

POISONING WITH PARACETAMOL, IBUPROFEN AND ASPIRIN. HOW MUCH IS DUE TO PRESCRIBED MEDICATION?

CL Sheen, Clinical Research Fellow, Medicines Monitoring Unit, JF Dillon, Consultant Gastroenterologist, Department of Gastroenterology, both Ninewells Hospital, Dundee; DN Bateman, Reader in Clinical Pharmacology and Consultant Physician, Scottish Poisons Information Bureau, KJ Simpson, Consultant Hepatologist, Scottish Liver Transplant Unit, both Royal Infirmary, Edinburgh; TM MacDonald, Professor of Clinical Pharmacology and Pharmacoepidemiology, Medicines Monitoring Unit, Ninewells Hospital, Dundee

SUMMARY

Paracetamol, ibuprofen and aspirin are used frequently in self-poisoning attempts. They are available both over the counter (OTC) and on prescription. Measures have been taken to limit OTC supply, particularly for paracetamol. To effectively target any limitation in the supply of drugs used for self-harming, however, it is important to understand from where the drugs are obtained.

This paper has examined the proportion of paracetamol, aspirin and ibuprofen prescribed in the Tayside region of Scotland.

Using databases within the Medicines Monitoring Unit (MEMO) in Ninewells Hospital, Dundee, data on dispensed paracetamol, ibuprofen or aspirin were record-linked to admissions for poisoning with paracetamol, aspirin or non-steroidal anti-inflammatory drugs (NSAIDs) respectively.

Up to 15% of hospitalisations were associated with a prescription dispensed up to one month before admission.

It appears that most admission to hospital for self-poisoning with paracetamol, aspirin or ibuprofen are not associated with prescribed drugs. Measures to reduce the incidence of self-poisoning with these drugs needs to be aimed at the OTC supply.

INTRODUCTION

Paracetamol, aspirin and ibuprofen are the major non-opioid analgesics available OTC, but they may also be prescribed. They are all associated with self-poisoning, although paracetamol is most frequently used and has risks of severe hepatic injury and death.

People who attempt self-poisoning often use whatever tablets come most readily to hand, be they prescribed or OTC drugs.^{1,2} Other studies have reported that both prescription and OTC drugs are used.³⁻⁵ To plan the most effective way to reduce poisoning it is important to understand sources of drugs used. For example, there would be little point in changing the legal status of an OTC drug if that drug is predominantly obtained from a prescription when used in self-poisoning attempts.

This study identifies the proportion of poisoning associated with paracetamol, aspirin and ibuprofen prescribed in the Tayside region of Scotland.

METHODS

The Medicines Monitoring Unit at Ninewells Hospital, Dundee contains databases of all dispensed prescriptions in Tayside (the Tayside Script Facility – TSF) and discharge diagnoses (Scottish Morbidity Record 01 – SMR 01). The TSF is created in MEMO by manual data entry from prescriptions, which are sent to MEMO after the Prescription Pricing Authority has processed them. The Information and Statistics Division of the Scottish Office provides MEMO with SMR 01.

The hospitalisation database identifies the patient by their Community Health Index number (CHI) and the reason for admission by the ICD-9 code. It also lists other data such as the date of admission. The CHI number is a unique patient identification number that is used throughout Tayside on all primary and secondary care medical information. The TSF database records all prescriptions encashed by a patient, again identified by the CHI number. TSF also records the dispensing date and type of drug, dose, frequency and duration. For the purposes of research these data were anonymised prior to record-linkage.

Using the ICD-9 codes representing poisoning with paracetamol, aspirin and NSAIDs, which include ibuprofen, the number of episodes for 1995 were identified including the date of admission (Table 1). The ICD coding system is unable to differentiate between different NSAIDs and so all poisonings due to NSAIDs were identified in this search of the database.

Two other codes are also frequently used in recording drug toxicity. These are;

- E950.0 – Suicide and self-inflicted poisoning by analgesics, antipyretics and anti-rheumatics.
- E980.0 – Injury undetermined whether accidentally or purposely inflicted, poisoning by analgesic, antipyretic or anti-rheumatic.

These codes are non-specific and are usually used in conjunction with a more specific code, e.g. 965.1 and

Table 1
Codes used.

Paracetamol	
965·4	Aromatic analgesic poisoning not elsewhere classified (NEC*)
E850·2	Accidental poisoning by aromatic analgesics (NEC)
NSAID	
965·6	Anti-rheumatic poisoning
E850·4	Accidental poisoning by anti-rheumatics
Aspirin	
965·1	Salicylate poisoning
E850·1	Accidental poisoning by salicylates
*NEC – Not Elsewhere Classified	

E950·0 would mean salicylate poisoning from suicide or self-inflicted poisoning. These codes are not specific enough to differentiate between the three classes of drugs and were therefore excluded from the search. This means that the number of overdoses counted could be lower than the true number if there were any instances where one of these non-specific codes has been used alone.

The TSF database contains a library of all drugs entered into it. To search for prescribed drugs, a drug list for each drug type of interest (i.e. paracetamol, aspirin and ibuprofen) was created that included proprietary drug names (Table 2). The name of each drug was checked in the British National Formulary that was current in 1995 to verify that they contained the constituent drugs of interest. Using these drug lists, the dispensed prescribing database was searched to identify who had received prescriptions for a drug containing

TABLE 2
Drugs searched for.

Paracetamol	Aspirin
Aspirin/Paracetamol/Codeine Combination	Aloxiprin
Calpol Extra	Aspav
Calpol Paediatric	Aspirin
Calpol Paediatric Sugar Free	Aspirin Acid
Cocodamol	Aspirin Dispersible
Cocodamol Dispersible	Aspirin Dispersible
Codydramol	Aspirin Nuseals
Coproxamol	Aspirin Paediatric
Disprol Adult	Aspirin/Paracetamol/Codeine Combination
Disprol Paediatric Sugar Free	Benoral
Junior Disprol	Benorylate
Kapake	Caprin
Paldesic	Caprin Enteric Coated
Panadol	Cocodaprin
Panadol Junior	Cocodaprin Dispersible
Panadol Ultra	Disalcid
Panaleve	Disprin Cardiovascular
Panaleve 6+ Sugar Free	Sodium Salicylate
Panaleve Junior	
Paracetamol/Codeine Phosphate	Ibuprofen
Paracetamol	Apsifen
Paracetamol Effervescent	Arthrofen
Paracetamol Paediatric	Brufen
Paracetamol Pain Relief	Brufen Retard
Paracetamol Sugar Free	Codafen Continus
Paracetamol Soluble	Fenbid
Paracodol	Ibuprofen
Remedeine	Junifen
Remedeine Forte	Junifen Sugar Free
Salzone	Motrin
Solpadeine	Proflex Sugar Free
Solpadol Caplets	
Solpadol Effervescent	
Tylex	

paracetamol, aspirin or ibuprofen, including the dispensing date.

A dispensed prescription and an overdose event were linked using a unique identifier. This enabled the identification of patients who had been hospitalised for an overdose of paracetamol, aspirin or NSAID in 1995 and who had been dispensed the associated index drug as used in the overdose (paracetamol, aspirin or ibuprofen) up to a month prior to the admission. Thus the dispensed prescribing database was searched from 1 December 1994 to 31 December 1995.

Validity of SMR 1 Codes

The SMR 1 codes used were the same as those used routinely by the medical records departments of Ninewells Hospital and the Royal Infirmary of Edinburgh, and also by the Information and Statistics Division of the Scottish Office (personal communications). The paracetamol codes were further verified by the General Register Office for Scotland (personal communication) and have been used in other papers (Sheen – unpublished data) and Christopherson *et al.*⁶

Results

The results are shown in Table 3. The actual drugs prescribed in subjects with overdoses were aspirin 75 mg (one case), co-codamol (20 cases), co-proxamol (22 cases), co-dydramol (seven cases), Calpol® (one case), paracetamol 500 mg (four cases), ibuprofen 400 mg (seven cases) and Codafen Continus® (one case).

The proportions of poisonings associated with a prescription of the index drug in the month prior to hospital admission for poisoning were 11.6%, 1.8% and 15% of hospitalisations for paracetamol, aspirin and NSAID poisoning respectively.

DISCUSSION

This study has shown that in 88.4%, 98.2% and 85% of overdoses, due to paracetamol, aspirin or ibuprofen respectively, the drug was not obtained from a prescription in the month prior to the hospital admission. The drug may have been obtained OTC or from other sources such as another person's medication

or from residual unused drugs from previous prescriptions (the 'bathroom cabinet effect').

In keeping with our results, other studies have also shown that drugs used in self-poisoning are obtained infrequently from prescriptions.^{7,8} The hepatotoxicity of paracetamol is well recognised and has been highlighted to the public in television hospital dramas and 'soap operas'.⁹⁻¹² Aspirin is regarded as safe by the public despite being a common cause of gastric irritation and bleeding and rarely hepatotoxicity.^{13,14} However, aspirin poisoning can be very serious and result in death even with aggressive management. Ibuprofen is generally considered safe by consumers and regulatory authorities and is probably safe in overdose.^{15,16} Any method aimed at reducing drug toxicity must therefore focus on the more toxic analgesics paracetamol and aspirin. Methods of limiting availability such as changing the legal classification of the drugs to 'prescription only' or changing their supply to pharmacy only may need to be considered.

Further studies on the pharmacoeconomics and impact on the health service of the poisoning of these drugs and modelling effects of limiting their sale need to be performed.

Advantages and limitations of this study

Due to the completeness of the records in the MEMO databases and the fact that all records pertaining to a single patient can be identified from the anonymous unique identifier, this study has been able to reliably link dispensed drug and SMR 01 codes. These associated instances have been isolated from a large population (of 385,000 people) with verified data rather than relying on the reports of patients or relatives at the time of hospital presentation. Other studies have only been able to use smaller patient groups and questionnaires and so bias in reporting may have reduced the accuracy of their data.

This study has used previously verified codes for poisoning. However, it does rely on the accurate and appropriate recording of the event (i.e. a paracetamol poisoning was truly due to a paracetamol-containing drug) and of the drugs prescribed. In addition, there may

TABLE 3
Poisonings and prescriptions in Tayside in 1995.

	Paracetamol	Aspirin	NSAID poisoning/ ibuprofen prescription
All poisoning episodes in 1995	447	57	53
Dispensed prescriptions 1/12/94 – 31/12/95	238,983	82,891	40,933
Poisoning episodes in patients with prescriptions in 1995	52	1	8

have been an element of 'double counting' if a patient claimed to have overdosed on more than one of the index drugs.

In the case of ibuprofen for which there is no single ICD9 code, the numbers included under the poisoning include all drugs in the anti-rheumatic class (e.g. other NSAIDs) thus the instances of ibuprofen poisoning may be grossly overestimated in this study.

Another weakness of this study is that it attributed only those drugs dispensed in the month prior to poisoning. In reality, drugs from prior prescription could have been used and even drugs from another person in the same household. Thus, although this study can conclude that drugs were not likely to have been obtained via a prescription, it cannot definitively conclude that drugs were obtained OTC.

Nevertheless, it seems likely that OTC drugs are the most likely source of medication in those patients taking an overdose who have had no prior prescriptions.

CONCLUSION

Most patients admitted to hospital for self-poisoning with paracetamol, aspirin or ibuprofen are most likely to have used OTC purchased drugs and not prescribed medication. Measures aimed at reducing the incidence of poisoning with these drugs must therefore be directed at modifying the OTC supply.

REFERENCES

- 1 Carlsten A, Allebeck P, Brandt L. Are suicide rates in Sweden associated with changes in the prescribing of medicines? *Acta Psychiatr Scand* 1996; **94**:94–100.
- 2 Crombie IK, McLoone P. Does the availability of prescribed drugs affect rates of self poisoning? *Br J Gen Pract* 1998; **48**:1505–6.
- 3 Buckley NA, Whyte IM, Dawson AH *et al.* Correlations between prescriptions and drugs taken in self-poisoning. Implications for prescribers and drug regulation. *Med J Aust* 1995; **162**:194–7.
- 4 Alsen M, Ekedahl A, Lowenhielm P *et al.* Medicine self-poisoning and the sources of the drugs in Lund, Sweden. *Acta Psychiatr Scand* 1994; **89**:255–61.
- 5 MacNamara AF, Riyat MS, Quinton DN. The changing profile of poisoning and its management. *JR Soc Med* 1996; **89**:608–10.
- 6 Christopherson O, Rooney C, Kelly S. Drug-related mortality: methods and trends. *Popul Trends* 1998; **93**:29–37.
- 7 Gazzard BG, Davis M, Spooner J *et al.* Why do people use paracetamol for suicide? *Br Med J* 1976; **1**:212–13.
- 8 Gustafsson LL, Boethius G. Utilization of analgesics from 1970 to 1978. Prescription patterns in the county of Jamtland and in Sweden as a whole. *Acta Med Scand* 1982; **211**:419–25.
- 9 Clissold SP. Paracetamol and phenacetin. *Drugs* 1986; **32** (Suppl 4):46–59.
- 10 Prescott LF, Roscoe P, Wright N *et al.* Plasma-paracetamol half-life and hepatic necrosis in patients with paracetamol overdose. *Lancet* 1971; **1**:519–22.
- 11 Prescott LF. Paracetamol overdose. Pharmacological considerations and clinical management. *Drugs* 1983; **25**:290–314.
- 12 Prescott LF, Lasagna L, Erill S *et al.* Dose response relationships in toxicology. Conference: The Esteve Foundation Symposium III 1989; Dose-response relationships in man. 13–15 Oct 1988; Mallorca, Spain.
- 13 Schaller JG. Chronic salicylate administration in juvenile rheumatoid arthritis: aspirin 'hepatitis' and its clinical significance. *Pediatrics* 1978; **62**:916–25.
- 14 Bjorkman D. Nonsteroidal anti-inflammatory drug-associated toxicity of the liver, lower gastrointestinal tract, and esophagus. *Am J Med* 1998; **105**:17–21S.
- 15 Royer GL, Seckman CE, Welshman IR. Safety profile: fifteen years of clinical experience with ibuprofen. *Am J Med* 1984; **77**:25–34.
- 16 Doyle G, Furey S, Berlin R *et al.* Gastrointestinal safety and tolerance of ibuprofen at maximum over-the-counter dose. *Aliment Pharmacol Ther* 1999; **13**:897–906