JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH

How to cite this article:
DURGA BISTA, ARCHANA SAHA, PRANAYA MISHRA, SUBISH PALAIAN, P R SHANKAR. PATTERN OF POTENTIAL DRUG-DRUG INTERACTIONS IN THE INTENSIVE CARE UNIT OF A TEACHING HOSPITAL IN NEPAL: A PILOT STUDY. Journal of Clinical and Diagnostic Research [serial online] 2009 August [cited: 2009 August 7]; 3:1713-1716.Available from http://www.jcdr.net/back_issues.asp?issn=0973-709x&year=2009&month=August &volume=3&issue=4&page=1713-1716 &id=417

LETTER TO EDITOR

Pattern of Potential Drug-Drug Interactions in the Intensive Care Unit of a Teaching Hospital in Nepal: a Pilot Study.

DURGA BISTA*, ARCHANA SAHA, PRANAYA MISHRA***, SUBISH PALAIAN****, P R SHANKAR******

* Lecturer, Department of Clinical Pharmacology Nepal Medical College Teaching Hospital, Kathmandu, ** Department of Pharmacology, *** Department of Hospital and Clinical Pharmacy, **** Assistant Professor, Manipal Teaching Hospital, Pokhara, Nepal.

Corresponding Author:
Durga Bista B.Pharm, M.Sc Pharmacology
Lecturer, Department of Clinical Pharmacology
Nepal Medical College, Kathmandu, Nepal.
E-mail: durgabista40@hotmail.com

Dear Editor,

With the increase in the number of patients with multiple diseases and complex therapeutic regimens, polypharmacy becomes unavoidable.[1] When more than one drug is used, the risk for Drug-Drug Interactions (DDIs) increases. The consequences of DDIs are often not considered seriously, though they are a preventable cause of morbidity and mortality.[1,2,3] A drug interaction (DIs) is said to occur when the effects of one drug are changed by the presence of another drug, food, drink or an environmental chemical agent. The result of DIs may be an additive effect, antagonism, alteration of an effect or idiosyncratic effects.[4] Studies about DDIs are lacking in Nepal. A retrospective study from Nepal showed a high prevalence of polypharmacy. During the hospital stay, 73% of patients received more than five drugs concurrently.[5]

The present study was conducted with the objective of identifying the potential DDIs in the Intensive care unit (ICU) of Manipal Teaching Hospital (MTH), to categorize the potential DDIs based on their severity, onset, and documentation and to study the association, if any, of potential DDIs with various parameters like age, sex, smoking, alcohol consumption, disease state and the number of drug prescribed.

A prospective, cross sectional study was conducted in the ICU of MTH, a 700 bedded tertiary care teaching hospital located at Pokhara city in the Western region of Nepal. The study was conducted for a period of fifteen days (Jan 1- 15, 2006). All patients admitted to the ICU of MTH were included in the study. Out patient department (OPD) patients, patients admitted to wards other than the ICU, patients taking only one drug, patients not taking any drugs and also patients on herbal drugs and multivitamins were excluded from the study. A self developed structured patient profile form was used for the collection of patient details in the study. The Micromedex[6] electronic source for integrated drug information was used to categorize the DDIs based on severity (major, moderate, minor), onset (rapid, delayed, not specified) and documentation (excellent, good, fair, poor and unlikely). It also gives information on the mechanism of DDIs, clinical outcomes and ways to manage them.

Among the 26 patients admitted during the study period, 15 (57.7%) encountered at least one DDI during their stay in the ICU. The average number of drugs prescribed among the patients who were at the risk of developing DDIs was 10.67 (n=15) and for the patients who were not at risk for DDIs was 8.23 (n=26). A higher incidence of potential DDIs was observed among the age group of 51-60 years at 40%. Male patients

encountered more number of potential DDIs 9 (60%). Smokers (11.53%) and alcoholics (23.07%) were found to be at a risk of developing potential DDIs than those who were not taking these drugs.

According to the Micromedex electronic database classification, most of the potential DDIs encountered, were of 'Moderate' severity [39 (72.23%)] and of 'Good' documentation [35 (64.82%)]. Cardiovascular drugs were the most common therapeutic category at high risk for DDIs [50 (46.3%)]. [Table/Fig 1] shows the details regarding the therapeutic category at a higher risk for DDIs.

Table/Fig 1. Therapeutic category of the interacting drugs

Therapeutic category of Interacting Drugs	Number	Percentage
Cardiovascular drugs	50	46.3
Drugs acting on blood	19	17.6
Drugs acting on GIT	9	8.3
Antimicrobials	7	6.5
Antitubercular drugs	7	6.5
Centrally acting drugs	6	5.6
Respiratory	3	2.8
Steroids	2	1.9
Endocrine	2	1.9
Miscellaneous	3	2.8

Aspirin was the most common high risk drug responsible for interaction in both the phases. [Table/Fig 2] has the list of the top thirteen high risk drugs prescribed during the study period.

[Table/Fig 3] shows the commonest high risk interactions found during the study period.

Table/Fig 2. High risk drugs for developing DDIs (n=108)

S.No	Drugs	Number	Percentage
1	Aspirin	13	12.04
2	Frusemide	12	11.11
3	Digoxin	9	8.33
4	Enalapril	7	6.48
5	Omeprazole	5	4.63
6	Alprazolam	4	3.70
7	Propranolol	4	3.70
8	Rifampicin	4	3.70
9	Low molecular weight heparin (LMWH)	3	2.78
10	Ramipril	3	2.78
11	Theophylline	3	2.78
12	Warfarin	3	2.78
13	Miscellaneous	38	35.19

Table/Fig 3. Commonest high risk DDIs

S.No	Drugs	Number (%)
1	Aspirin-ACEIs	5 (9.26)
2	Aspirin-LMWHs	3(5.56)
3	Alprazolam-omeprazole	3(5.56)
4	Digoxin-spironolactone	3(5.56)
5	Warfarin-PPIs	2(3.70)
6	Digoxin-Frusemide	2(3.70)
7	Frusemide-Propranolol	2(3.70)
8	Frusemide-ACEIs	2(3.70)
9	Miscellaneous	32(59.26)

The incidence of potential DDIs during our study was 57.7%. A review of nine epidemiological studies reported an incidence of 0% to 2.8%.[7] Similarly, a study from USA reported DDIs to be responsible for nearly 2% of adverse events in acute hospital in-patients.[8] Another study from South India, carried out in a community pharmacy, reported an incidence of 26%.[9] Our study had a higher incidence of potential DDIs. The difference might be due

to the inclusion of patients from the ICU, where usually various chronically ill patients with multiple drugs are admitted.

We found that the incidence of potential DDIs was higher in the age group of 51-60 years. In consonance with other studies, [9, 10] our study has also shown an increase in the number of potential DDIs with the patient's increasing age. Similarly, a study from Sweden reported that 31% of the DDIs were found in elderly patients.[11] In general, it has been observed that elderly patients use more medications and hence, they are at an increased risk of developing DDIs. Moreover, they also have impaired homoeostatic mechanisms that might otherwise counteract some of the unwanted effects. In these patients, the consequences of DDIs are likely to be serious.[1] It has been stated that potential DDIs are common in elderly people who use many drugs as part of a normal drug regimen.[12]

The present study observed the practice of polypharmacy (10.67 drugs per prescription). A study conducted in USA found the risk of adverse drug interactions (ADIs) to be 13% for patients taking two medications and 82% for those taking 7 or more medications.[13]A retrospective study from Nepal showed a high prevalence of polypharmacy where during hospital stay, 73% patients received more than five, 54% received more than eight, and 24% received more than nine drugs concurrently, predisposing them to DDIs.[5] Our study was similar to these results with respect to the observation that the number of interactions increased with increase in the number of drugs prescribed.

The severity of the DDIs was graded as per the Micromedex[6] electronic database classification. We found 72.23% of the potential DDIs to be moderately severe. The 'Major' severity type accounted for 16.67% of DDIs and 11.12% were of 'Minor' severity. Our values are higher than the findings reported from a study conducted in USA, which reported 7.3% of Major DDIs in a surgical intensive care unit.[14] A South Indian study found 15% of DDIs to be severe in nature and 12% to have a significance level of one (severe reaction and well-documented interaction), which is again higher than our values.[8]

In our study, 51.86% of the potential DDIs had delayed onset as per the Micromedex electronic database. In general, DDIs usually have a specific time course i.e. onset and duration and this makes them more predictable and preventable than ADRs.[15] This finding suggests that one should be careful while prescribing drugs that can cause delayed type of DDIs. These patients should also be counseled for careful monitoring of symptoms suggestive of the occurrence of DDIs.

A study by Doucette and coworkers also found cardiovascular and psychotropic medications to be more frequently involved in DDIs.[16] In general, the ICU had a significant number of cardiac patients in our hospital. This could be a reason attributable for the higher number of cardiac drugs in our study. We found aspirin (12.04%) followed by frusemide (11.11%), digoxin (8.33%), enalapril (6.48%) and omeprazole (4.63%) to be the drugs at a high risk for developing DDIs. A South Indian study identified antitubercular drugs, analgesics and antipyretics, bronchodilators, diuretics, antiplatelet drugs, H2-receptor blockers and proton pump inhibitors to be commonly responsible for causing DDIs.[8] Though some of the drugs involved were similar, our study has focused on the pattern of the interaction of the drugs used in the ICU.

The commonest potential DDIs observed during the study were between aspirin-ACEIs (9.26%), followed by aspirin-LMWH (5.56%). Unlike our findings, a study done in an elderly population found that the most common DDIs in them were between beta-blockers and antidiabetics, followed by potassium-sparing diuretics and potassium and between carbamazepine and dextropropoxyphene.[10]

This study provided some basic information regarding the pattern of DDIs in the ICU setting in Nepal. Our findings suggest the need for further studies in this area

References

1. Lee A, Stockley IH. Drug interactions In Walker R, Edwards C. *Clinical Pharmacy and Therapeutics*. 3rd edition. Churchill Livingstone, Philadelphia 2003: 21-31.
2. Seymour R.M, Routledge P.A. Important drug-drug interactions in the elderly. Drugs Aging 1998; 12: 485- 94.
3. Juurlink DN, Mamdani M, Kopp A, Laupacis A, Redelmeier DA. Drug-drug interactions among elderly patients hospitalized for drug toxicity. J Am Med Assoc 2003; 289: 1652- 8.
4. Stockley I H. Drug interaction: a source book of adverse interaction, their mechanisms, clinical importance and management.5th ed. Pharmaceutical Press, London 1999.
5. Joshi MP, Sugimoto T, Santoso B. Geriatric prescribing in the medical wards of a teaching hospital in Nepal. Pharmacoepidemiol Drug Saf 1997; 6: 417- 21.
6. Klasco RK (Ed): DRUG-REAX® System. Thomson Micromedex, Greenwood Village, Colorado (Vol. 130 [Expires12/2006]).
7. Jankel C A, Fitterman L K. Epidemiology of drug-drug interactions as a cause of hospital admissions. Drug safety 1993; 9: 55- 9.
8. Leape L, Brennam T A, Laired N et al. The nature of adverse events in hospitalized patients: results of the Harvard Medical Practice Study II. N Engl J Med 1992; 324: 377- 84.
9. Nagavi BG, Singhal R. Drug interactions in prescription from selected Indian community pharmacies. J Pharm Pract Res 2005; 35: 332.
10. J, Liedholm H, Lindblad U *et al*. Prescriptions with potential drug interactions dispensed at Swedish pharmacies in January 1999: cross sectional study. Br Med J 2001; 323: 427-8.
11. Bergendal L, Friberg A, Schaffrath AM. Potential drug-drug interactions in 5,125 mostly elderly out-patients in Gothenburg, Sweden. Pharm World Sci 1995; 17:152-7.
12. Biorkman IK, Fastbom J, Schmidt IK, Bernsten CB. Drug-drug interactions in the elderly. Ann Pharmacother 2002; 36: 1675- 81.
13. Goldberg RM, Mabee J, Chan L, Wong S. Drug-drug and drug-disease interactions in the ED: analysis of a high-risk population. Am J Emerg Med 1996; 14; 447- 50.
14. Oeser DE, Polansky M, Thomas NP, Varon J. Incidence of major drug interactions and associated adverse drug events in a surgical intensive care unit. Internet J Pharmacol 2003; 2.
15. Johnson MD, Newkirk G, Jr White JR. Clinically significant drug interactions: what you need to know before writing prescriptions. Postgrad Med 1999; 105:193- 5, 200, 205- 6.
16. Doucet J, Chassagne P, Trivalle C et al. Drug-drug interactions related to hospital admissions in older adults: a prospective study of 1000 patients. J Am Geriatr Soc. 1996; 44: 944- 8.