

Adverse Drug Reactions in Adults Leading to Emergency Department Visits

Shiju K S^a, Prabhakar K^a, Jayaram^a

a. Department of Internal Medicine, Sri Devraj Urs Medical College, Kolar, Karnataka*

ABSTRACT

Published on 27th June 2013

Background: Medication-related visits to the emergency department are an important but poorly understood phenomenon. A large number of adverse drug event-related visits and admissions are preventable which highlights the importance of public education on the proper use of drugs.

Methodology: A prospective observational study was conducted including selected adults presenting to the emergency department over a period of 1 year. Drug-related visits were assessed by two physicians. Discrepancies were adjudicated by two independent reviewers.

Results: Among the 133 patients included in the study, the emergency department visit was identified as drug-related adverse reactions for 50 patients (37.59%); of these 9 visits (18%) were deemed preventable. Severity was classified as mild in 14%, moderate in 68% and severe in 18%. The most common Adverse drug reactions (ADR) were neuropsychiatric events (n=10 [28.57%]), gastrointestinal reactions (n=13 [37.14%]) and angioedema (n=4 [11.42%]). The most common drug classes involved were NSAID (n=16 [32%]), Glucocorticoids (n=10 [20%]), Fluoroquinolones (n=4 [8%]) and Insulin (n=8 [16%]). The factors associated with Adverse drug reaction related visits to the emergency department found in this study were the number of co morbidities a patient has, total number of pharmacy visits, total number of physicians prescribers and total number of medications a patient takes at a given period. A patient having one or more co morbidities (p-value 0.0002) has a more chance of developing an ADR. A patient going to more than one physician (p value 0.0124) and pharmacy (p value 0.0002) along with a daily intake of more than two medications (p value <0.0001) has a greater chance of developing an ADR. Another observation made during this study is that patients usually make multiple visits to the local pharmacy with the same prescription and get the drugs over the counter.

Discussion: A high proportion of preventable adverse drug events were around a small number of drugs. Effective safety practices directed to reduce the incidence of medication errors are needed. 45% (n=72) of Adverse drug events were detected at the Emergency Department and 55% (n = 88) were detected during hospitalization. 62.3% of Adverse drug events were considered potentially avoidable (n = 109). 38.1% of adverse drug events were serious, 40.0% moderate and 21.9% mild. Drugs most commonly involved in the Adverse drug events sample studied included: antimicrobials (24.0%), systemic corticoids (15.4%), NSAIDs (11.4%), diuretics (10.3%), digoxin (9.1%), insulin and oral hypoglycemic agents (5.7%), anticoagulants and heparin (5.7%)

Elderly age group patients are at high risk of developing drug related adverse effects because of increased sensitivity to the unintended side effects or adverse drug reactions of medications that could result from incorrect dosing, and their use of more medications. Because of the increasing number of drugs, regimen complexity, continuously changing drug interactions and adverse effects, physician memory can no longer serve as a reliable bridge between research advances and clinical practice. We must remember that “there are no biologically safe drugs; there are only safe physicians”

Most studies reviewed above, suggest that a significant percentage of Adverse drug events and drug related problems (DRPs) are preventable.

Conclusion: More than 1 in 100 emergency department visits are due to drug-related adverse events, a potentially preventable problem in our health care system. Patients prescribed with more than 2 drugs and going to more than one pharmacy and physician for treatment have higher risk for developing adverse drug reactions. Physicians should prescribe NSAIDs and glucocorticoids with caution to patients along with adequate counseling regarding their adverse drug reactions.

Keywords: Adverse drug reaction, Emergency room, Drug related problems

*See End Note for complete author details

BACKGROUND

Adverse drug-related events have recently been evaluated in ambulatory care settings and among patients admitted to hospital,¹⁻⁵ and it has been

estimated that 5%–25% of hospital admissions are drug-related.^{3,4} Unfortunately, emergency department visits are not reflected in most hospital studies, because patients seen in the emergency department for an adverse drug-related event are typically not admitted.⁶

Corresponding Author:

Dr. Shiju K S, Department of Internal Medicine, Sri Devraj Urs Medical College, Kolar, Karnataka.
E-mail: sleebashiju@yahoo.co.in

Adverse drug events (ADEs) account for a sizable proportion of all visits to a medical emergency unit and some are serious enough to require hospitalization. A large number of adverse drug event-related visits and admissions are preventable which highlights the importance of public education on the proper use of drugs, and also the need for regulation of the practice of unregistered medical practitioners in developing countries.

In addition, most research evaluating drug-related visits to the emergency department has involved retrospective studies or analysis of administrative data.⁷⁻⁹ Retrospective studies may underestimate the incidence of drug-related visits because information may be missing or inaccurately documented.¹⁰ Finally, studies performed to date have used variable definitions of “drug-related events,” which limits comparative evaluation and generalizability. The studies on drug-related visits to the medical emergency department and hospital can contribute to a more comprehensive evaluation of drug related problems that arise from prescriptions of general practitioners.

The information generated from such prospective studies can be utilized in such a manner, to try and establish as to what proportion these events are avoidable, so that an intervention can be carried out in future.

Adverse drug events (ADEs) are a substantial cause of hospital admissions. However, little is known about the frequency, preventability and severity of Adverse drug events resulting in emergency department visits. To address this issue, we need to conduct a study confining to the region of kolar.

METHODOLOGY

The present study was a prospective observational study. All visits to the emergency room of R.L Jalappa hospital, Kolar over duration of one year (January 2011 to January 2012) were recorded. R.L Jalappa hospital is an 850-bedded tertiary care hospital. The residents on round-the-clock duty in the emergency room informed about the study objectives. They were asked to elicit information from all patients regarding whether the patient’s visit was due to an ADR, drug interaction, or patient non-compliance. Drug-related visits were assessed by two physicians (Figure 1). Discrepancies were adjudicated by two independent reviewers. Also, all patients (relatives, if patients were unconscious) were interviewed to elicit more information and reassess the causes for the emergency room visit and

hospital admission.

For each patient, the following information was recorded: demographic characteristics, diagnosis, drug history, type of ADE and clinical condition. The cases of suspected ADEs were followed-up to find out whether they were discharged from the emergency room itself, or whether they subsequently required hospitalisation.

An emergency department visit was deemed to be related to medication use if the presentation was directly related to the presenting chief complaint and could be classified into 1 of 8 predefined drug-related categories: adverse drug reaction, drug interaction, improper drug selection, untreated indication, sub therapeutic dosage, suprathreshold dosage, non adherence and drug use without indication.

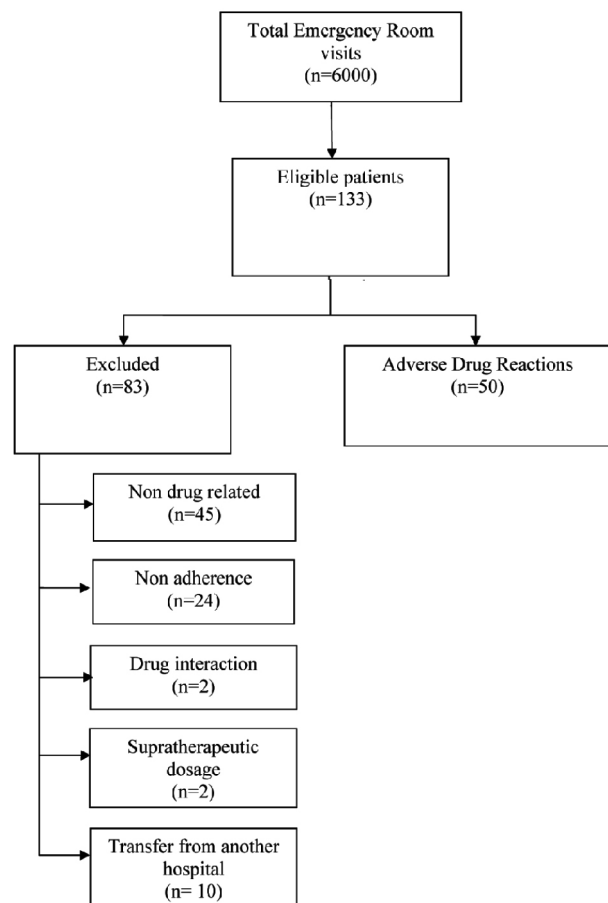


Figure 1. Patient flow in a study of medication related visits to the emergency department

Definitions

The World Health Organisation (1970) defines an adverse drug reaction as: “Any response to a drug which is noxious and unintended and that occurs at doses used in man for prophylaxis, diagnosis or therapy”.

Causality was determined by both the modified World Health Organization algorithm and the modified algorithm of Naranjo and associates. An adverse drug-related event was considered to be present if assessment by the World Health Organization algorithm indicated a “certain” or “probable” drug-related event, or if assessment by the Naranjo algorithm indicated a “definite” or “probable” drug related event.

Severity was classified as mild (laboratory abnormality or symptom not requiring treatment), moderate (laboratory abnormality or symptom requiring treatment or admission to hospital or resulting in non-permanent disability), severe (abnormality or symptom that was life-threatening or resulted in permanent disability) or fatal.

Drug-related visits were defined as preventable if drug treatment or lack thereof, was inconsistent with current best practice. Such inconsistencies included inappropriate drug, dosage, route or frequency for the patient’s clinical condition, age, weight or renal function; known drug allergy or previous reaction to drug; known drug interaction; nonadherence; lack of laboratory monitoring; and prescribing, dispensing or administration errors

STATISTICAL ANALYSIS

Students ‘t’ test was used to compare the mean number of drugs prescribed between patients whose visit was due to an ADE, and patients whose visit was not due to an ADE. The chi-square test was used to compare the percentage of ADE that occurred between different age groups of patients. A ‘p’ value of less than 0.05 was considered to be statistically significant. The Statistical Package for the Social Sciences (SPSS) programme was used for analysis.

RESULTS

Among the 133 patients included in the study, the emergency department visit was identified as drug-related adverse reactions for 50 patients (37.59%); of these 9 visits (18%) were deemed preventable. Age distribution of the patients studied showed 60% (n=30) were above the age of 50 years (Table 1). Gender distribution showed 58% (n=29) were females and 42% (n=21) were males (Table 2). The most common Adverse events were neuropsychiatric events (n=10 [28.57%]), gastrointestinal reactions (n=13 [37.14%]) and angio edema (n=4 [11.42%]). The most common drug classes involved were NSAID (n=16 [32%]), Glu-

cocorticoids (n=10 [20%]), fluoroquinolones (n=4 [8%]) and Insulin (n=8 [16%]) (Figure 2). The factors associated with adverse drug reaction related visits to the emergency department (Table 8) found in this study were the number of co morbidities a patient has, total number of pharmacy visits, total number of physicians prescribers and total number of medications a patient takes at a given period. A patient having one or more co morbidities (p-v alue 0.0002) has a more chance of developing an ADR (Table 3). A patient going to more than one physician (p value 0.0124) (Table 4) and pharmacy (p value 0.0002) (Table 5) along with a daily intake of more than two medications (p value <0.0001) (Table 6) has a greater chance of developing an ADR. Severity was classified as mild in 14%, moderate in 68% and severe in 18% (Table 7) of visits among adverse drug events. Another observation made during this study is that patients usually make multiple visits to the local pharmacy with the same prescription and get the drugs over the counter.

Table 1. Age distribution of patients studied

Age category (yr)	No. of Patients (%)
20-29	5 (10)
30-39	6 (12)
40-49	9 (18)
50-59	9 (18)
60-69	19 (38)
70-79	2 (4)

Table 2. Sex distribution

Sex	No. of Patients (%)
Male	21(42)
Female	29(58)

Table 3. Number of Comorbidities

Number of Co Morbidities	No. of Patients (%)
0	26(52)
1	21(42)
2	3(6)

Table 4. Number of Physician prescribers

Number of Physician prescribers	No. of Patients (%)
<1	17(34)
Greater than 1	33 (66)

Table 5. Number of Pharmacies

Number of pharmacies	No. of Patients (%)
<1	8(16)
Greaterthan1	42 (84)

Number of medications By category	
1-3	41(82)
4-6	9(18)

Mild N=7	Moderate N=34	Severe N=9
14%	68%	18%

Factor	ADR N=50	Non Drug Related N=45	95% CI	P value
No. of co morbidities, mean (SD)	0.54 (0.61)	0.13 (0.34)	0.2- 0.61	0.0002
Total No. of medications, mean (SD)	2.52 (1.16)	1.13 (0.59)	1.00-1.77	<0.0001
Greater than one Pharmacy	42/50 (0.84)	15/45 (0.33)	0.31-0.93	0.0002
> 1 Physician Prescriber	33/50 (0.66)	19/45 (0.42)	0.14-1.11	0.0124
Age, mean (SD)	50.11 (16.30)	45.56 (17.21)	-2.99 – 12.10	0.2327

DISCUSSION

In a large hospital based study, more than 14% of elderly admissions were due to drugs.¹¹ In another study, the incidence of drug related adverse events in the elderly population was 28.2%.¹² Elderly age group patients are at high risk of developing drug related adverse effects because of increased sensitivity to the unintended side effects or adverse drug reactions of medications that could result from incorrect dosing, and their use of more medications. Because of the increasing number of drugs, regimen complexity, continuously changing drug interactions and adverse effects, physician memory can no longer serve as a reliable bridge between research advances and clinical practice. We must remember that “there are no biologically safe drugs; there are only safe physicians”.¹³

In a study, on multivariate analysis, only age and the number of medications taken were significantly associated with adverse events. In total, 410 drugs were incriminated in the occurrence of 328 adverse drug events. The most frequently incriminated drug

classes were: (i) psychotropic agents (n=84; 20.5%); (ii) diuretics (n=48; 11.7%), anticoagulants (n=38; 9.3%) and other cardiovascular drugs (n=63; 15.4%); and (iii) analgesics, including NSAIDs (n=57; 13.9%). Preventability could be assessed in 280 of the 328 cases. In 106 cases (37.9%), the adverse drug events was judged to be preventable.¹ In another study, 30% of ADEs were preventable. Many health care delivery systems, especially in hospitals, could be redesigned to significantly reduce the likelihood of error.¹⁴

A high proportion of preventable adverse drug events were around a small number of drugs. Effective safety practices directed to reduce the incidence of medication errors are needed. 45% of Adverse drug events were detected at the Emergency Department (n = 72) and 55% (n = 88) were detected during hospitalization. 62.3% of adverse drug events were

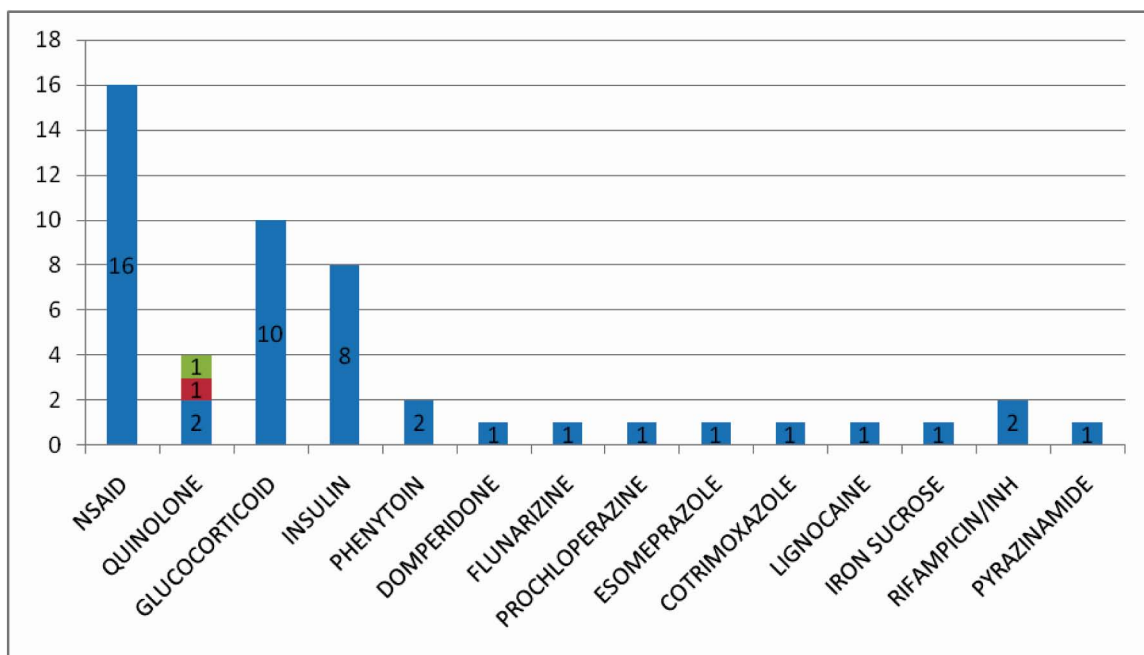


Figure 2. Common drugs used that caused adverse drug events.

considered potentially avoidable (n = 109). 38.1% of adverse drug events were serious, 40.0% moderate and 21.9% mild. Drugs most commonly involved in the Adverse drug events sample studied included: antimicrobials (24.0%), systemic corticoids (15.4%), NSAIDs (11.4%), diuretics (10.3%), digoxin (9.1%), insulin and oral hypoglycaemic agents (5.7%), anticoagulants and heparin (5.7%).¹⁵

A total of 4764 patients were included in a study. 5.9% of all visits were considered to be drug-related. The highest percentage of adverse drug events was observed in the age group less than 20 and more than 80 years. Adverse drug reactions accounted for 45% of all adverse drug events, followed by patient non-compliance (28%). Patient and physician non-compliance were the main causes of drug-related hospital admissions. 52% of all adverse drug events -related visits and 55% of adverse drug events -related admissions were considered to be preventable. Non-steroidal anti-inflammatory agents, oral hypoglycemic and antitubercular drugs were responsible for 37% of all adverse drug reactions. Non-compliance was mainly seen in hypertensives, asthmatics and epileptics.¹⁶

Most studies reviewed above, suggest that a significant percentage of adverse drug events and DRPs are preventable.

CONCLUSION

More than 1 in 100 emergency department visits are due to drug-related adverse events, a potentially preventable problem in our health care system. Patients prescribed with more than two drugs and going to more than one pharmacy and physician for treatment have higher risk for developing adverse drug reactions. Physicians should prescribe NSAIDs and glucocorticoids with caution to patients along with adequate counseling regarding adverse drug reactions.

LIMITATION

Our study has a few limitations. Although the team used a standardized approach, bias may have occurred in the determination of whether a visit was drug-related. We attempted to minimize this potential bias through an independent adjudication process. Increased attention to the subject of drug-related visits resulting from this study may have heightened emergency physicians' awareness of drug-related issues and introduced a Hawthorne effect. Given the study location, our results are not necessarily generalizable to community, rural or pediatric hospitals.

END NOTE

Author Information

1. Dr. Shiju K S, Department of Internal Medicine, Sri Devraj Urs Medical College, Kolar, Karnataka. E-mail: sleebashiju@yahoo.co.in
2. Dr. Prabhakar K, Associate Professor, Department of Internal Medicine, Sri Devraj Urs Medical College, Kolar, Karnataka.
3. Dr. Jayarama N, Professor, Department of Internal Medicine, Sri Devraj Urs Medical College, Kolar, Karnataka.

Abbreviations

- ADR - Adverse Drug Reactions
ADE - Adverse Drug Event
NSAID - Non steroidal anti inflammatory drug
SPSS - Statistical Package for the Social Sciences

Conflict of Interest: None declared

Cite this article as: Shiju K S, Prabhakar K, Jayaram. Adverse Drug Reactions in Adults Leading to Emergency Department Visits. Kerala Medical Journal. 2013 Jun 27;6(2):36-41

REFERENCES

1. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: A meta-analysis of prospective studies. *JAMA*. 1998 Apr 15;279(15):1200-5.
2. Gurwitz JH, Field TS, Harrold LR, Rothschild J, Debellis K, Seger AC, et al. Incidence and preventability of adverse drug events among older persons in the ambulatory setting. *JAMA*. 2003 Mar 5;289(9):1107-16.
3. Samoy LJ, Zed PJ, Wilbur K, Balen RM, Abu-Laban RB, Roberts M. Drug-related hospitalizations in a tertiary care internal medicine service of a Canadian hospital: a prospective study. *Pharmacotherapy*. 2006 Nov; 26(11):1578-86.
4. Pirmohamed M, James S, Meakin S, et al. Adverse drug reactions as a cause of admission to hospital: prospective analysis of 18 820 patients. *BMJ* 2004; 329:15-9.
5. Baker GR, Norton PG, Flintoft V, et al. The Canadian Adverse Events Study: the incidence of adverse events among hospital patients in Canada. *CMAJ* 2004; 170:1678-86.
6. Zed PJ. Drug-related visits to the emergency department. *J Pharm Pract* 2005; 18: 329-35.
7. Budnitz DS, Pollock DA, Weidenbach KN, Mendelsohn AB, Schroeder TJ, Anest JL. National surveillance of emergency department visits for outpatient adverse drug events. *JAMA*. 2006 Oct 18; 296(15):1858-66.
8. Budnitz DS, Shehab N, Kegler SR, Richards CL. Medication Use Leading to Emergency Department Visits for Adverse Drug Events in Older Adults. *Ann Intern Med*. 2007 Dec 4;147(11):755-65.
9. Hohl CM, Robitaille C, Lord V, Dankoff J, Colacone A, Pham L, et al. Emergency physician recognition of adverse drug-related

- events in elder patients presenting to an emergency department. *Acad Emerg Med.* 2005 Mar;12(3):197–205.
10. Nagurney JT, Brown DFM, Sane S, Weiner JB, Wang AC, Chang Y. The accuracy and completeness of data collected by prospective and retrospective methods. *Acad Emerg Med.* 2005 Sep;12(9):884–95.
 11. Malhotra S, Karan RS, Pandhi P, Jain S. Drug related medical emergencies in the elderly: role of adverse drug reactions and non-compliance. *Postgrad Med J.* 2001 Nov 1;77(913):703–7.
 12. Col N, Fanale JE, Kronholm P. The role of medication noncompliance and adverse drug reactions in hospitalizations of the elderly. *Arch Intern Med.* 1990 Apr; 150(4):841–5.
 13. Bhatt AD. Drug-related problems and adverse drug events: negligence, litigation and prevention. *J Assoc Physicians India.* 1999 Jul; 47(7):715–20.
 14. Leape LL. Error in medicine. *JAMA.* 1994 Dec 21;272(23):1851–7.
 15. Sánchez Muñoz LA, Castiella Herrero J, Sanjuán Portugal FJ, NayaManchado J, Alfaro Alfaro MJ. [Usefulness of MBDS in detection of adverse drug events]. *An Med Interna.* 2007 Mar; 24(3):113–9.
 16. Malhotra S, Jain S, Pandhi P. Drug-related visits to the medical emergency department: a prospective study from India. *Int J Clin Pharmacol Ther.* 2001 Jan; 39(1):12-8.