ORIGINAL RESEARCH ARTICLE

Drug Saf 2011; 34 (1): 59-71
0114-5916/11/0001-0059/$49.95/0

Detecting Medication Errors in the New Zealand Pharmacovigilance Database

A Retrospective Analysis

Desireé L. Kunac and *Michael V. Tatley*

New Zealand Pharmacovigilance Centre, Department of Preventive and Social Medicine, University of Otago, Dunedin, New Zealand

Abstract

Background: Despite the traditional focus being adverse drug reactions (ADRs), pharmacovigilance centres have recently been identified as a potentially rich and important source of medication error data.

Objective: To identify medication errors in the New Zealand Pharmacovigilance database (Centre for Adverse Reactions Monitoring [CARM]), and to describe the frequency and characteristics of these events.

Methods: A retrospective analysis of the CARM pharmacovigilance database operated by the New Zealand Pharmacovigilance Centre was undertaken for the year 1 January–31 December 2007. All reports, excluding those relating to vaccines, clinical trials and pharmaceutical company reports, underwent a preventability assessment using predetermined criteria. Those events deemed preventable were subsequently classified to identify the degree of patient harm, type of error, stage of medication use process where the error occurred and origin of the error.

Results: A total of 1412 reports met the inclusion criteria and were reviewed, of which 4.3% (61/1412) were deemed preventable. Not all errors resulted in patient harm: 29.5% (18/61) were 'no harm' errors but 65.5% (40/61) of errors were deemed to have been associated with some degree of patient harm (preventable adverse drug events [ADEs]). For 5.0% (3/61) of events, the degree of patient harm was unable to be determined as the patient outcome was unknown. The majority of preventable ADEs (62.5% [25/40]) occurred in adults aged 65 years and older. The medication classes most involved in preventable ADEs were antibacterials for systemic use and anti-inflammatory agents, with gastrointestinal and respiratory system disorders the most common adverse events reported. For both preventable ADEs and 'no harm' events, most errors were incorrect dose and drug therapy monitoring problems consisting of failures in detection of significant drug interactions, past allergies or lack of necessary clinical monitoring. Preventable events were mostly related to the prescribing and administration stages of the medication

use process, with the majority of errors 82.0% (50/61) deemed to have originated in the community setting.

Conclusions: The CARM pharmacovigilance database includes medication errors, many of which were found to originate in the community setting and reported as ADRs. Error-prone situations were able to be identified, providing greater opportunity to improve patient safety. However, to enhance detection of medication errors by pharmacovigilance centres, reports should be prospectively reviewed for preventability and the reporting form revised to facilitate capture of important information that will provide meaningful insight into the nature of the underlying systems defects that caused the error.

Background

Medications are a leading source of unintended patient harm in hospitals worldwide.[1-4] These adverse drug events (ADEs) are costly,[5,6] can cause or prolong hospitalization[6,7] and are associated with significant morbidity and mortality.[6-8] An ADE is an actual injury or harm resulting from use of a medicine;[5] ADEs may arise due to an adverse drug reaction (ADR) to a usual recommended dose of medicine, or due to an error in the use of a medicine (preventable ADE). Whilst not all errors in medication use result in patient harm ('no harm' medication errors), the finding that up to 56% of ADEs may be due to medication errors (termed preventable ADEs)[3,9,10] has made these events a global priority for patient safety solutions[11] and research.[12]

ADRs as a source of patient harm have long been recognized[13] and ADR surveillance systems operated by regional or national pharmacovigilance centres are now well established, along with an international network linking around 100 countries to facilitate global ADR monitoring through the WHO's International Drug Monitoring Programme.[14] Despite the traditional focus being ADRs, pharmacovigilance centres have recently been identified as a potentially rich and important source of medication error data. As part of a pilot project built by the World Alliance for Patient Safety in collaboration with the WHO Programme for International Pharmacovigilance, a retrospective review of 1300 ADEs reported to the Moroccan Pharmacovigilance Centre (2003–6) revealed that 14.4% (n = 187) were considered preventable.[15] Furthermore, in a prospective study of ADRs spontaneously reported to the Regional Drug Monitoring Centre of Tours, France, over a 1-year period, 17% of patients were adjudged to have experienced an avoidable ADR secondary to inappropriate prescribing.[16] The WHO has highlighted the importance of identifying medication errors and is now working toward expansion of existing roles of pharmacovigilance centres to include monitoring of medication errors.[17,18] Pharmacovigilance centres are beginning to work collaboratively to prospectively identify medication errors.[19]

New Zealand implemented a national ADR surveillance scheme in 1965 and was one of the earliest members of the WHO International Drug Monitoring Programme when it was established in 1968. Today, the New Zealand Pharmacovigilance Centre, based within the University of Otago, Dunedin, is the national centre responsible for monitoring adverse reactions to therapeutic products in New Zealand, through the Centre for Adverse Reactions Monitoring (CARM).[20] Given the considerable contribution of medication errors to patient harm and the emerging role of pharmacovigilance centres in identification of these events, the New Zealand Pharmacovigilance Centre initiated this study to contribute to this critical international initiative from a New Zealand perspective.

The aim of this study was to identify medication errors in the CARM pharmacovigilance database, and to describe the frequency and characteristics of these events.

Methods

Study Design

A retrospective analysis of the CARM pharmacovigilance database operated by the New Zealand Pharmacovigilance Centre was undertaken for the year 1 January–31 December 2007.

Selection Criteria

All ADR reports notified to CARM during the study period, involving medications, were considered for inclusion. Reports relating to vaccines, clinical trials and pharmaceutical company reports were excluded as these are intended as a subject for future analysis. Those reports where the event and medicine were considered unrelated (see causality assessment in the Classification of ADRs section) were also excluded from further analysis.

Classification of Adverse Drug Reactions

All ADR reports received by CARM undergo evaluation and assessment by a medical assessor. Full details of this process have been previously described,[20] but include the following:

- *Clinical evaluation:* The description of the event, as outlined by the reporter in the ADR report, is evaluated by a medical assessor and coded to standardized terms from the WHO Adverse Reactions Terminology (WHO-ART) dictionary. This dictionary organizes terms under System Organ Class (SOC) headings, with subhierarchies within each SOC to facilitate analysis. Each event is then assessed for severity, seriousness and patient outcome. The term 'severe' is used to describe the intensity (severity) of a specific event, whereas the term 'serious' relates to the patient/event outcome.[21,22]
- *Causality assessment:* The degree of association (causality) between the suspect medicine(s) and the reported event is determined according to WHO definitions.[21] The criteria consider the nature of the event, its timing, the dose of the medicine being taken, possible confounding factors and information on dechallenge or rechallenge with the suspected medicine. A causality assessment of 'certain', 'probable' or 'possible' assigned to an event identifies a reaction, whereas an adverse event deemed 'unlikely' to be causally associated with the medicine are considered unrelated.
- *Classification of medicine classes:* The WHO guidelines for the Anatomical Therapeutic Chemical classification system were used to classify medicine classes.[23]

Preventability Assessment

To determine whether the event may be associated with an error, each report was assessed for preventability using predetermined criteria,[24] as shown in table I. Confidence about the preventability classification was rated on a 4-point scale[25] (table II). Assessment was undertaken independently by two medical assessors; the assessors were asked to judge an event as preventable if it was believed an error had occurred with the use of a medicine. These tools have been found to have 'moderate' to 'fair' reliability for preventability assessment of ADEs in a paediatric inpatient population.[26]

Characterization of Preventable Events

Preventable events with a confidence score of 1 or 2 were then further classified to identify the following:

- Degree of patient harm, using the National Coordinating Council for Medication Error

Table I. Preventability assessment criteria[24]

Answering 'yes' to one or more of the following questions suggests that the event in question may have been preventable	
A	Was the drug involved in the event *not* considered appropriate for the patient's clinical condition?
B	Was the dose, route of administration or frequency of administration *not* appropriate for the patient's baseline characteristics (i.e. age, weight, disease state)?
C	Was the necessary medication monitoring omitted (i.e. therapeutic drug monitoring or other necessary laboratory tests not performed)?
D	Did the patient have a history of allergy or known previous reactions to the drug?
E	Was a drug-drug, drug-food, drug-laboratory interaction involved in the event?
F	Was a toxic or sub-therapeutic serum drug level documented?
G	Was poor patient adherence involved in the event?

Table II. Confidence score regarding preventability decision[25]a

1	Definitely preventable
2	Probably preventable
3	Probably not preventable
4	Definitely not preventable

a Assessors were asked to rate the strength of evidence for preventability using these scores.

Reporting and Prevention (NCC MERP) taxonomy of medication errors, which is a previously validated index for categorizing medication errors.[27] The term 'harm', as contained in the definition of ADE, included the entire range of seriousness, from very minor harm to life-threatening events or death. Where the error resulted in no actual harm to the patient, these were classified as 'no harm' medication errors (table III). The frequency of preventable ADEs versus 'no harm' medication errors was then determined.

- Type of error, using the NCC MERP taxonomy of medication errors.[28]
- Stage(s) in the medication use process (prescribing, dispensing, administration and monitoring) where the error occurred.
- Origin of the error, either during hospital admission or in the community.

Results

A total of 2783 reports were received by CARM for the period 1 January–31 December 2007; 1371 reports did not meet the inclusion criteria (vaccines 898, clinical trials 7, pharmaceutical company 439, causally 'unrelated' event 27) and were excluded. The remaining 1412 reports were included in the final analysis.

Preventability of Reported Events

Through application of the preventability assessment tools, 18 reports were deemed 'definitely' preventable and 43 'probably' preventable, resulting in 4.3% of reports (61/1412) being considered preventable events arising due to error. However, only 1.0% of reports (14/1412) were considered preventable events by a medical assessor when using the standardized pharmacovigilance coding terms from the WHO-ART dictionary.

Characterization of Preventable Events

The age of individuals who experienced a preventable event ranged from 1 month to 95 years, among which 39 were female and 22 male. Over half of the events (n = 32) occurred in adults aged 65 years and older, with 13 of these occurring in individuals aged 80 years and older (figure 1).

Frequency of Preventable Adverse Drug Events (ADEs) and 'No Harm' Medication Errors

Of the preventable events, 65.5% (40/61) were adjudged associated with patient harm (termed preventable ADEs) and 29.5% (18/61) 'no harm' medication errors. For 4.9% of events (3/61), which all involved drug exposure of podophyllotoxin during pregnancy, the degree of patient harm was unable to be determined as the patient outcome was unknown at the time of the report (table III). A greater number of harmful events (preventable ADEs) than 'no harm' errors were found to be experienced by individuals at the two extremes of age. However, by far the majority of harmful events (25/40) occurred in adults aged 65 years and over, with 12 of these involving individuals aged 80 years and over (figure 2).

Medication Class

The medication classes most involved in preventable ADEs (table IV) were antibacterials for

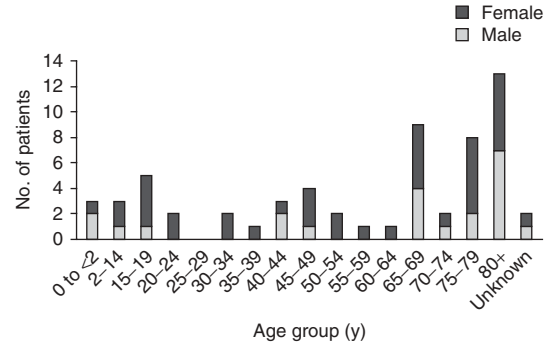

Fig. 1. Age and sex distribution of patients who experienced preventable events.

Table III. Classification of preventable events by degree of patient harm

Classification	NCC MERP category[a]	Definition	Number of events
No error	A	Circumstances or events that have the capacity to cause harm (near miss)	0
Error, no harm	B	An error occurred that did not reach the patient (near miss)	0
	C	An error occurred that did reach the patient but did not cause patient harm	6
	D	An error occurred that reached the patient and monitoring was required to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm	12
Error, harm	E	An error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention	7
	F	An error occurred that may have contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalization	25
	G	An error occurred that may have contributed to or resulted in permanent patient harm	2
	H	An error occurred that required an intervention necessary to sustain life	3
Error, death	I	An error occurred that may have contributed to or resulted in the patient's death	3
Unknown	U	Outcome unknown	3
Total			**61**

a Categories B–D were classified as 'no harm' medication errors and categories E–I were classified as preventable adverse drug events.

NCC MERP = National Coordinating Council for Medication Error Reporting and Prevention.

systemic use, anti-inflammatory agents, psychoanaleptics, psycholeptics, analgesics and lipid modifying agents. Thirty different medications were involved in preventable ADEs, with nitrofurantoin, roxithromycin, celecoxib and simvastatin being the most commonly implicated.

For 'no harm' medication errors, the medication classes most involved were drugs for obstructive airway diseases, antithrombotics, antibacterials for systemic use and anti-inflammatory agents. Fourteen medications were implicated in 'no harm' medication errors, with salbutamol and warfarin being most involved.

System Organ Class

Gastrointestinal and respiratory system disorders were the most common adverse event reported for preventable ADEs, whilst for 'no harm' medication errors, the most commonly reported adverse effects related to the SOCs 'skin and appendage disorders' and 'body as a whole' (table IV).

Type of Error

For both preventable ADEs and 'no harm' medication errors, most errors were incorrect dose and drug therapy monitoring problems consisting of failures in detection of significant drug interactions, past allergies or lack of necessary clinical monitoring. Incorrect dosing errors resulted in overdosage for preventable ADEs, but for 'no harm' medication errors, underdosing was an issue (table IV).

Stage(s) in the Medication Use Process where Error Occurred

Errors occurred at each stage of the medication use process, from prescribing, dispensing, administration and monitoring (table IV). The majority of preventable ADEs were related to the prescribing stage followed by the administration stage, whereas 'no harm' medication errors mostly

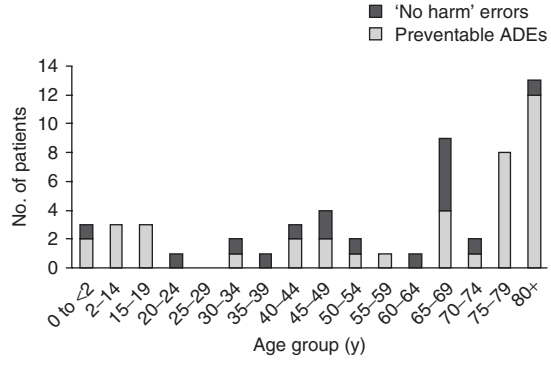

Fig. 2. Age distribution of patients who experienced 'no harm' medication errors and preventable adverse drug events (ADEs).

Table IV. Characteristics of preventable events

Code/abbreviation	Description	All preventable events	Preventable adverse drug events	'No harm' medication error	Unknown outcome
ATC code	**Medicine class**				
A01	Stomatological preparations	1	0	1	0
B01	Antithrombotic agents	4	1	3	0
C01	Cardiac therapy	2	1	1	0
C10	Lipid modifying agents	3	3	0	0
D01	Antifungals for dermatological use	1	1	0	0
D04	Anaesthetics for topical use	1	1	0	0
D06	Antibiotics for dermatological use	3	0	0	3
J01	Antibacterials for systemic use	13	11	2	0
J05	Antivirals for systemic use	1	1	0	0
L04	Immunosuppressive agents	2	1	1	0
M01	Anti-inflammatory products	8	6	2	0
N02	Analgesics	4	3	1	0
N03	Antiepileptics	2	2	0	0
N05	Psycholeptics	4	3	1	0
N06	Psychoanaleptics	5	4	1	0
P02	Anthelmintics	1	1	0	0
R03	Drugs for obstructive airway diseases	4	0	4	0
Z	Herbal preparations	2	1	1	0
SOC code	**SOC**				
0100	Skin and appendage disorders	8	4	4	0
0200	Musculoskeletal system disorders	5	5	0	0
0300	Collagen disorders	1	0	1	0
0410	Central and peripheral nervous system	8	6	2	0
0432	Hearing and vestibular disorders	3	3	0	0
0500	Psychiatric disorders	4	4	0	0
0600	Gastrointestinal disorders	9	9	0	0
0700	Liver and biliary system disorders	2	2	0	0
0800	Metabolic and nutritional disorders	3	3	0	0
0900	Endocrine disorders	1	1	0	0

Continued next page

Table IV. Contd

Code/abbreviation	Description	All preventable events	Preventable adverse drug events	'No harm' medication error	Unknown outcome
1030	Heart rate and rhythm disorders	1	1	0	0
1040	Vascular disorders	1	0	1	0
1100	Respiratory system disorders	10	9	1	0
1210	Red blood cell disorders	2	2	0	0
1220	White cell and RES disorders	1	1	0	0
1230	Platelet, bleeding and clotting disorders	7	5	2	0
1300	Urinary system disorders	1	1	0	0
1420	Reproductive disorders, female	1	0	1	0
1500	Fetal disorders	2	1	1	0
1810	Body as a whole – general disorders	10	6	4	0
NCC MERP Code	**Type of error**				
2	Incorrect dose				
	2.1 Resulting in overdosage	16	13	3	0
	2.2 Resulting in underdosage	4	0	4	0
3	Incorrect strength/concentration	2	1	1	0
4	Incorrect drug	1	1	0	0
5	Incorrect dosage form	1	1	0	0
6	Incorrect medication administration technique	1	1	0	0
11	Incorrect patient	1	0	1	0
12	Drug therapy monitoring problem				
	12.1 Drug-drug interaction	18	13	5	0
	12.3 Documented allergy	5	3	2	0
	12.4 Drug-disease interaction	2	1	1	0
	12.5 Clinical (e.g. blood pressure)	7	7	0	0
13	Deteriorated drug	1	0	1	0
14	Other	11	8	3	3
Abbreviation	**Stage of error in medication use process**				
P	Prescribing	28	23	5	0
D	Dispensing	13	10	3	0
A	Administration	26	13	13	3
M	Monitoring	10	8	2	0

ATC = Anatomical Therapeutic Chemical; **NCC MERP** = National Coordinating Council for Medication Error Reporting and Prevention; **RES** = Reticulo-endothelial System; **SOC** = System Organ Class.

occurred in the administration stage, followed by the prescribing stage. Sub-analysis revealed that incorrect dosage most often involved the administration stage, and drug therapy monitoring problems were mostly associated with the prescribing stage.

Origin of the Error

The majority of errors (82% [50/61]) were deemed to originate in the community setting, with the remaining 18% (11/61) arising during hospital admission.

Preventable ADEs in Adults Aged 65 Years and Older

Incorrect doses resulting in overdosage and drug therapy monitoring problems were the main error types involved in the 25 preventable ADEs occurring in adults aged 65 years and over (table V). The causes include inappropriate dose for patient age and renal function, lack of recognition of a significant drug interaction (particularly combinations with warfarin therapy), not taking into account a history of allergy to the specific medicine, inadequate monitoring (particularly of nitrofurantoin) and lack of gastroprophylaxis with anti-inflammatory medications.

Discussion

The principal finding of the present study is that whilst pharmacovigilance systems are primarily targeted to ADR surveillance, these systems may also be a useful source of medication error data, particularly for those errors arising in the community setting. In the present study, use of the preventability assessment tool enhanced detection of medication errors with a yield of 4.3% compared with 1.0% when using the standard pharmacovigilance coding system. Medication errors occurred more commonly in females than males and over half of all errors occurred in the 65 years and older age group. Not all medication errors identified resulted in patient harm; 29.5% were 'no harm' medication errors, but 65.5% of errors were deemed to have been associated with some degree of patient harm (preventable ADEs).

Frequency of Preventable Events

Much of what is known about the epidemiology of medication errors and preventable ADEs has been gleaned from work undertaken in hospitals using intensive event detection methods, and it appears that only a few studies have estimated the frequency of medication errors reported to pharmacovigilance centres.[15,16] Comparisons between studies regarding rates of events are problematic as the rates of events are influenced not only by health systems and settings but also to a major degree by the methods of event detection; the more comprehensive data collection using multiple strategies, the higher the yield of events.[30,31] Therefore, as expected, the frequency of preventable ADEs identified through review of pharmacovigilance data harvested through voluntary reporting[32] and tailored to ADR detection is much lower than prospective observational cohort studies of hospitalized inpatients that employ multifaceted approaches to preventable ADE detection and report frequencies of up to 56%.[3,9,10,33]

In the present study, retrospective review of 1412 reports to the New Zealand CARM pharmacovigilance database over 1 year (2007) revealed that 4.3% (n = 61) were deemed preventable. Using a similar retrospective review methodology, of 1300 ADEs reported to the Moroccan Pharmacovigilance Centre over 3 years (2003–6), 14.4% (n = 187) were considered preventable.[15] This variance in rate of preventable events may be explained by a number of factors, such as differences in the study setting and associated differences in healthcare delivery between countries; differences in methods, specifically the different preventability assessment tools used; that the Moroccan Pharmacovigilance Centre also receives reports of accidental poisonings as it is also a Poisons Control Centre; and the higher denominator for events due to a higher overall rate of reporting of events in New Zealand. Thus, any differences in rates should not be interpreted simply as reflecting differing levels of the quality of care between countries, but more as reflecting differences in study setting and methodologies employed and possibly even indicative of differences in pharmacovigilance practices between countries.

Table V. Type of error and medications involved in the 25 preventable adverse drug events in adults aged 65 years and over

Type of error	Medicine	Reported adverse event	Comments
Incorrect dose			
Resulting in overdosage	Diclofenac	Acute renal failure, confusion	Dose too high
	Erythromycin	Deafness	Dose too high
	Galantamine	QT interval prolonged	Patient self-administered too high a dose
	Simvastatin	Myopathy, hepatic enzymes increased	Dose too high
	Simvastatin	Muscle weakness, nausea	Dose too high, combination with diltiazem
Drug therapy monitoring problem			
Drug-drug interaction	Azathioprine	Anaemia, leukopenia	Combination with allopurinol
	Celecoxib	Haemorrhagic gastric and duodenal ulcers	Combination with prednisone and aspirin (acetylsalicylic acid)
	Fluoxetine[a]	Epistaxis	Combination with warfarin
	Miconazole	INR increased	Combination with warfarin
	Roxithromycin	INR increased, hepatic function abnormal	Combination with warfarin, paroxetine, amoxicillin/clavulanic acid (Augmentin®)
	Roxithromycin	INR increased, haemorrhage	Combination with warfarin
	Roxithromycin	INR increased	Combination with warfarin
	Simvastatin	Rhabdomyolysis, myalgia, myoglobinuria	Combination with diltiazem
	Venlafaxine	Serotonin syndrome, rhabdomyolysis, multiple organ failure	Combination with paroxetine
Documented allergy	Cotrimoxazole	Stevens-Johnson syndrome	History of allergy to cotrimoxazole
	Dextropropoxyphene[a]/paracetamol (acetaminophen)	Deafness, tinnitus	History of allergy to dextropropoxyphene
Clinical	Amiodarone[a]	Interstitial lung disease	Inadequate monitoring
	Fluoxetine	Hyponatraemia	Inadequate monitoring
			Combination with omeprazole and valproate
	Lithium	Hypothyroidism, constipation	Inadequate monitoring
	Nitrofurantoin[a]	Alveolitis, pulmonary fibrosis	Inadequate monitoring
	Nitrofurantoin[a]	Interstitial lung disease	Inadequate monitoring
	Nitrofurantoin[a]	Interstitial lung disease	Inadequate monitoring
	Nitrofurantoin[a]	Pulmonary fibrosis	Inadequate monitoring, continuous treatment for 2 years
Other			
	Celecoxib	Haemorrhagic duodenal ulcer, duodenitis	Lack of gastroprophylaxis, also in combination with aspirin
	Indometacin[a]	Haemorrhagic duodenal ulcer	Non-compliance with gastroprophylaxis and unable to attend follow-up appointments

a Medications that should be avoided in older adults according to Beers criteria.[29]

INR = international normalized ratio.

Interestingly, we found 1.0% reports were assessed and coded as 'medication error' when using the standardized coding terms from the WHO-ART dictionary. This finding is remarkably consistent with a review of the WHO Individual Case Report pharmacovigilance database, which contains collated data from around 100 contributing countries, where, cumulatively, medication errors comprise 0.9% of reports (Pal S, personal communication). However, based on the findings of the present study, this is likely to be an underestimate of the frequency of preventable events

contained in the international database. It is important to distinguish between ADRs and medication errors as the approaches to management will differ. The causes of medication errors are usually related to failures in the systems or processes of medicine use, whereas ADRs are related to the inherent pharmacological properties of the medicine. Application of the preventability assessment tools enabled those events amenable to system or process improvements to be more readily identified, providing greater opportunity to improve patient safety.

Characteristics of Preventable Events

The pattern of events in the present study is consistent with the findings of previous work, which also found an elderly and female predominance of preventable events.[15] An important new finding of the present study is that by far the majority of preventable events were found to originate in the community setting and very few errors that originate in hospitals are currently identified through the New Zealand pharmacovigilance voluntary reporting programme. This suggests that pharmacovigilance centres may be a potentially valuable source of primary care data.

In the present study, antibacterials for systemic use and anti-inflammatory agents were the medication classes implicated in both preventable ADEs and 'no harm' medication errors. Specifically, nitrofurantoin, roxithromycin, celecoxib and simvastatin were the medicines most often associated with preventable ADEs. The most common adverse effects reported were gastrointestinal disorders followed by respiratory system disorders for preventable ADEs, with skin and appendage disorders the main adverse effects reported for 'no harm' medication errors. These findings are again consistent with previous reviews of spontaneous reports to pharmacovigilance centres.[15,16]

We found most medication errors were due to incorrect dose and drug therapy monitoring problems, particularly due to failures in detection of significant drug interactions, past allergies or lack of necessary clinical monitoring. Previous work has also found most medication errors were due to wrong dose, non-respect of documented allergy or contraindications and interactions.[15] McDonnell and Jacobs[34] reported that most medication errors occurred as a result of inadequate monitoring of therapy or inappropriate dose. Patient non-compliance, drug-drug interactions, contraindication to therapy and documented allergy were also associated with these events.

In our study, the prescribing and administration stages were identified as the most common stages of the medication use process where preventable ADEs and medication errors occur, in line with previous reports.[10,35,36] We also found that incorrect dosage most often involved the administration stage, and drug therapy monitoring problems were mostly associated with the prescribing stage.

We observed that individuals at the two extremes of age experienced a greater number of harmful than 'no harm' errors. Both the elderly[37] and children, particularly neonates and infants,[35] are recognized as high-risk patient groups for harmful events. Our study further emphasizes that these age groups should be a target for prevention strategies. In the sub-analysis of preventable events in the elderly population aged 65 years and older, 8 of the 25 cases involved potentially inappropriate medication use according to the Beers criteria[29] for safe medication use in elderly patients. The five medications involved in these eight cases (fluoxetine, dextropropoxyphene, nitrofurantoin, amiodarone, indometacin) are among the list of 48 individual medications that should be avoided in older adults, independent of diagnoses or conditions.

Limitations

The present study relied solely on voluntary reports of events to the Pharmacovigilance Centre. Under-reporting is a recognized limitation of pharmacovigilance spontaneous reporting programmes,[38] and as the system does not primarily focus on encouraging reports of error it therefore reflects an underreporting bias for medication errors, which likely explains the low number of preventable events found in our study. Consequently, despite the limitation of the data-

base, our study illustrates that even such databases have value in identifying medication errors, particularly when the primary reason for reporting is not error. Also, with reporting forms tailored to data collection of ADR information, details regarding patient weight, dose of medication, and eventual patient outcome were often lacking. Retrospective analysis meant that events could not be easily followed up to obtain this further information or to clarify any details provided. Complete information is necessary when making the preventability assessment and, as such, some errors may have been missed, leading to a lower than actual preventable event rate. In addition, possible causal factors were not captured using the ADR form, limiting the ability to undertake root cause analyses and form conclusions about why the event occurred. Nevertheless, the ADR reporting card in its present form does at least provide a mechanism to enable identification of preventable events that could be further investigated if reviewed in a prospective manner.

Future Direction

To improve detection of preventable events in a pharmacovigilance database and to improve the utility of data obtained, the New Zealand Pharmacovigilance Centre ADR reporting form needs to be revised to enhance capture of relevant medication error data. For example, important patient information, such as a child's weight or the degree of renal impairment in an older adult, is required to detect dosing errors. Also, details about the event, particularly any possible contributing factors to the error would provide greater insight into the likely causes of the event, better informing prevention strategies. Furthermore, application of the preventability assessment tools prospectively on incoming ADR reports would allow timely follow-up for incomplete information, strengthening the ability to make preventability judgements. Based on these findings, the New Zealand Pharmacovigilance Centre has adapted the methodology to allow prospective review of incoming reports on a routine basis.

This study highlights the importance of integrating medication error recognition systems within or with very close working relationships with national centres undertaking ADR monitoring, as ADR reports may contain events that reflect preventable ADEs.

We found the preventability assessment tools very easy to use and their application provided a higher yield of preventable events than through application of the current pharmacovigilance standardized coding terms. We encourage these methods, and any new approaches,[39] be piloted by other pharmacovigilance centres to not only allow comparison of findings between centres but to also determine the reliability of preventability assessment tools prior to potential wider routine use by pharmacovigilance centres.

Conclusions

The New Zealand CARM pharmacovigilance database includes medication errors, many of which were found to originate in the community setting and were reported as ADRs. Error-prone situations were more readily identified, providing greater opportunity to improve patient safety. However, to strengthen detection of medication errors by pharmacovigilance centres, reports should be prospectively reviewed for preventability and the reporting form revised to facilitate capture of important information that will provide meaningful insight into the nature of the underlying systems defects that caused the error.

Acknowledgements

We acknowledge the invaluable contributions of our New Zealand Pharmacovigilance Centre colleagues, Dr Ruth Savage, who, along with Dr Michael Tatley, was involved in event assessment, and Janelle Ashton for assistance with data extraction. We also thank Dr Joanne Hart (Medsafe) who offered thoughtful comments on drafts of this manuscript.

This study was supported by a grant awarded to the authors by the Department of Preventive and Social Medicine, University of Otago, Dunedin, New Zealand. The authors' work was independent of the funders. The authors have no conflicts of interest to declare.

References

1. Leape LL, Brennan TA, Laird N, et al. The nature of adverse events in hospitalized patients: results of the Harvard Medical Practice Study II. N Engl J Med 1991 Feb 7; 324 (6): 377-84

2. Wilson RM, Runciman WB, Gibberd RW, et al. The Quality in Australian Health Care Study. Med J Aust 1995; 163 (9): 458-71
3. Bates DW, Leape LL, Petrycki S. Incidence and preventability of adverse drug events in hospitalized adults. J Gen Intern Med 1993; 8 (6): 289-94
4. Davis P, Lay-Yee R, Briant R, et al. Adverse events in New Zealand public hospitals: principal findings from a national survey. Occasional paper no. 3. Wellington: Ministry of Health [online]. Available from URL: http://www.moh.govt.nz/moh.nsf/pagesmh/1240?Open [Accessed 2010 Sep 28]
5. Bates DW, Spell N, Cullen DJ, et al. The costs of adverse drug events in hospitalized patients. Adverse Drug Events Prevention Study Group. JAMA 1997; 277 (4): 307-11
6. Classen DC, Pestotnik SL, Evans RS, et al. Adverse drug events in hospitalized patients: excess length of stay, extra costs, and attributable mortality. JAMA 1997 Jan 22-29; 277 (4): 301-6
7. Briant R, Ali W, Lay-Yee R, et al. Representative case series from public hospital admissions 1998: I. Drug and related therapeutic adverse events. N Z Med J 2004 Jan 30; 117 (1188): U747 [online]. Available from URL: http://www.nzma.org.nz/journal/117-1188/747/content.pdf [Accessed 2010 Oct 11]
8. Phillips DP, Christenfeld N, Glynn LM. Increase in US medication-error deaths between 1983 and 1993. Lancet 1998 Feb 28; 351 (9103): 643-4
9. Bates DW, Boyle DL, Vander Vliet MB, et al. Relationship between medication errors and adverse drug events. J Gen Intern Med 1995; 10 (4): 199-205
10. Bates DW, Cullen DJ, Laird N, et al. Incidence of adverse drug events and potential adverse drug events: Implications for prevention. JAMA 1995; 274 (1): 29-34
11. WHO Collaborating Center for Patient Safety Solutions. Nine life-saving patient safety solutions. Jt Comm J Qual Patient Saf 2007 Jul; 33 (7): 427-62
12. Bates DW, Larizgoitia I, Prasopa-Plaizier N, et al. Global priorities for patient safety research. BMJ 2009; 338: 1242-4
13. McBride WG. Thalidomide and congenital abnormalities. Lancet 1961; II: 1358 [online]. Available from URL : http://www.jameslindlibrary.org/illustrating/records/thalidomide-and-congenital-abnormalities/whole_articles [Accessed 2010 Sep 28]
14. Uppsala Monitoring Centre (UMC). WHO Programme for International Drug Monitoring [online]. Available from URL: http://www.who-umc.org/DynPage.aspx?id=13140&mn=1514 [Accessed 2010 Jan 12]
15. Alj L, Touzani MDW, Benkirane R, et al. Detecting medication errors in pharmacovigilance database: capacities and limits. Int J Risk Saf Med 2007; 19 (4): 187-94
16. Jonville-Bera AP, Saissi H, Bensouda-Grimaldi L, et al. Avoidability of adverse drug reactions spontaneously reported to a French regional drug monitoring centre. Drug Saf 2009; 32 (5): 429-40
17. WHO. Patient safety: extending the scope of pharmacovigilance centres. WHO Pharmaceuticals Newsletter No. 6. Geneva: WHO, 2007
18. Bencheikh RS, Benabdallah G. Medication errors: pharmacovigilance centres in detection and prevention. Br J Clin Pharmacol 2009 Jun; 67 (6): 687-90
19. Benkirane RR, Abouqal R, Haimeur CC, et al. Incidence of adverse drug events and medication errors in intensive care units: a prospective multicenter study. J Patient Saf 2009 Mar; 5 (1): 16-22
20. Kunac D, Harrison-Woolrych M, Tatley M. Pharmacovigilance in New Zealand: the role of the New Zealand Pharmacovigilance Centre in facilitating safer medicines use. N Z Med J 2008; 121 (1283): 76-89
21. Edwards IR, Biriell C. Harmonisation in pharmacovigilance. Drug Saf 1994 Feb; 10 (2): 93-102
22. ICH Steering Committee. ICH harmonised tripartite guideline. Clinical safety data management: definitions and standards for expedited reporting [online]. Available from URL: http://www.ich.org/LOB/media/MEDIA436.pdf [Accessed 2009 Sep 16]
23. WHO Collaborating Centre for Drugs Statistics Methodology. Guidelines for ATC classification and DDD assignment [online]. Available from URL: http://www.whocc.no/atc_ddd_index/ [Accessed 2010 Sep 28]
24. Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. Hosp Pharm 1992; 27 (6): 538
25. Dubois RW, Brook RH. Preventable deaths: who, how often, and why? Ann Intern Med 1988; 109 (7): 582-9
26. Kunac DL, Reith DM, Kennedy J, et al. Inter- and intra-rater reliability for classification of medication related events in paediatric inpatients. Qual Saf Health Care 2006 Jun; 15 (3): 196-201
27. Forrey RA, Pedersen CA, Schneider PJ. Interrater agreement with a standard scheme for classifying medication errors. Am J Health Syst Pharm 2007 Jan 15; 64 (2): 175-81
28. NCC MERP. NCC MERP taxonomy of medication errors [online]. Available from URL: http://www.nccmerp.org/aboutMedErrors.html [Accessed 2009 Sep 12]
29. Fick DM, Cooper JW, Wade WE, et al. Updating the Beers criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. Arch Intern Med 2003 Dec 8-22; 163 (22): 2716-24
30. Morimoto T, Gandhi TK, Seger AC, et al. Adverse drug events and medication errors: detection and classification methods. Qual Saf Health Care 2004 Aug; 13 (4): 306-14
31. Kozer E, Scolnik D, Jarvis AD, et al. The effect of detection approaches on the reported incidence of tenfold errors. Drug Saf 2006; 29 (2): 169-74
32. Cullen DJ, Bates DW, Small SD, et al. The incident reporting system does not detect adverse drug events: a problem for quality improvement. Jt Comm J Qual Improv 1995; 21 (10): 541-8
33. Kunac D, Kennedy J, Austin NC, et al. Incidence, preventability and impact of adverse drug events (ADEs) and potential ADEs in hospitalized children in New Zealand. Pediatr Drugs 2009; 11 (2): 153-60
34. McDonnell PJ, Jacobs MR. Hospital admissions resulting from preventable adverse drug reactions. Ann Pharmacother 2002 Sep; 36 (9): 1331-6
35. Kaushal R, Bates DW, Landrigan C, et al. Medication errors and adverse drug events in pediatric inpatients. JAMA 2001; 285 (16): 2114-20

36. Kunac DL, Reith DM. Preventable medication-related events in hospitalised children in New Zealand. N Z Med J 2008; 121 (1272): 17-32
37. Hanlon JT, Schmader KE, Koronkowski MJ, et al. Adverse drug events in high risk older outpatients. J Am Geriatr Soc 1997 Aug; 45 (8): 945-8
38. Hazell L, Shakir SA. Under-reporting of adverse drug reactions: a systematic review. Drug Saf 2006; 29 (5): 385-96
39. Aronson JK, Ferner RE. Preventability of drug-related harms - part II: proposed criteria, based on frameworks that classify adverse drug reactions. Drug Saf 2010; 33 (11): 995-1002

Correspondence: Dr *Desireé L. Kunac*, New Zealand Pharmacovigilance Centre, Department of Preventive and Social Medicine, University of Otago, PO Box 913, Dunedin, New Zealand.
E-mail: desiree.kunac@otago.ac.nz