Investigation into the reasons for preventable drug related admissions to a medical admissions unit: observational study

R L Howard, A J Avery, P D Howard, M Partridge

Objective: To describe the drugs and types of medicine management problems most frequently associated with preventable drug related admissions to an acute medical admissions unit.

Design: Observation study.

Setting: Medical admissions unit in a teaching hospital in Nottingham, UK.

Participants: 4093 patients seen by pharmacists on the medical admissions unit between 1 January and 30 June 2001.

Main outcome measures: Proportion of admissions that were drug related and preventable, classification of the underlying causes of preventable drug related admissions, and identification of drugs most commonly associated with preventable drug related admissions.

Results: Of the admissions seen by pharmacists, 265 (6.5%) were judged to be drug related and 178 (67%) of these were judged to be preventable. Preventable admissions were mainly due to problems with prescribing (63 cases (35%)), monitoring (46 cases (26%)), and adherence to medication (53 cases (30%)). The drugs most commonly implicated were NSAIDs, antiplatelets, antiepileptics, hypoglycaemics, diuretics, inhaled corticosteroids, cardiac glycosides, and beta-blockers.

Conclusions: Potentially preventable drug related morbidity was associated with 4.3% of admissions to a medical admissions unit. In 91% of cases these admissions were related to problems with either prescribing, monitoring, or adherence.

METHODS

Selection of participants

The local research ethics committee approved the study. All patients admitted to the medical admissions unit (box 1) and seen by a pharmacist between 1 January and 30 June 2001 were included in the study. The pharmacists saw patients as part of their routine work Mondays to Fridays. They recorded details of all patients seen and reported patients with any suspected drug related morbidity to the principal investigator.
Preventable drug related admissions

8781 admissions between 1 January 2001 and 30 June 2001
- 4688 admissions not screened by the admissions ward pharmacists
- 3784 admissions screened by the admissions ward pharmacists and
- 309 by the principal investigator (total 4093 admissions screened)
- 3512 admissions screened as not drug related by the admissions ward pharmacists and principal investigator
- 581 admissions screened as possibly drug related by the admissions ward pharmacists and principal investigator
- 170 possible drug related admissions excluded after follow-up by the principal investigator
- 411 admissions assessed by the panel
- 146 admissions classified as not drug related
- 265 admissions classified as drug related
- 87 admissions classified as drug related and not preventable
- 178 admission classified as drug related and preventable

Figure 1 Flow of patients through the study.

Box 2 Details included in the case summaries
- Unique identifier
- Patient’s age
- Sex
- Date of admission
- Date of discharge
- Presenting complaint
- Medication history (before admission to hospital)
- Medication on discharge
- Events leading up to the admission
- Summary of hospital treatment
- Test results
- Diagnosis made by the physicians caring for the patient in hospital

(RH). Similar methods have been used successfully in at least five previous studies."

The principal investigator assessed possible cases using a combination of:
- medical note review (throughout the admission and on discharge);
- contact with general practitioners, where necessary, to obtain medication histories, test results, and information regarding the management of patients in primary care;
- interviewing patients, where possible, about the type and duration of symptoms and medication use, using an interview schedule. Those not interviewed included patients discharged home before being seen by the principal investigator, patients too unwell to be interviewed, and patients unable to speak English.

Following assessment by the principal investigator, some cases were excluded from further review (fig 1). These included cases where further investigation suggested that drug related morbidity was unlikely—for example, a low probability VQ scan in a case of suspected pulmonary embolism in a woman taking a combined oral contraceptive. In order to ensure that some patients were included in the study who had been admitted at weekends, the principal investigator identified patients with potential drug related morbidity through medical note review and patient interview on alternate weekends (fig 1).

Classification of potential drug related admissions
Following discharge from hospital, the principal investigator prepared detailed case summaries on patients with suspected

Box 3 Criteria used to review possible drug related admissions cases

Amended Hallas criteria for causality
(1) Known adverse drug reaction, toxic reaction, response to omission of treatment or inadequate treatment.
(2) Reasonable temporal relationship between commencement or cessation/omission of treatment and onset of problem.
(3) Risk of further problems likely to be reduced by dose reduction or increase, discontinuation, closer monitoring or commencement of treatment.
(4) Not explained by any other known condition of predisposition to the patient, or this condition/predisposition is likely to be exacerbated by the presence/absence of the drug.
(5) For drug toxicity:
- symptoms re-appeared upon re-exposure;
- laboratory tests showed toxic drug levels or drug induced metabolic disturbances that explained the symptom;
- symptoms resolved on dose reduction or discontinuation of the drug.
For drug omission:
- symptoms resolved upon re-introduction of the drug or dose increase.

Score = 5: criteria fulfilled then definite.
Score = 4: criteria fulfilled then probable
Score = 3: criteria fulfilled then possible
Score = 2 or less criteria fulfilled then either, not drug related or unvaluable

Hepler criteria for preventability
(1) Drug related morbidity (DRM) preceded by a recognisable drug therapy problem (DRP).
(2) Given the DRP, the DRM would have been reasonably foreseeable.
(3) The cause of DRM would have been identifiable with reasonable probability (Hallas criteria probable or definite for causality).
(4) The cause of the DRM could have been reasonably controllable within the context and objectives of treatment.

All four criteria must be fulfilled to confirm preventability.

Contribution of drug related problem to hospital admission
Score = 4 [dominant]: the suspected symptoms were the main reason for admission and no other symptoms contributed significantly.
Score = 3 [partly contributing]: the suspected symptoms played a substantial role in admission, but other factors also contributed significantly.
Score = 2 [less important]: the suspected symptoms played a minor or uncertain role, and the patient would probably have been admitted without them.
Score = 1 [not contributing]: other symptoms/circumstances were the reason for hospitalisation.

Hepler definitions for classification of drug related admissions
Score = 1: inappropriate prescribing.
Score = 2: inappropriate delivery (unavailable when needed, inappropriate formulation, failure to administer, dispensing error).
Score = 3: inappropriate behaviour by the patient (non-compliance).
Score = 4: patient idiosyncrasy (response to drug, mistake, or accident).
Score = 5: inappropriate monitoring.
Score = 6*: potentially preventable with interventions which are not standard care at present.

*Category 6 is additional to the original Hepler classification
drug related morbidity (box 2). These summaries provided reviewers with information on temporal relationships between medications and symptoms, the nature of patients’ symptoms, medication changes resulting from the admission, and the diagnoses made by physicians caring for the patients. The case summaries were independently scored by a hospital physician (PH), an academic general practitioner with a special interest in prescribing (AA), and a clinical pharmacist (RH). Each reviewer scored the cases using explicit criteria for causality, preventability, contribution to the admission, and classification of the underlying cause of the drug related morbidity (box 3). All the criteria were validated in pilot study work where 46 possible cases of drug related morbidity were reviewed to ensure the criteria were reliable and gave reasonable agreement between the reviewers. After scoring the cases the reviewers met up and, in keeping with standard practice in this field, a majority decision was used to classify the cases where there was disagreement on any of the review criteria.

Admissions were classified as drug related if two or more reviewers scored 4 or 5 using the amended Hallas criteria and judged the drug to have made a dominant or partial contribution to the admission. Admissions were classified as potentially preventable if the above criteria were fulfilled and two or more reviewers scored 4 using the Hepler criteria for preventability.

Recording of data
For all admissions to the medical admissions unit age, sex, and date of admission were recorded on an ACCESS 97 database. The hospital routinely records details of primary diagnoses of patients admitted, classified according to the International Classification of Diseases and Related Health Problems, 10th revision. These data were available for 7962 (91%) of all patients admitted. To assess inter-reviewer reliability, case review scores were compared using Cohen’s kappa and intraclass correlation coefficients (moderate to substantial agreement is indicated by kappa 0.41–0.80). The proportion of patients considered to have a drug related admission was calculated as the percentage of patients seen by a pharmacist who were classified as having definite or probable drug related morbidity that had made a dominant or partial contribution to the admission. We also calculated the proportion of drug related admissions that were considered potentially preventable. The proportion of patients considered to have a potentially preventable drug related admission was calculated as the percentage of patients seen by a pharmacist who were judged to have a preventable drug related admission.

RESULTS
Patient characteristics
The flow of patients through the study is shown in box 2. Of the 8781 patients admitted to the medical admissions unit, 4093 (47%) were seen by a pharmacist. The mean (SD) age of patients seen was 62.6 (20.7) years and the mean (SD) age of patients not seen by a pharmacist was 62.0 (20.6) years. Of the patients seen by a pharmacist 2002 (49%) were female and 2091 (51%) were male, and of the patients not seen by a pharmacist 2399 (51%) were female and 2289 (49%) were male.

Comparing patients who were either seen or not seen by a pharmacist, there were no significant differences in age

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Primary diagnoses of patients admitted to the medical admissions unit where there was a statistically significant difference between the numbers of patients seen and not seen by a pharmacist.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary diagnoses classified by ICD-10 chapter heading</td>
<td>Patients seen by pharmacist (n=3799)</td>
</tr>
<tr>
<td>Certain infectious and parasitic diseases</td>
<td>101 (2.7)</td>
</tr>
<tr>
<td>Diseases of the nervous system</td>
<td>153 (4.0)</td>
</tr>
<tr>
<td>Mental and behavioural disorders</td>
<td>84 (2.2)</td>
</tr>
<tr>
<td>Diseases of the respiratory system</td>
<td>702 (18.5)</td>
</tr>
<tr>
<td>Diseases of the skin and subcutaneous tissue</td>
<td>51 (1.3)</td>
</tr>
<tr>
<td>Diseases of the musculoskeletal system and connective tissue</td>
<td>106 (2.8)</td>
</tr>
</tbody>
</table>

Values are no (%). *Based on χ² tests (1 degree of freedom).

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Reviewer agreement in scoring case summaries calculated using kappa and intraclass correlation coefficients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Kappa for RH*TA</td>
</tr>
<tr>
<td>Causality</td>
<td>0.81</td>
</tr>
<tr>
<td>Preventability</td>
<td>0.77</td>
</tr>
<tr>
<td>Contribution to admission</td>
<td>0.74</td>
</tr>
<tr>
<td>Cause of suboptimal outcome</td>
<td>0.78</td>
</tr>
</tbody>
</table>

Data were exported to SPSS version 10.0 for statistical analysis. To assess differences between the groups of patients seen and not seen by a pharmacist, patient characteristics were compared using an independent t test for age on admission and χ² tests for sex, day of admission, and primary diagnosis (available for 7962 (91%) of all patients admitted). To assess inter-reviewer reliability, case review scores were compared using Cohen’s kappa and intraclass correlation coefficients (available for 7962 (91%) of all patients admitted). The proportion of patients classified as having a drug related admission was calculated as the percentage of patients seen by a pharmacist who were classified as having definite or probable drug related morbidity that had made a dominant or partial contribution to the admission. We also calculated the proportion of drug related admissions that were considered potentially preventable. The proportion of patients considered to have a potentially preventable drug related admission was calculated as the percentage of patients seen by a pharmacist who were judged to have a preventable drug related admission.
In this large observational study we found that 6.5% of admissions screened by pharmacists on a medical admissions unit were judged to be drug related and 67% of these were considered preventable. The drugs most commonly associated with potentially preventable drug related admissions were NSAIDs, low-dose aspirin, beta-blockers, antiepileptics, diuretics, sulphonylureas, digoxin, inhaled corticosteroids, nitrates, and insulin. These admissions were mainly attributed to problems with prescribing, monitoring, and patient adherence.

In order to minimise the risk of misclassifying cases, we used a methodology which compares well with the most rigorous studies previously reported. We used explicit criteria to guide the assessment of cases and a three member panel of reviewers to independently classify each case. Despite the varied backgrounds of the reviewers, kappa and intraclass correlation coefficients showed good to excellent levels of agreement. Only those admissions where the drug related morbidity was judged to be the dominant cause, or partially contributing, to the admission were included as drug related admissions. Also, when we classified drug related admissions as preventable, it was our view that the problems identified were predictable and controllable in terms of the treatment (Box 4). Nevertheless, our results could be questioned in terms of the extent to which they reflect the true preventability of the observed outcomes. For example, a recent study of hospital deaths that were attributed to medical error suggested that in many cases the error made relatively little difference to expected fatal outcomes in seriously ill patients. While these results are not directly comparable to our study, we recognise that some of the patients in our study were at very high risk of hospital admission regardless of any preventable medication related adverse event.

### Table 3

<table>
<thead>
<tr>
<th>British National Formulary class</th>
<th>Adverse drug event</th>
<th>Prescribing problem</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-steroidal anti-inflammatory drugs</td>
<td>Gastrointestinal toxicity</td>
<td>Prescription in patients with two or more risk factors without gastrointestinal prophylaxis†</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Renal tubular necrosis</td>
<td>Concurrent prescription of two full dose non-steroidal anti-inflammatory drugs without monitoring renal function</td>
<td>1</td>
</tr>
<tr>
<td>Antiplatelet drugs</td>
<td>Gastrointestinal toxicity</td>
<td>Prescription in patients with two or more risk factors without gastrointestinal prophylaxis</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Thrombotic event</td>
<td>Failure to prescribe in patients needing secondary prevention</td>
<td>4</td>
</tr>
<tr>
<td>Beta-adrenoceptor blocking drugs</td>
<td>Congestive cardiac failure</td>
<td>Prescription of standard dose beta-blocker in patient with known congestive cardiac failure</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Tachycardia</td>
<td>Co-prescription of atenolol with verapamil*</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Bleeding oesophageal varices</td>
<td>Sudden cessation</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Chest pain</td>
<td>Cessation without prescription of alternative</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Failure to maximise anti-anginal therapy despite ongoing symptoms over a period of time*</td>
<td>2</td>
</tr>
<tr>
<td>Antiepileptics</td>
<td>Fitting</td>
<td>Subtherapeutic prescription</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Inappropriate cessation</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Subtotal</td>
<td>6</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td>38†</td>
</tr>
</tbody>
</table>

*If a drug related admission involves more than one causative drug it may be recorded more than once in the table.
†Further details on “other” drug categories are available on the QSHC website (www.qshc.com/supplemental).
at reducing medication related morbidity in primary care. Combining evidence from this review with results from the study presented here means that we are able to suggest the types of interventions that may be most successful in reducing the incidence of preventable drug related admissions.

In terms of prescribing related problems, our study suggests that it may be worth focusing on preventing morbidity associated with NSAIDs and antiplatelet drugs. We know that patients with two or more risk factors for gastrointestinal bleeds are at high risk, and that various interventions can reduce the risks of these drugs. For example, co-prescription with ulcer healing drugs can reduce the risk of gastrointestinal bleeds and educational interventions have been shown to improve the safety of GP prescribing. Indeed, in a large Australian study an educational intervention focusing on NSAIDs reduced by 70% the rate of hospital admissions for upper gastrointestinal bleeding. The results of these studies may not be applicable to other drugs, but they suggest that nurse led monitoring clinics, computerised decision support systems, patient education and involvement, and patient self-management may help to improve control through improved monitoring. In our systematic review we did not find many other studies that looked at medication monitoring in primary care, and we believe that there is a need for further research in this area.

In terms of patient adherence, a number of studies have shown that improved education and approaches that provide greater involvement of patients in decision making improve patient adherence and may reduce drug related admissions. However, few studies have attempted to show clinical benefits. Our study suggests that priority should be given to patients taking the drugs listed in table 5.

Many of the problems identified in this study arise from medicines management in primary care, but it should be recognised that drug related admissions are relatively rare from the primary care perspective. For example, while NSAIDs were responsible for 12.4% of potentially preventable admissions in

### Table 4

<table>
<thead>
<tr>
<th>British National Formulary class</th>
<th>Adverse drug event</th>
<th>Problem</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loop diuretics</td>
<td>Overdiuresis causing dehydration ± renal failure ± electrolyte imbalance</td>
<td>Failure to monitor fluid balance, renal function, electrolytes etc*</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Congestive cardiac failure</td>
<td>Failure to monitor following cessation of angiotensin converting enzyme inhibitor and diuretics*</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Dizziness</td>
<td>Failure to check electrolytes</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Hyponatraemia</td>
<td>Subtotal</td>
<td>10</td>
</tr>
<tr>
<td>Potassium sparing diuretics</td>
<td>Overdiuresis causing dehydration ± renal failure ± electrolyte imbalance</td>
<td>Failure to monitor fluid balance, renal function, electrolytes etc*</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Hyponatraemia</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Dizziness</td>
<td>Unnecessary polypharmacy*</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Subtotal</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>Sulphonylureas</td>
<td>Hypoglycaemia</td>
<td>Failure to monitor blood sugar and renal function</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Hyperglycaemia</td>
<td>Failure to monitor blood sugar</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Subtotal</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>Cardiac glycosides</td>
<td>Digoxin toxicity</td>
<td>Failure to monitor renal function and/or digoxin levels at least annually</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Fast atrial fibrillation</td>
<td>Failure to ensure that digoxin levels were therapeutic</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Dizziness</td>
<td>Unnecessary polypharmacy*</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Subtotal</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Thiazide and related diuretics</td>
<td>Overdiuresis causing dehydration ± renal failure ± electrolyte imbalance</td>
<td>Failure to monitor fluid balance, renal function, electrolytes etc.*</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Hypotension ± hyponatraemia</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Subtotal</td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Antiepileptics</td>
<td>Toxicity</td>
<td>Failure to monitor phenytoin levels</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Fitting</td>
<td>Failure to review patient after increasing carbamazepine dose</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Subtotal</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td>27†</td>
</tr>
</tbody>
</table>

*If a drug related admission involves more than one causative drug it may be recorded more than once in the table.
†Further details on “other” drug categories are available on the QSHC website (www.qshc.com/supplemental).

### Table 5

<table>
<thead>
<tr>
<th>British National Formulary class</th>
<th>Adverse drug event</th>
<th>Problem</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loop diuretics</td>
<td>Congestive cardiac failure</td>
<td>Not taking medication*</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Ascites</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dehydration</td>
<td>Taking too much</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Subtotal</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>Antiepileptics</td>
<td>Fitting</td>
<td>Not taking medication</td>
<td>7</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Exacerbation of asthma</td>
<td>Not taking medication</td>
<td>7</td>
</tr>
<tr>
<td>Nitrites</td>
<td>Chest pain</td>
<td>Not taking medication*</td>
<td>5</td>
</tr>
<tr>
<td>Insulins</td>
<td>Hyperglycaemia</td>
<td>Not taking medication</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Hypoglycaemia</td>
<td>Not eating and continuing to use same dose of insulin</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Subtotal</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td>35†</td>
</tr>
</tbody>
</table>

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†Further details on “other” drug categories are available on the QSHC website (www.qshc.com/supplemental).
Our study, a German study estimated that NSAIDs were associated with just 5.5 hospital admissions per 10,000 patients treated with these drugs in primary care. This may have important implications for encouraging general practitioners and health service managers that drug related admissions are important enough to justify potentially significant changes in medicines management. The types of changes outlined above could mean increased costs associated with gastroprotection for patients taking NSAIDs, more frequent monitoring for patients receiving oral anticoagulants, and the use of computerized decision support systems. Nevertheless, these changes might improve safety for patients and protect healthcare professionals from litigation.

ACKNOWLEDGEMENTS

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REFERENCES

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