Paracetamol availability and recent changes in paracetamol poisoning: is the 1998 legislation limiting availability of paracetamol being followed?

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ORIGINAL ARTICLE

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Objective: To determine the degree of adherence to legislation introduced in 1998 restricting the availability of over the counter paracetamol.
Design: A prospective observational study.
Setting: An emergency department in an inner city London teaching hospital. Pharmacy and non-pharmacy outlets in south London.
Main outcome measures: (1) The source of paracetamol ingested by 107 patients presenting with an acute paracetamol overdose (2001–2003) and (2) the ability to purchase paracetamol from pharmacy and non-pharmacy outlets in a manner contravening paracetamol pack size legislation (2004).
Results: Potentially toxic amounts of paracetamol in excess of pack size restrictions were purchased in 70% (17 of 24) of outlets. Forty six per cent of patients who had ingested a potentially toxic dose of paracetamol obtained the tablets in a manner contravening the 1998 legislation.
Conclusion: Legislation limiting the availability of over the counter paracetamol is not being adhered to in south London. A significant number of patients ingesting a potentially toxic dose of paracetamol report purchasing the tablets in a manner contravening the legislation. Studies that attempt to assess the impact of the legislation need to be interpreted in the context of these results. Measures to enforce current legislation may help to reduce the severity of paracetamol poisoning in the UK.

Paracetamol is the most common drug taken in non-fatal overdoses in the UK.[1] During 1993–98 there were about 150–200 deaths each year in England and Wales secondary to acute liver failure caused by paracetamol overdose.[2 3]

In an attempt to limit the number of cases of fatal paracetamol poisoning, legislation was introduced in September 1998 limiting pack sizes and the amount of over the counter (OTC) paracetamol available to the public in pharmacy and non-pharmacy outlets.[4] The rational behind the legislation was to reduce the total amount of paracetamol available in households for short term ingestion at any one time.[5 6] Pharmacies are allowed to sell a maximum of 32 tablets containing 500 mg of paracetamol (16 g total as one or more blister packs); non-pharmacy outlets were limited to selling a maximum of 16 tablets containing 500 mg of paracetamol (8 g total). A potentially hepatotoxic dose of paracetamol for an average adult weighing 70 kg is considered to be 150 mg/kg–11.5 g (23 paracetamol 500 mg tablets).[7 8] This potentially fatal dose is halved (75 mg/kg, 5.25 g, 11 tablets) for people at high risk of paracetamol induced hepatotoxicity (those with reduced hepatic stores of glutathione or induced hepatic P450 enzymes). Although not formally required by the legislation, blister packs have been introduced for all paracetamol pack sizes.

There have been a number of studies examining the impact of the 1998 legislation on paracetamol overdose related morbidity and mortality.[10 11] These studies have shown varying results for different outcomes.[9 11] A systematic review by Morgan and Majeed found that the 1998 legislation has been associated with a decrease in hospital attendances after paracetamol overdose and a decrease in liver unit admissions and liver transplants secondary to paracetamol overdoses.[11] However they found that five of eight studies published in the period 1998–2003 did not report a reduction in the severity of paracetamol poisoning.[11]

Recently published data seem to show a decrease in deaths attributed to paracetamol and a decrease in the number of patients requiring liver transplantation as a result of paracetamol induced acute liver failure during 1999–2001.[10 12] These findings have been attributed largely to the effect of the 1998 legislation limiting the amount of OTC paracetamol available for purchase at one time and therefore theoretically limiting the total amount of paracetamol available for a single ingestion, obtained either from home stocks of paracetamol or from an impulse purchase of a toxic quantity of paracetamol. The findings of these studies are based on the assumption that the legislation has been adhered to and patients have less paracetamol available to ingest in overdose. However, there is a scarcity of published data examining the degree of adherence to this legislation.[13] Morgan *et al* reported that during the period 1993 to 2002 mortality rates attributable to paracetamol poisoning declined, however they concluded that the contribution of the 1998 legislation to these findings is unclear.[12] Morgan *et al* also saw an overall decline in the rate of fatal poisonings for other drugs such as antidepressants, suggesting that the recent observed decline in the severity of paracetamol poisoning may be attributable to secular trends, rather than a result of the legislation.[13] A conclusion that the 1998 legislation limiting OTC paracetamol availability is primarily responsible for a recent decrease in morbidity and mortality associated with paracetamol overdose cannot be made without evidence that the legislation is being followed.

The aim of this study was to investigate the degree of adherence to the 1998 legislation limiting the availability of OTC paracetamol tablets.

Table 1 Characteristics of 107 patients presenting to the emergency department after an acute overdose of paracetamol

	All patients (107)	Female (51%)	Male (49%)
Age range (years)	16–93	16–85	18–93
Average age (years)	35	31	38
Multiple drug ingestion	33%	32%	34%

METHODS

Source of paracetamol taken in overdose

Patients who presented to an inner city London teaching hospital emergency department during a 16 month period (November 2001–March 2003) after a history of acute overdose of paracetamol tablets were questioned within 12 hours of tablet ingestion to determine the source of the tablets. Patients were questioned by a specialist registrar or consultant in clinical toxicology. All patients were asked if they had ingested tablets they already had stored at home or if they had purchased the tablets for the purpose of taking an overdose. Significant paracetamol ingestion was confirmed by measuring serum paracetamol concentration and plotting this on the Prescott treatment nomogram.[14] A serum paracetamol concentration requiring antidotal treatment was considered to confirm a significant ingestion.

If the patient who had ingested more than 16 paracetamol tablets had purchased the tablets OTC they were asked to describe the number and type of outlets they had purchased the tablets from, and the number of tablets purchased in each individual outlet. The information is recorded as part of a structured clinical toxicology history, which is recorded by the clinical toxicology team for all patients presenting to our facility who have ingested a potentially toxic amount of a drug. The information is entered into a dedicated electronic clinical toxicology database.

Purchase of paracetamol from pharmacy and non-pharmacy outlets

During March 2004 the authors attempted to purchase in excess of the restricted amount of paracetamol tablets in a total of 24 different shops (both pharmacy and non-pharmacy outlets) in south London. Individual postcodes were randomly selected from known postcodes in south London. The authors went to these areas using public transport and then selected the first available shop in each category (supermarket, corner shop, petrol station, and pharmacy). We attempted to buy 64 paracetamol 500 mg tablets by choosing the packs off the shelf and purchasing them at the shop or pharmacy counter. If the packs were only available behind the counter we simply asked for ''4 packets of paracetamol''. If the pharmacist or shop assistant questioned the purchase, no attempt was made to coerce the person into agreeing to sell an inappropriate number of tablets.

RESULTS

Patients presenting to an emergency department

Of 107 patients who presented to the emergency department after an acute overdose of paracetamol, 77 patients reported ingesting more than 16 paracetamol tablets (greater than one standard pack size). The source of paracetamol tablets was recorded for 73 of these patients. A total of 34 of 107 patients ingested multiple drugs in overdose. Coingestants included ibuprofen (7), aspirin (6), selective serotonin reuptake inhibitors (6), amitriptyline (5), codeine phosphate (4), cocaine (3), diazepam (3), cocodamol (3), coproxamol, heroin, zopiclone, amoxicillin, dothiepin, temazepam. Two patients who ingested paracetamol tablets also ingested a compound preparation containing paracetamol. There were no deaths. Table 1 shows demographic data for the 107 patients.

Paracetamol had been purchased specifically for the overdose by 35 (48%) of the 73 patients who reported ingesting more than 16 tablets. The remaining 38 (52%) patients reported that the paracetamol tablets were already stored at home through previous purchases or a doctor's prescription (table 2). Patients who ingested 16 or less paracetamol tablets seem more likely ($p<0.01$, χ^2 value 6.94) to have ingested tablets stored at home (80% of cases) rather than purchasing the tablets for the purpose of taking an overdose (table 2).

Paracetamol blood concentrations showing possible hepatotoxicity and requiring treatment with *N*-acetylcysteine (NAC) were found in 32 of the 35 patients who reported buying greater than 16 paracetamol tablets (500 mg) for the purpose of taking an overdose, confirming the ingestion of a toxic quantity of paracetamol. In addition, two patients were treated with NAC on the basis of a history of staggered paracetamol ingestion. One patient did not have a significant detectable blood paracetamol concentration. Table 3 summarises the sources of paracetamol obtained for ingestion by these 35 patients.

As shown in table 3, nearly half (46%) of patients who reported ingesting more than 16 paracetamol 500 mg tablets and had purchased them for the purpose of taking an overdose, purchased the tablets in a manner contravening the 1998 legislation. A further 43% of this group purchased more than 16 tablets by visiting multiple different outlets, the remaining 11% obtained paracetamol tablets legally by purchasing them from a single pharmacy.

Table 2 Comparison of patients who ingested 16 or less paracetamol (500 mg) tablets in overdose with patients who ingested greater than 16 paracetamol (500 mg) tablets

	Ingested 16 or less 500 mg paracetamol tablets (30)			Ingested greater than 16500 mg paracetamol tablets (77)		
Patients' sex	All	Female	Male	All	Female	Male
Age range (years)	17–85	17–85	18–54	16–93	16–69	22–93
Average age (years)	32	34	30	35	28	39
Had tablets at home	24 (80%)	15 (79%)	9 (82%)	40 (52%)	21 (55%)	19 (50%)
Purchased for overdose	6 (20%)	4 (21%)	2 (18%)	37 (48%)	18 (45%)	19 (50%)

Table 3 Source of paracetamol obtained by patients who reported ingesting more than 16 tablets (500 mg) and had purchased the tablets for the purpose of taking an overdose

Source of paracetamol	Number (%) of patients
Purchased from multiple different stores	15 (43)
Purchased from pharmacy according to legislation	4 (11)
Purchased from store contravening legislation	16 (46)
1 pharmacy (>32 tablets)	
15 non-pharmacy outlets (>16 tablets)	
Total number of patients who purchased paracetamol for the purpose of taking an overdose	35 (100)

Purchase of paracetamol tablets

Table 4 summarises the number of paracetamol 500 mg tablets purchased in different outlets by the authors. In four of eight pharmacies we were able to purchase more than the restricted amount of paracetamol (at least 48 or more tablets instead of the maximum of 32).

More than the restricted amount of paracetamol was purchased from four of six supermarkets and 9 of 10 newsagents, petrol stations and corner stores. In 9 of the 16 non-pharmacy outlets we were able to purchase at least double the potentially toxic dose of paracetamol (48 or more tablets).

Overall we were able to purchase paracetamol in a manner contravening the 1998 legislation in 70% of the outlets. Less than 20% of supermarkets, newsagents, corner stores, and petrol stations restricted the amount of paracetamol we attempted to purchase. In 54% of outlets we were able to purchase 48 or more 500 mg paracetamol tablets.

DISCUSSION

Our study shows that legislation limiting OTC availability of paracetamol is not being followed in south London, and furthermore that many patients still have a potentially toxic supply of paracetamol at home. Half of patients who ingested greater than 16 tablets used stocks at home. Our study shows that 80% of non-pharmacy outlets in south London that were surveyed sold paracetamol in a manner contravening the 1998 legislation.

Although the total number of patients who ingested a potentially toxic amount of paracetamol and who had purchased the tablets for the purpose of taking the overdose is small (35), nearly half (16) of these patients purchased the tablets in a manner contravening the 1998 legislation. This finding suggests that enforcement of the legislation may help to reduce the severity of paracetamol poisoning. The methods used to obtain paracetamol tablets (that is, if the tablets were purchased in a manner contravening the legislation) by the 72 patients who did not purchase a toxic amount of paracetamol for the purpose of taking an overdose were not recorded.

Although strict enforcement of the legislation would have only reduced the total number of overdoses by 15% in this study, one of the indirect aims of the legislation was to decrease the severity of poisoning and this would have been achieved in 21% (16 of 77) of potentially toxic overdoses.

This is a small study, examining a discrete community in south London. Our findings may not be reflective of nationwide practice in regards to the 1998 legislation. The numbers of outlets in our study is too small to enable analysis by type of outlet and therefore the overall conclusions cannot be generalised to particular types of outlet. There is potential for bias and inaccuracy when patients provide information regarding methods used to obtain paracetamol tablets. This small study needs to be repeated on a larger scale before nationwide conclusions can be made.

Although studies have examined the impact of 1998 legislation limiting the OTC availability of paracetamol,[2 10 11] a recent review article highlights the limitations and conflicting findings of currently published studies, and concludes that although the 1998 legislation seems to have been associated with reduced paracetamol related morbidity, further research is needed to fully evaluate the impact of the legislation.[11 12]

Attributing the legislation as the primary cause of any apparent changes in paracetamol overdose related morbidity requires evidence that the legislation is achieving its primary goal—to reduce the availability of paracetamol stores in the home at any one time and hence the amount of paracetamol available to be ingested in overdose.[5] Sales data show that although pack sizes of paracetamol decreased from an average of 35 tablets (1996–7) to 24 tablets (1998–9), the total number of tablets sold increased from 520 million (1996–7) to 580

Key points

- Legislation introduced in 1998 restricting the availability of OTC paracetamol is not being adhered to in south London.
- Further studies are needed to determine the degree of nationwide adherence to this legislation.
- The legislation may not be achieving the goal of reducing stores of paracetamol in the community available for overdose.

Table 4 Number of 500 mg paracetamol tablets purchased from different outlets

Outlet	Number of tablets permitted under legislation	Number of 500 mg paracetamol tablets purchased in each outlet	Number of outlets exceeding 1998 legislation
Pharmacies	32	16, 16, 32, 32, 48, 48, 48, 64	4 of 8
Supermarkets	16	16, 16, 32, 32, 64, 64	4 of 6
Corner shops, newsagents, petrol stations	16	16, 32, 32, 48, 48, 48, 48, 48, 64, 64	9 of 10

million (2001–2).[10] Total sales of compound analgesic tablets containing paracetamol also increased.[10] These findings cannot be explained by an increase in the UK population (population growth averaged 0.3% per year 1991–2003[15]). These figures do not support the assumption that the 1998 legislation has lead to a decrease in the amount of paracetamol stored in the average UK home available for short term ingestion. The legislation may have reduced the peak availability in terms of number of tablets available in the home at any one time for a single ingestion; however there are currently no published data available illustrating this. Half of our study population who ingested a potentially toxic dose of paracetamol did so by using stocks stored at home.

Other studies have illustrated poor adherence to guidelines or legislation limiting the availability of paracetamol in the community. A study in Ireland showed poor compliance among non-pharmacy outlets with guidelines limiting paracetamol sales at a time when hospital admissions for paracetamol overdose were increasing.[16] A 2001 study in London showed poor compliance with the new legislation in pharmacies, supermarkets, and corner stores.[17] Gunnell *et al* found that compared with England and Wales paracetamol related morbidity and mortality were less in France where the quantity of paracetamol in a single purchase is limited, suggesting a link between paracetamol availability in the community and paracetamol related morbidity and mortality.[18]

Currently there is no published evidence showing that the 1998 legislation has reduced the total mass of paracetamol available in household stocks to be ingested in overdose, and our study shows that, in south London at least, there is poor adherence with the legislation. Further research is needed to determine the degree of adherence to the 1998 legislation throughout the UK and to assess whether any observed changes in paracetamol poisoning are attributable to the legislation itself or other factors. If other studies confirm poor adherence, measures must be introduced to enforce the legislation.

CONTRIBUTORS

SG, PD, PL, and AJ designed the study and collected study data. SG and PD conducted data analysis. SG wrote the draft report and PD, PL, and AJ reviewed and finalised the report. All four authors will act as guarantors.

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Ethics: this observational study was not considered by the local hospital ethics committee. Information obtained from patients is part of the standard toxicology history taken by the Clinical Toxicology team at St Thomas's Hospital. The clinical toxicology database has been discussed with the local research ethics committee.

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