Characterization of Drug-Related Problems in Elderly Patients on Admission to a Medical Ward

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ABSTRACT

The incidence, types, avoidability and risk factors associated with drug-related problems (DRPs) in geriatric patients on admission to a medical ward of the Toronto Hospital were assessed. The admission note and laboratory data of 150 consecutive admissions were reviewed for the presence of an adverse drug reaction, inappropriate dose, non-compliance, drug interaction, or lack of required medication. The avoidability (avoidable, possibly avoidable, or unavoidable) and contribution to hospitalization (major reason, contributing or non contributing) of each DRP was characterized.

On admission, 41% of patients had a DRP identified, of which most were potentially avoidable (96.8%) and involved commonly prescribed drugs. The DRP was the major or contributing reason for admission in 31% of cases.

Polypharmacy was a statistically significant risk factor for a DRP, particularly for male patients (p=0.0010). In this elderly population, DRPs were not statistically correlated to age greater than 65 years, gender, renal function, native language, or duration of hospital stay.

The incidence of DRPs and hospitalizations in the elderly can potentially be reduced by improving medication use. Enhanced communication, particularly between hospital and community pharmacists and their patients, may be a key mechanism.

Key Words: *drug related problems, geriatrics, hospitalization, polypharmacy*

Can J Hosp Pharm 1995; 48:161-166

RÉSUMÉ

On a évalué, chez les personnes âgées qui étaient admises à une unité de soins médicale du Toronto Hospital, l'incidence et les types de problèmes d'origine médicamenteuse (POM), ainsi que le caractère évitable et les facteurs de risque associés à ces derniers. Les dossiers d'admission et les données de laboratoires concernant 150 patients admis de façon consécutive ont été passés en revue. On recherchait les réactions indésirables à un médicament, les doses inappropriées, le manque de fidélité au régime non-observance thérapeutique, les interactions médicamenteuses ou la sous-médication. Le caractère évitable (évitable, possiblement évitable, inévitable) et le facteur de contribution à l'hospitalisation (majeur, présent, absent) de chaque POM ont été spécifiés.

À l'admission, 41 % des patients présentaient un POM qui, dans la majorité de ces cas, soit (96.8 %) était évitable et associé à un médicament d'ordonnance courant. Dans 31 % des cas, le POM était un facteur de contribution majeur ou présent à l'hospitalisation.

La polypharmacie constituait un facteur de risque de POM statistiquement significatif, particulièrement chez les hommes (p = 0,0010). Dans cette population, il n'a pas été possible d'établir de corrélation statistique entre les POM et l'âge supérieur à 65 ans, le sexe, l'état de la fonction rénale, la langue maternelle ou la durée de l'hospitalisation.

L'incidence des POM et de l'hospitalisation chez les personnes âgées pourrait être réduite en rationalisant l'utilisation des médicaments. Une meilleure communication, particulièrement entre les hôpitaux, d'une part, et les pharmaciens communautaires et leurs patients, d'autre part, serait tout probablement une solution clé.

Mots clés : *hospitalisation, personnes âgées, problèmes d'origine médicamenteuse*

INTRODUCTION

It has long been established that drugs may directly cause or contribute to hospital admissions,[1,2] with the incidence increasing with the number of medications.[3,4] The elderly are particularly at risk for drug-related hospitalizations[5,6] secondary to altered pharmacodynamics and pharmacokinetics;[7] and increased number of concomitant disease states and medications.

Adverse effects of drugs are more prevalent in the elderly[8,9] and are often incorrectly attributed to the aging process or a worsening of the disease state. Thus, drug-related problems (DRPs) are often not reported by elderly patients and not detected by their physician or family.[10] Additional agents may be prescribed to deal with the symptoms of adverse effects and potentiate the problem of polypharmacy.

The reported incidence of hospital admissions secondary to adverse drug reactions and non-compliance in geriatric patients ranges from 10% to 31%.[2,10-16] A large proportion of drug-related hospitalizations are believed to be avoidable.[13,17,18] Few studies addressing this issue have been conducted in Canada.[11,19] The present study was undertaken to determine the incidence, types, avoidability and risk factors associated with DRPs in geriatric patients admitted to a medical ward. The data highlight specific areas which should be targeted by hospital and community pharmacists and other health professionals in order to reduce drug-related hospitalizations.

METHODS

The study was conducted at The Toronto Hospital, a large, two-site, tertiary teaching hospital located in Toronto, Ontario. The study was limited to the medical ward at the General Division which reserves 20 beds for geriatric patients admitted with acute medical problems. The remaining 12 beds of the ward are for adults of all ages with acute medical problems. All patients admitted to the ward were included in the study, with the exception of patients less than 65 years of age and patients transferred from the Western Division of The Toronto Hospital or from other hospitals.

The pharmacy resident collected data by concurrent chart review of 150 consecutive admissions from September 28, 1992 to February 14, 1993, inclusive. Admissions were reviewed for the presence of five drug-related problems: inappropriate drug dosing (incorrect dose or frequency); adverse drug reactions; drug interactions; non-compliance; and lack of required drug therapy. The World Health Organization's definition for adverse drug reactions was followed — a noxious, unintended drug reaction that occurs at doses normally used in man for prophylaxis, diagnosis or therapy.[17] Dose-related adverse effects were classified as an inappropriate dose rather than as an adverse drug reaction in accordance with Strand et al.[20]

Data collected included clinical signs and symptoms, laboratory values, past medical history, medications taken, impression of the admitting physician, and plasma drug concentrations when available. Normal laboratory values for The Toronto Hospital were used to determine the presence of abnormalities, with the exception of blood glucose. Less than 14 mmol/L is considered an acceptable two-hour postprandial blood glucose level in elderly patients;[21] therefore, patients were considered to be hyperglycemic if their blood glucose was greater than 15 mmol/L. Plasma drug levels were evaluated in conjunction with the patient's clinical signs and symptoms since therapeutic ranges in the elderly may differ from normal laboratory values reported for younger adults.

Renal function was estimated using the Cockroft-Gault equation for creatinine clearance.[22] The ideal body weight of females less than five feet tall was assumed to be 45 kg. When height and weight data were unavailable, the average ideal body weight of the study population was employed: 52 kg for females and 64.5 kg for males. When only a patient's weight was available, this weight was assumed to be ideal, unless the patient was noted to be obese.

Each patient was characterized by the pharmacy resident as having a DRP or no DRP on admission. Adverse drug reactions were reported when supported by the literature since causality was not determined clinically by withdrawing the drug and rechallenging the patient. Non-compliance and lack of required drug therapy were reported only if documented by the admitting physician. Patients requiring changes in drug therapy based on a newly diagnosed medical condition or a rapid worsening of an existing medical condition were not characterized as having a DRP on admission.

Identified DRPs were evaluated for their contribution to hospital admission and avoidability. Definitions were adapted from Hallas et al.[17] A DRP's contribution to hospitalization was classified as: i) the "major reason" if it was the chief complaint and no other reason for hospitalization existed; ii) "contributing" to admission if other factors also played a role in the reason for admission; or, iii) "not contributing" if the patient had medical reasons sufficient to result in admission which were unrelated to the DRP. When a patient had more than one DRP identified, the DRP most contributing to hospitalization was used to categorize the case. Patients who had a DRP which was the major reason for or contributed to hospitalization were characterized as having a drug-related hospital admission.

The avoidability of a DRP was classified as: i) "avoidable" if the drug treatment was obviously inappropriate or contraindicated, no measures were taken to counteract known effects of the drug, or the patient was noncompliant or insufficiently educated about their medications; ii) "possibly avoidable" if the patient's disease state was considered to be potentially changing thereby resulting in the need for altered drug therapy; or iii) "unavoidable" if the DRP was unpredictable (e.g., an idiosyncratic reaction or secondary to a rapidly changing disease or metabolic state) or an acceptable, clinically insignificant adverse effect.

Patients characterized as having a DRP were compared to those without a DRP. A two-tailed, unpaired t-test was employed to test for significant differences ($p < 0.05$) between the number of medications taken, age, renal function and duration of hospital stay. Gender and native language (English-speaking or not) were compared using Chi-square analysis with the Yates correction applied. A

subset analysis by gender was performed using a two-tailed, unpaired t-test to determine if statistical differences existed between males and females within and between each group (i.e., with and without a DRP) with respect to number of medications and age.

RESULTS

The study population consisted of 88 women and 62 men, aged 65 to 108 years (average 78 years). On admission, the number of medications per patient ranged from 0 to 17 (average 5.7).

The incidence of DRPs on admission was 41.3%; 46 patients had a drug-related hospital admission, and an additional 16 patients had a DRP which did not contribute to hospitalization (Table I). Almost all identified DRPs were potentially avoidable (40 avoidable and 20 possibly avoidable) and involved drugs which are often prescribed for elderly patients (Table II). The majority of DRPs were secondary to inappropriate doses and adverse drug reactions. The drugs and manifestations resulting from these two DRPs are listed in Tables III and IV, respectively.

No statistical correlation was found when age, gender, renal function, language or duration of hospitalization was compared between patients with and without a DRP (Table V). However, polypharmacy was an obvious risk factor for a DRP (p = 0.0003). Subset analysis by gender revealed that the number of drugs taken by patients with a DRP versus without a DRP was statistically significant for males (p = 0.0010) but not for females (Table VI). Within the group of patients with a DRP, males were taking more drugs than females (p = 0.049), accounting for the observed gender-specific influence of polypharmacy. Male and female patients did not differ in age within or between groups or in the number of medications in the groups without a DRP.

Table I: Characterization of identified drug-related problems (DRPs)

DRP	No.	Contribution[a]			Avoidability[b]		
		major	partial	not	yes	possible	no
inappropriate dose	35	5	16	14	20	15	0
adverse drug reaction	16	8	7	1	9	5	2
non-compliance	9	7	1	1	9	0	0
drug interaction	1	0	1	0	1	0	0
lack of therapy	1	1	0	0	1	0	0
Total	62	21	25	16	40	20	2

[a] Contribution to hospitalization:
   1) major – The DRP was the chief complaint and no other reason for admission existed
   2) partial – The DRP contributed to admission but other medical factors were also present which required hospitalization
   3) not – The DRP did not contribute to hospitalization
[b] Avoidability:
   1) yes – The DRP was avoidable (e.g. inappropriate or contraindicated drug therapy, non-compliance)
   2) possible – The DRP may have been avoided if drug therapy had been altered to match changes in the patient's disease state
   3) no – The DRP was unavoidable (e.g. unpredictable or known acceptable side effects)

Table II: Drugs identified as causing a drug-related problem (DRP) in more than one patient

Drug	Number	% of DRPs (n=62)
Hypoglycemic agents	10	16
Digoxin	8	13
Diuretics ± potassium supplements	8	13
Anti-hypertensive agents*	7	11
Nonsteroidal anti-inflammatory agents	5	8
Warfarin	3	5
Lithium	3	5
Nitrates	2	3
Antibiotics	2	3

* beta-blockers, calcium channel blockers and angiotensin converting enzyme inhibitors

DISCUSSION

Forty-one percent of the geriatric patients admitted had one or more DRPs. This incidence is higher than previously reported in the literature (10% to 31%). However, other studies in the elderly have only assessed the incidence of hospital admissions secondary to two DRPs: adverse drug reactions and non-compliance.[2,10-16] In fact, the observed 41% incidence is likely an underestimate of the true incidence of DRPs in this population due to limitations of the study design. Information regarding chronic disease states, drug prescribing and compliance is not routinely gathered from the patient or recorded by the admitting physician; identification of lack of therapy and non-compliance was, therefore, limited. In addition, two other potential DRPs (the patient is taking a drug for which there is no medical indication; and, the patient is receiving the wrong drug or drug product[20] could not be accurately assessed from the medical chart alone at the time of admission and were, therefore, not recorded. Thus, the detection of DRPs was limited by the study design, particularly the fragmented medication history and the decision to identify a limited number of DRPs.

DRPs were either the major or a contributing reason for admission for 31% of patients. Four hundred and eight days of hospitalization might have been prevented in 18 patients for whom avoidable DRPs were the major reason for admission (seven cases of non-compliance, six cases of adverse drug reactions, four cases of inappropriate dose, and one case of lack of therapy).

The high incidence and avoidability of drug-related problems and hospital admissions observed leads to the conclusion that the medical management of the elderly patient in the community requires modification. Although this study was conducted in a large teaching hospital offering tertiary care, by excluding patients transferred from other hospitals, the sample population represents the elderly in the community. In addition, the medical problems and medications of the sample population are commonly encountered in this age group. The drugs most frequently implicated as causing a DRP are often prescribed (Table II). Patients who are prescribed these drugs warrant more careful and consistent pharmaceutical care to identify, prevent and resolve DRPs.

The risk of a DRP in this elderly study population (minimum 65 years old) was not associated with age, duration of hospitalization or renal function. Although previous studies have shown the risk of a DRP is increased in elderly patients compared to young adults,[5,6] most studies have not shown this risk to continue to increase beyond the age of 65 years.[2, 13, 19] The majority of the medications taken by our group of elderly patients were hepatically eliminated; therefore, renal function would not be expected to be correlated to DRPs.

Polypharmacy was a statistically significant risk factor for a DRP. Previous studies have shown polypharmacy to be a risk factor for drug-related hospitalizations,[2, 15, 19] including studies of all age groups.[3, 4, 6] It should be noted that patients taking more medications may have a higher risk of a DRP secondary to multiple, concurrent disease states. Grymonpre et al[19] found that the number of medications taken by patients was correlated to the number of disease states and that both variables were risk factors for drug-related hospital admissions.

Females tended to have an increased incidence of DRPs which could not be attributed to polypharmacy or age (Table VI). Other investigators[3, 4, 19]

Table III: Identified cases of inappropriate dose or drug schedule

Drug(s)	Dose	Manifestation	No. (%) of cases (n=35)
Hypoglycemic agents	low	hyperglycemia	9 (26)
Digoxin	low	subtherapeutic	5 (14)
Furosemide	low	edema, elevated JVP	4 (11)
Warfarin	high	elevated INR	3 (8.6)
Anti-hypertensive agents*	low	hypertension	3 (8.6)
Nitrates	too frequent #	tolerance	2 (5.7)
Potassium supplements	low	hypokalemia	2 (5.7)
Potassium supplements	high	hyperkalemia	1 (2.8)
Allopurinol	high	none noted	1 (2.8)
Co-trimoxazole	high	none noted	1 (2.8)
Lithium	low	subtherapeutic	1 (2.8)
Glyburide	high	hypoglycemia	1 (2.8)
Hydrochlorothiazide + Triamterene	high	dehydration	1 (2.8)
Theophylline	low	subtherapeutic	1 (2.8)

*   enalapril; captopril + furosemide; metoprolol + lisinopril
\#   QID with no nitrate free period

Table IV: Identified cases of adverse drug reactions

Drug(s)	Manifestation	No. (%) of cases (n=16)
Nonsteroidal anti-inflammatory agents	gastrointestinal bleed	3 (19)
	epigastric pain	1 (6.2)
	gastropathy	1 (6.2)
Digoxin	bradycardia	1 (6.2)
	arrhythmia	1 (6.2)
	nausea, vomiting, weakness	1 (6.2)
Cefaclor	diarrhea	1 (6.2)
Doxepin + Furosemide + Diltiazem	postural hypotension	1 (6.2)
Lithium	tremors, hypercalcemia	1 (6.2)
	confusion, anorexia	1 (6.2)
Propoxyphene	confusion	1 (6.2)
Captopril	hyperkalemia	1 (6.2)
Enalapril + Furosemide	hypotension	1 (6.2)
Hydroxyzine + Cyclobenzaprine	sedation, cognitive impairment	1 (6.2)

have reported an increased risk of adverse drug reactions in female patients. All three of these studies included patients less than 65 years of age. The present study lends support to this conclusion in elderly female patients: 12.5% (11 of 88) of females admitted had an adverse drug reaction compared to 8.1% (five of 62) of males. The reasons for the higher incidence of adverse drug reactions in females have not been studied.

Although not statistically significant, a trend towards increased incidence of non-compliance in non-English speaking patients was observed. The nine cases of non-compliance identified included four patients who spoke English, one who spoke both German and English, and four who spoke other languages. Only 21% of the study population was non-English-speaking; however, this group accounted for 44% of the compliance problems. The observed trend may represent a communication problem between physicians, phar-macists and their patients. It is important for patients to be counselled in their own language to improve compliance.

Non-compliance was the most common cause of avoidable hospi-talization. According to the physi-cians' admitting notes, in all nine cases the patients were either not taking their medications or were only taking them sporadically. This DRP is likely more frequent than the 6% incidence observed in this study. Drug-related hospital admissions second-ary to non-compliance have been reported to occur in 3% to 28%[15, 19, 23] of elderly patients. Patients can be reluctant to tell a physician that they have not been compliant with medi-cation. A thorough medication history performed by a pharmacist may have resulted in a higher frequency of detection of non-compliance[24] and, potentially, a reclassification of some "inappropriate doses" as patient non-compliance. Community pharmacists can play an active role in reducing this cause of unnecessary hospital-ization by continually counselling their patients. Pharmacists should attempt to discover the compliance history by asking patients how they have been taking the medication and ascertaining if the interval between refills is appropriate.

Identification and prevention of DRPs in geriatric outpatients will be an important step towards reducing hospital admissions. In addition to improving compliance, community pharmacists can help reduce drug-related hospitalizations by asking patients about adverse reactions when refills are obtained, monitoring for drug interactions and ensuring drugs are discontinued by the prescribing physician when they are no longer required by the patient. Patients should be encouraged to utilize only one pharmacy, where their complete patient profile is maintained, in order to prevent drug interactions or recurrence of adverse reactions.

Actual or potential DRPs identified in hospital need to be relayed to the patient's community pharmacist, physician, and other caregivers. A communication system needs to be developed and implemented to allow hospital pharmacists to forward recommendations and monitoring plans to community pharmacists. Documentation could be provided in writing to the patient prior to discharge from hospital. The patient would then be responsible for taking this information to the community pharmacist and physician. The use of patient medical cards containing all relevant patient information, such as the SMART CARD proposed by the Ontario government, or computer systems linking pharmacists and physicians to patient databases, could further benefit patients by ensuring health professionals have complete access to the patient's medical file, including a complete drug history.

By increasing awareness of the potential for DRPs, it is hoped that these problems will be recognized

Table V: Factors associated with drug-related problems. Data are presented as the mean ± standard deviation.

Factor	DRP	No DRP	p value
Number of drugs	6.92 ± 3.06 (n=62)	4.83 ± 3.66 (n=88)	0.0003*
Age (years)	78.2 ± 8.1 (n=62)	78.6 ± 9.0 (n=88)	0.78*
% Female	62.9 (n=62)	55.7 (n=88)	>0.25#
Creatinine clearance (mL/min)	29.0 ± 12.4 (n=60)	32.0 ± 11.8 (n=79)	0.16*
% English speaking	77.4 (n=53)	80.8 (n=73)	>0.5#
Hospital stay (days)	18.7 ± 21.0 (n=62)	18.1 ± 20.0 (n=88)	0.87*

*   two-tailed, unpaired t-test
\#   Chi square test with Yates correction
n   denotes sample size

Table VI: Subset analysis by patient gender. Data are presented as the mean ± standard deviation.

Factor	DRP	No DRP	p value
Number of drugs per female	6.33 ± 2.86	5.16 ± 3.18	0.077
Number of drugs per male	7.91 ± 3.20	4.41 ± 4.19	0.0010
Age of females (years)	79.2 ± 8.4	79.8 ± 9.7	0.72
Age of males (years)	76.6 ± 7.5	77.1 ± 7.9	0.84
Number drugs per female vs male	p = 0.049	p = 0.34	
Age of females vs males	p = 0.24	p = 0.15	

p values calculated using a two-tailed, unpaired t-test

earlier and corrected before hositalization is required. This will require a co-operative effort between patients, physicians, pharmacists and other caregivers within the community and hospital. ▣

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