available" period. OTC = over-the-counter formulation.

and 765 presentations (255 per year) in the comparison periods (Box 2). There was no significant change in the percentages of presentations due to paracetamol or ibuprofen, but a significant increase in aspirin DSP ($P = 0.043$).

There were 21 864 calls regarding accidental paediatric poisonings to the NSW PIC during the recall periods in 2000, and 73 525 calls (24 508 per year) in the comparison periods (Box 3). There was no significant change in calls about accidental paediatric ingestions of paracetamol or aspirin, but a significant increase in calls regarding ibuprofen ($P = 0.001$).

DISCUSSION

Availability is reported to be the most common reason for patients choosing to take paracetamol in overdose.[17] In Australia, during a period of restricted availability of paracetamol, an overall reduction in the number of DSPs with paracetamol was not observed. However, there was a significant increase in DSP with the next most available OTC analgesics.

It is not clear why there was no overall reduction in paracetamol DSP. However, in the first recall period there was a non-significant reduction in paracetamol DSP. Recall 1 affected most brands available from supermarkets, whereas recall 2 affected only one brand available in supermarkets and had a greater impact on pharmacies. Thus, recall 1 had more effect on readily available paracetamol, suggesting that availability is important in the type of medication used for DSP.

Presentations to HATS with aspirin DSP were significantly increased during the recall periods. Significant overdoses of aspirin cause early symptoms, including nausea, vomiting and tinnitus,[18] that are likely to result in presentations to hospital, compared with ibuprofen, where there are often few clinical manifestations.[19] Calls to NSW PIC were more often from the public than from hospitals managing DSPs. This may explain why there was a significant increase in ibuprofen DSP and not aspirin in NSW PIC data, with the reverse being true for HATS.

Accidental paediatric ingestion of medication in the home is an important public health issue. The total number of accidental ingestions is related to the access that children have to medications.[16] Hence, if parents purchase alternative analgesics owing to a restriction of paracetamol and there are no changes to access in the home, this should lead to an increase in accidental paediatric ingestions of these alternative agents. During the recall periods, there was a significant increase in paediatric ingestions of ibuprofen tablets. There is no reason to think access in the home changed in this period.

Paracetamol is relatively non-toxic in children,[20] and there are no reported confirmed deaths from acute poisoning.[21] However, although in most circumstances ibuprofen causes minimal clinical effects, there are reports of paediatric ingestion of ibuprofen leading to serious complications.[22,23] The important public health issue is reducing the total number of accidental paediatric ingestions (eg, by improving packaging) rather than restricting particular types of medication (which may only increase ingestions of more toxic medications).

In this study, we have presented rates of paracetamol, aspirin and ibuprofen poisonings as a proportion of the total number of accidental or deliberate poisonings. This approach has been used in similar studies, for example in a study which looked at the effects of limiting the size of paracetamol and salicylate packs in reducing self-poisoning in the UK.[7] Because we conducted an observational study, it was not possible to control for confounding factors. However, by presenting the data as proportional incidence rates, we have been able to adjust the rate of overdose for the differences in the total number of poisonings in the periods of interest. Similarly, the absolute incidence of paediatric accidental poisonings is only affected by access to medications,[16] and there is no evidence that this changed in the time of the study. For this reason, proportional incidences were also used for paediatric accidental poisonings.

Although there are limitations of the small sample size in the HATS data, Fisher's exact test was used for analysis and we have presented our data with confidence intervals so that the imprecision in the estimates is clear. As this was an opportunistic study, it was not possible to increase the sample size. However, our conclusions are based on two different datasets, with a large sample size for the NSW PIC data.

Although this was a retrospective comparison study, two different data sources demonstrated the same changes. Both showed no significant changes in paracetamol DSP, but significant increases in DSP using the next most available analgesics. There is no evidence that changing paracetamol availability will decrease the total

number of DSPs. Thus, our data support previous suggestions that reducing paracetamol availability increases the use of other medications for deliberate and accidental poisonings.[12,14] Unless availability of other medications is controlled, the removal of one readily available medication, such as paracetamol, could lead to deliberate and accidental poisonings with more toxic medications.

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COMPETING INTERESTS

None declared.

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