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Frequency and characteristics of hospital admissions associated with drug-related problems in paediatrics

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Aim
To determine the frequency of paediatric hospital admissions associated with drug-related problems (DRPs) at two Australian hospitals.

Methods
The investigator and ward pharmacists prospectively screened eligible patients. A multidisciplinary panel reviewed data and established causality, preventability and clinical significance classifications.

Results
Over 22 weeks of data collection, a total of 11 564 patients were admitted, 2933 met eligibility criteria. Of those eligible, 127 [4.3%, 95% confidence interval (CI) 3.6, 5.0] were judged to have hospital admissions associated with DRPs. Direct costs associated with DRPs identified totalled £100 707. Of the 81 cases assessed for preventability, 46.9% were deemed preventable.

Conclusions
This research has provided information on the nature and characteristics of paediatric DRPs associated with hospital admissions.

Introduction

Problems associated with the use of medications comprise a broad set of clinical situations and can result in significant drug-related morbidity and mortality. Substantial costs are associated with drug-related problems (DRPs), as highlighted by a study from the USA which estimated the economic burden arising from drug-related morbidity and mortality to range between £17.3 billion and £75 billion annually [1].

Studies investigating the frequency, causality, clinical significance and possible preventability of drug-related admissions have been conducted in adults. The corresponding epidemiological and economic data within the paediatric population are limited. An extensive review of the literature found a total of 10 studies investigating aspects of DRPs in children [2–11]. Seven of the studies investigated adverse drug reactions (ADRs) and cannot be extrapolated to the broader set of events encompassed by DRPs [3–5, 8–11]. Further research is required to establish if the frequency and characteristics of hospital admissions associated with DRPs reported in the remaining three studies provide a

representative reflection of the impact of such events. Our aim was to determine the frequency and characteristics of paediatric admissions associated with DRPs to two hospitals in order to provide baseline information on such events.

Methods

This study involved paediatric patients (patients ≤17 years) at the following two Australian hospitals: Royal Children's Hospital (RCH), a specialist paediatric teaching hospital which provides primary, secondary and tertiary care and is the major trauma and referral centre for paediatric patients within South-eastern Australia; and Geelong Hospital (GH), a general regional teaching hospital which is the sole provider of public acute health services within a large regional area. Ethics approval to conduct this study was granted at each hospital, and by Monash University Standing Committee on Ethics in Research in Humans.

All unplanned paediatric medical (excluding trauma or oncology) patients admitted to a ward of RCH or GH over the periods of data collection were considered for inclusion. The practical constraints operating within each hospital meant that the duration of data collection was based upon convenience. A hospital admission was considered a study case if an association between the admission and a DRP was established. We used the eight DRP categories defined by Strand *et al.* and listed in Table 1 [12].

The investigator and ward pharmacists prospectively screened eligible patients admitted to hospital. Information was sought from other healthcare professionals, medical records and by review of hospital admission preliminary diagnoses on each consecutive day of data collection. Information was not sought from patient interview, except in the course of provision of normal pharmacy services. A checklist was completed if an admission was deemed to be possibly associated with a DRP. The investigator then conducted a preliminary review of the medical histories of all patients identified. If, at the end of this preliminary review, an association between the hospital admission and a DRP was possible, admission details were recorded to allow subsequent analysis by a multidisciplinary panel. The panel consisted of seven independent members from a variety of disciplines including paediatric medicine, pharmacy, paediatric clinical pharmacology and nursing. The panel reviewed information collected for each patient identified and established the likelihood of an association between the hospital admission and a DRP. Where such an association was established a DRP category along with a causality [13], preventability [13, 14] and clinical significance classification [2] was determined.

Two members of the panel reviewed each case on an independent basis. At least one was required to be a medical practitioner. Any discrepancies in classifications were recorded. In cases where discrepancies arose, the reviewed cases were annotated with the classifica-

Table 1
The eight drug-related problem (DRP) categories defined by Strand *et al.*

DRP categories	The patient has a medical condition:	Frequency of cases, no.	Number preventable, no.
1	That requires drug therapy (a drug indication), but the patient is not receiving a drug for that indication	5	2
2	For which the wrong drug is being taken	2	2
3	For which too little of the correct drug is being taken	4	1
4	For which too much of the correct drug is being taken	2	2
5	Resulting from an adverse drug reaction*	29	3
6	Resulting from a drug–drug, drug–food or drug–laboratory interaction	1	1
7	That is the result of not receiving the prescribed drug (non-adherence)	38	27
8	That is the result of taking a drug for which there is no valid medical indication (accidental or intentional poisoning)	46	Not applicable
Total		127	38

*No., Number. *An adverse drug reaction was defined as 'any response to a drug that is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis or treatment of disease, or for the modification of physiological function'.*

tions and any other comments made by the panel members. These were returned to the panel members who were asked to discuss the relevant case and reach a consensus. The consensus opinions were recorded as the final DRP category, causality and preventability classifications.

The direct costs associated with data obtained were estimated using a clinical costing approach [15]. Direct costs are those borne mainly by the healthcare system in treating the illness in question, and include medical care expenditures incurred in the diagnosis, treatment and rehabilitation of illness [16]. A clinical costing approach derives a cost per patient built up from the recorded utilization of individual products. Put simply, this means that costs are attached to individual products, such as specific laboratory tests or types of drugs, and the number of these products used by a patient over the course of their hospital stay is then multiplied by the cost per product. The cost per individual product is then summed to reach the total cost per patient.

The data were analysed using the Statistical Package for the Social Sciences (SPSS) for Windows version 10 (SPSS Inc., Chicago, IL, USA). χ^2, Mann–Whitney *U*- and the Kruskal–Wallis *H*-tests were used to detect significant differences between groups. A significance level of 0.05 was selected for all tests. The 95% confidence intervals (95% CI) for frequencies reported were determined using CIs for a proportion.

Results

Data collection was conducted over an 18-week period at RCH (11 May 1998 to 13 September 1998) and a 4-week period at GH (7 June 1999 to 4 July 1999).

Combined data for RCH and GH

Combining data for the two hospitals, a total of 11 564 patients were admitted over the 22-week period of data collection. Of these, 2933 (2745 RCH, 188 GH) met eligibility criteria. Eligible patients from the two hospitals were not significantly different in terms of gender ($P = 0.1149$) or age ($P = 0.079$).

One hundred and twenty-seven cases were judged to have hospital admissions associated with DRPs (119 at RCH and eight at GH). Drug-related problems were not associated with any deaths; however, eight cases were admitted to intensive care units.

The frequency of hospital admissions associated with DRPs was 4.3% (95% CI 3.6, 5.0). More specifically, 4.3% (95% CI 3.5, 5.1) of eligible patients at RCH and 4.3% (95% CI 1.4, 7.2) at GH were determined to be associated with a DRP. A summary of the total number of cases allocated to the eight DRP categories is provided in Table 1.

Table 2
Allocated causality and clinical significance classifications

Causality classification	Clinical significance classification* Category A	Category B	Category C	Total
Definite	33	10	11	54
Probable	10	9	12	31
Possible	20	8	14	42
Total	63	27	37	127

**A drug-related problem that results in the patient being admitted to hospital: for up to 24 h (Category A); for 24–48 h (Category B); for a period greater than 48 h and/or requires admission to an intensive care unit (Category C).*

Table 2 outlines the causality and clinical significance classifications allocated to cases.

The preventability of each case, excluding those allocated to category 8, was established. A preventability classification was therefore determined for 81 of the 127 cases. Of the 81 cases, 46.9% were deemed preventable, 30.9% not preventable and in 22.2% preventability was unable to be determined. The number of cases judged preventable per DRP category is provided in Table 1.

Drugs involved in DRPs

A mean of 2.0 drugs (median 2.0 drugs, ±SD 1.4) per case were recorded to have been taken in the week prior to admission. This count included regular and nonregular drugs along with documented over-the-counter and alternative medications. (Nonregular drugs included drugs taken on a when-required basis along with drugs taken for which there was no valid medical indication.) A total of 243 drugs were recorded, of which 160 were specifically implicated in the 127 admissions associated with DRPs. The 14 most common drugs implicated were: beclomethasone; flucloxacillin; insulin-isophane; paracetamol; sodium valproate; insulin-neutral; budesonide; fluticasone; diazepam; theophylline; sodium cromoglycate; dothiepin; oxazepam; and Triple Antigen vaccine. Table 3 outlines the most common drugs implicated in each DRP category.

Costs of DRPs

The total direct costs incurred by the two hospitals as a result of the 127 hospital admissions associated with

Table 3
The most common drugs involved in each drug-related problem (DRP) category

DRP categories	Most common drugs involved
1 (drug indication)	Beclomethasone, fluticasone, sodium cromoglycate
2 (wrong drug)	Flucloxacillin, salbutamol
3 (too little)	Insulin-neutral, insulin-isophane, phenobarbitone, sodium valproate
4 (too much)	Aminophylline, phenytoin
5* (ADR)	Flucloxacillin, lamotrigine, triamcinolone/neomycin/gramicidin/nystatin, Triple Antigen
6 (drug interaction)	Erythromycin
7* (non-adherence)	Beclomethasone, budesonide, flucloxacillin, fluticasone, insulin-neutral, insulin-isophane, salmeterol, sodium cromoglycate
8* (poisoning)	Clonidine, diazepam, dothiepin, oxazepam, paracetamol, paracetamol/codeine, propranolol, theophylline

**A wide range of drugs were implicated in this DRP category, as such only those involved in two or more cases are included in the table. ADR, Adverse drug reaction.*

DRPs was £100 707, of which £61 543.20 was associated with DRPs determined by the panel to be preventable.

Discussion

The results presented confirm that hospital admissions are associated with DRPs within the Australian paediatric population.

The combined data revealed the frequency of hospital admissions associated with DRPs to be 4.3% (95% CI 3.6, 5.0). Three previous paediatric studies investigated hospital admissions associated with DRPs [2, 6, 7], one of which was conducted by us [2]. The two overseas studies (Lebanon, Israel) report the frequency of such admissions to range between 7.9% and 17.7% [6, 7], results that differ markedly from the results of the present study. The differences may primarily reflect variances in sample populations, as both studies included oncology patients [6, 7]. However, differences in methodologies were also apparent. For example, the two overseas paediatric studies utilized admission interviews in the process of data collection, a factor thought to contribute to a higher number of DRPs being identified.

In a review of Australian studies investigating drug-related admissions, Roughead *et al.* reported the frequency of such admissions in the adult population to range from 2.4% to 22% [17]. The 4.3% (95% CI 3.6, 5.0) of admissions reported in this study therefore falls within this range.

Three studies have investigated the issue of preventability in the Australian adult population, with the frequency of preventable admissions ranging from 32% to 69% [17]. Our percentage of 46.9% of preventable admissions falls within this range. It is therefore not unreasonable for the issue of DRPs occurring in the paediatric population to be given as much attention as that given to the adult population.

The drugs most frequently implicated in the DRPs identified in this study were in contrast to those reported by Roughead *et al.* in the Australian adult population [17]. It can be inferred that prevention strategies developed within the adult population may not be applicable to the paediatric population.

Certain limitations must be considered when interpreting our findings. First, as we excluded trauma and oncology patients, it may not be possible to generalize the results obtained to the entire paediatric population. However, given that oncology patients have been reported to be four times more likely to experience an ADR [10], it is likely that the frequency presented is a conservative estimate. Second, in reviewing the consistency of the frequencies reported, it must be acknowledged that because data collection was not undertaken over a 1-year period at either of the hospitals, it is possible that seasonal variations may have influenced the frequency of DRPs reported.

In conclusion, DRPs in children remain an important, costly and partly preventable problem. As the drugs implicated in the DRPs identified in this study differed from those reported within the adult population, the approach taken to reduce such problems may also differ.

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References

1 Johnson JA, Bootman JL. Drug-related morbidity and mortality: a cost-of-illness model. Ann Intern Med 1995; 155: 1949–56.

2 Easton KL, Parsons BJ, Starr M, Brien JE. The incidence of drug-related problems as a cause of hospital admissions in children. Med J Aust 1998; 169: 356–9.

3 Whyte J, Greenan E. Drug usage and adverse drug reactions in paediatric patients. Acta Paediatr Scand 1977; 66: 767–75.

4 McKenzie MW, Marchall GL, Netzloff ML, Cluff LE. Adverse drug reactions leading to hospitalization in children. J Pediatr 1979; 89: 487–90.

5 Mitchell AA, Lacouture PG, Sheehan JE, Kauffman RE, Shapiro S. Adverse drug reactions in children leading to hospital admission. Pediatrics 1988; 82: 24–9.

6 Major S, Badr S, Bahlawan L et al. Drug-related hospitalization at a tertiary teaching center in Lebanon: incidence, associations, and relation to self-medicating behavior. Clin Pharmacol Ther 1998; 64: 450–61.

7 Yosselson-Superstine S, Weiss T. Drug-related hospitalization in paediatric patients. J Clin Hosp Pharm 1982; 7: 195–203.

8 Martinez-Mir I, Garcia-Lopez M, Palop V et al. A prospective study of adverse drug reactions as a cause of admission to a paediatric hospital. Br J Clin Pharmacol 1996; 42: 319–24.

9 McKenney JM, Harrison WL. Drug-related hospital admissions. Am J Hosp Pharm 1976; 33: 792–5.

10 Collins GE, Clay MM, Falletta JM. A prospective study of the epidemiology of adverse drug reactions in pediatric hematology and oncology patients. Am J Hosp Pharm 1974; 31: 968–75.

11 Jonville-Bera AP, Giraudeau B, Blanc P, Beau-Salinas F, Autret-Leca E. Frequency of adverse drug reactions in children: a prospective study. Br J Clin Pharmacol 2002; 53: 207–10.

12 Strand LM, Morley PC, Cipolle RJ, Ramsey R, Lamsam GD. Drug-related problems. their structure and function. Ann Pharmacother 1990; 24: 1093–7.

13 Easton-Carter KL, Chapman CB, Brien JE. Emergency department attendances associated with drug-related problems in paediatrics. J Paediatr Child Health 2003; 39: 124–9.

14 Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. Hosp Pharm 1992; 27: 538.

15 Jackson T. Cost estimates for hospital inpatient care in Australia: evaluation of alternative sources. Aust NZ J Public Health 2000; 24: 234–41.

16 Hodgson TA, Meiners MR. Cost-of-illness methodology: a guide to current practices and procedures. Milbank Mem Fund Q 1982; 60: 429–61.

17 Roughead EE, Gilbert AL, Primrose JG, Sansom LN. Drug-related hospital admissions: a review of Australian studies published 1988–1996. Med J Aust 1998; 168: 405–8.