



FACTORS ASSOCIATED WITH UNNECESSARY DRUG THERAPY AND INAPPROPRIATE DOSAGE IN JIMMA UNIVERSITY SPECIALISED HOSPITAL, SOUTH WEST ETHIOPIA

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Received: 16-09-2013 / Revised: 09-10-2013 / Accepted: 19-10-2013

ABSTRACT

To assess factors associated with unnecessary drug therapy and inappropriate dosage in hospitalized patients. A hospital based cross-sectional study design was employed. The study was conducted in Jimma University Specialized Hospital, Jimma, which is 345 Km from South west of Addis Ababa. All patients who were admitted to medical ward from February 5 – March 21, 2011 were included in the study. Data on socio-demographic variables, past medical history, past medication history, current diagnosis, current medications, vital signs and relevant laboratory data were collected by using bed side patient interview guided semi-structured questionnaire and data abstraction formats for card review. The data were analysed by using SPSS version 16 for windows. Descriptive statistics, cross-tabs, chi-square and logistic regression were done. Out of 257 study participants 140(54.5%) had unnecessary drug therapy or inappropriate dosage. The only independent factors which predicted the unnecessary drug therapy in study population was polypharmacy while not considering organ function test, polypharmacy and clinically significant potential drug-drug interaction were independent factors associated with inappropriate dosage . The prevalence of unnecessary drug therapy or inappropriate dosage is significantly high.

Key words: unnecessary drug therapy, inappropriate dosage and polypharmacy.



INTRODUCTION

Drug therapy is growing more complex, thus making appropriate drug prescribing increasingly challenging. Drug-related problems (DRPs) are a major safety issue for hospitalized patients¹. Some of the DRPs existed at the time of admission to hospital, while others arose during hospital management². Studies evaluating drug-related hospitalization have estimated that approximately 5% to 10% of all hospital admissions are drug related³. At least 22% of the discharged patients in Spain suffered real or potential DRPs⁴.

On average 2.6 DRPs occur per patient in internal medicine ward and the presence of DRPs increased approximately linearly with the number of drugs used, for the range of one to > 11 drugs in Norway^{5,6}. According to a study done in five Norwegian hospitals the number of drugs at

admission is a risk factor for having an unnecessary drug, a nonoptimal drug or a non-optimal dose. The number of clinical/pharmacological risk factors which includes polypharmacy (defined as \geq five drugs at admission), reduced renal function (creatinine clearance below 50 ml/min or serum creatinine above normal range), reduced liver function [aspartate amino transferase (AST) or alanine aminotransferase (ALT) three times above normal values], confirmed diabetes mellitus, cardiac failure, history of allergy or adverse reactions to drugs, assumed noncompliance, use of drugs with a narrow therapeutic index, and other factors that could affect taking the drugs prescribed, including alcohol abuse and problems with swallowing, is a risk factor for having an interaction, non-optimal dose, need for laboratory tests or an additional drug. Age was only shown to be an independent risk factor for having an unnecessary drug².

MATERIALS AND METHODS

Patients and design: A facility based cross-sectional study design was employed. The study was approved by Ethical Review Board of Jimma University. From February 5, 2011 – March 21, 2011 two pharmacists and three graduating class pharmacy students have collected the data from medical ward of Jimma University Specialized Hospital, Jimma, which is 345 Km from South West of Addis Ababa. Patients who were discharged before the collected data was cross-checked are excluded from the study. Data on socio-demographic variables, past medical and medication history, social drug use, length of hospital stay, current diagnosis, laboratory values, vital signs and current medication were recorded for each patient.

Data collection: Pre-tested interview guided semi-structured questionnaire and data abstraction formats were used for data collection. The drug-related problems evaluation tool was prepared based on the categories and reasons in “pharmaceutical care practice the clinician’s guide.

The data collectors interviewed the patient and reviewed the patient chart. For identification of DRPs; Harrison’s principles of internal medicine, 17th edition, Pharmacotherapy: a pathophysiologic approach, 7th edition, Applied therapeutics: the clinical use of drugs, Uptodate®2009, Guidelines for management of opportunistic infections and anti retroviral treatment in adolescents and adults in Ethiopia, 2007 and Standard treatment guideline for general hospital, 2010 were used. Cockcroft-Gault equation was used to estimate glomerular filtration rate and the classification of creatinine clearance was done by considering glomerular filtration rate classification for chronic renal failure. The possible interactions between drugs was evaluated using the Micromedex® health care series soft ware and Stockley’s drug interactions 2009.

Operational definition

Clinically significant drug-drug interactions: Interactions said to have major or moderate severity and good or excellent documentations by Micromedex® health care series soft ware and interactions said to have a life threatening outcome, or where concurrent use is contraindicated by the manufacturers or concurrent use may result in a significant hazard to the patient and so dosage adjustment or close monitoring is needed by Stockley’s drug interaction, 2009.

Dosage: Includes the dose given, the frequency of administration and the duration of therapy.

Dosage too high: The drug dosage is too high to result in undesirable effects.

Dosage too low: The drug dosage is too low to produce the desired response.

Inappropriate dosage: Dosage too high or dosage too low

Polypharmacy: Concomitant use of five or more drugs on average per day.

Unnecessary drug therapy: A drug therapy when the patient does not have a clinical indication at the time of data collection.

Data analysis: The data from patient interview, data from abstraction formats and data from DRP evaluation questionnaire were cleaned, coded, entered to SPSS for windows, version 16 statistical software. The data was cleaned again after the entry by doing frequencies and observing inconsistencies. Descriptive statistical analysis and cross tabs were done. Chi-square and binary regressions with 95% confidence interval were done to find out statistical significance. P-value less than 0.05 was used to declare association.

Data quality control: The principal investigators were giving feedback and correction on daily basis for the data collectors before they were deployed to the wards. Completeness, accuracy, and clarity of the collected data were checked carefully. Any error, ambiguity and incompleteness which were not observed at supervision were addressed on the following day before starting next day activities. The DRP evaluation format was filled by a clinical pharmacist and an experienced internist. Three questionnaires which couldn’t be corrected in the following day were removed from the analysis.

RESULT

Socio-demographic characteristics and Drug-related problems: The study included 257 patients, 136(52.9%) patients were male, the mean age of study participants was 40.9 years with standard deviation of 16.82. 140 (54.5 %) patients had unnecessary drug therapy or inappropriate dosages. 47(18.3%) of the patients had unnecessary drug therapy while 93(36.2%) had inappropriate dosage.

Reasons for unnecessary drug therapy and inappropriate dosage: Twenty nine (61.7%) of the reasons which lead to unnecessary drug therapy were invalid indication for drug therapy at the time of prescribing. Among the reasons identified for low dosage 20 (41.7%) were the dose given was low. Twenty five (45.5%) of the reasons which

lead to high dosage were too short dosing frequency (Table 1).

Drugs involved with unnecessary drug therapy and inappropriate dosage: Twenty four (9.3%) study participants were prescribed antimicrobials unnecessarily. Twenty two (8.5%) of admitted patients were prescribed antimicrobials with low dosage. Fourteen (5.5%) of admitted patients were prescribed antimicrobials with high dosage (table 2).

Predictors of having unnecessary drug therapy: Patients who took five or more drugs per day on average were 5.96 times more likely to have unnecessary drug therapy than patients who took less than five drugs per day on average (AOR=5.963(2.611-13.621)). Clinically significant potential drug-drug interaction was not found to affect unnecessary drug therapy significantly, after adjusted for other variables (Table 3).

Patients whose organ function tests were not considered for drug prescribing were 8.50 times more likely to have inappropriate dosage than patients whose organ function tests were considered for drug prescribing (AOR=8.498(1.632-44.250)). Patients who took five or more drugs per day on average were 2.71 times more likely to have inappropriate dosage than patients who took less than five drugs per day on average (AOR=2.708(1.004-7.303)). Patients who had clinically significant potential drug-drug interaction in drug therapy regimen were 4.40 times more likely to have inappropriate dosage than patients who didn't have potential drug-drug interaction in drug therapy regimen (AOR=4.403(1.556-12.456)). Length of hospital stay and number of diagnosed disease anwere not found to affect inappropriate dosage significantly, after adjusted for other variables (Table 4).

DISCUSSION

Unnecessary drug therapy and inappropriate dosage reduce the therapeutic outcome of drug therapy by increasing adverse drug reactions and cost of treatment. Identification of associated factors is crucial to identify high risk patients and prevent and control the occurrence of the problems in an individual patient. The current study showed that 54.5% of patients admitted to internal medicine ward within the study period had unnecessary drug therapy or inappropriate dosage. 18.3% of admitted patients had unnecessary drug therapy. Invalid indication for the drug therapy (61.7%) and multiple drug products used for a condition that need a single drug therapy (38.3%) were reasons for unnecessary drug therapy. This finding was

similar to a study from Jordan⁹. Treatment duplicity was found to be a reason for unnecessary drug therapy by a study done in Spain⁴. Antibacterias like ceftriaxone were drugs prescribed without indication. The addition intravenous cimetidine on oral omeprazole and the combined use of oral and inhalation salbutamol were the common multiple drug product use while a single drug therapy was sufficient. In the present study 33.1% of admitted patients had inappropriate dosage(14.0% low dosage, 16.0% high dosage and 3.1% had both low and high dosages). Low dosage was mostly due to the reasons the dose given was low (41.7%) and potential drug-drug interaction which might decrease the concentration of a drug (39.6%). The other reasons for low dosage were the dosing frequency was too infrequent to produce the desired response (16.7%) and the duration of drug therapy was short to produce the desired response (2%). Similarly, study done in Jordan⁹ found low dose, inappropriate frequency, drug-drug interactions and short duration to be reasons for low dosage which was in agreement with the current finding except for low number of drug-drug interactions which decrease concentration of drugs. This difference might be due to differences in facilities of the hospitals like availability of drug interaction checker and the prevalence of tuberculosis and HIV/AIDS which drug therapies increase drug-drug interactions. Eventhough the set up was different a medication review study from Australia¹⁴ had mentioned low dose given as a reason for under dosage.

High dosage drug therapy was due to the reasons dosing frequency was too short (48.1%), the dose given was high (42.3%) and the duration of drug therapy was long for a given condition (9.6%). The current outcome was similar to findings from the study in Jordan⁹. Dose too high was found to be a reason for over dosage by study from Australia¹⁴ although the populations used were different.

In the present study 9.3%, 3.1%, 1.6% and 1.6% of patients were unnecessarily prescribed antimicrobials, salbutamol, beta blockers and acid secretion inhibitors, respectively. Antibiotics, β_2 agonists and acid secretion inhibitors were drug classes found to be involved with unnecessary drug therapy by a study from Jordan⁹. Acid secretion inhibitors were involved with unnecessary drug therapy in study from Australia⁷.

In current study 8.5% and 3.5% of admitted patients were prescribed antimicrobials and ACE-inhibitors with low dosage, respectively. On the other hand, 5.5%, 4.3% and 3.5% of admitted patients were prescribed antimicrobials, laxatives and steroids with high dosage, respectively. The

involvement of antimicrobials, ACE-inhibitors and steroids in inappropriate drug dosage was also found by similar studies^{2,9}. The Australian community based study was also found ACE-inhibitors involvement with wrong dose⁷. Polypharmacy (AOR=5.963, 95%CI (2.611-13.621)) was found to be the only independent risk factor to affect unnecessary drug therapy which was in agreement with similar studies^{2,6,9,15}. Considering organ function tests for drug prescribing (AOR=0.118, 95%CI (0.023-0.613)), polypharmacy (AOR=2.708, 95%CI (1.004-7.303)) and potential drug-drug interaction (AOR=4.403, 95%CI (1.556-12.456)) were independent risk factors for inappropriate dosage (high dosage or low dosage). The statistically significant effect of polypharmacy on inappropriate dosage was in agreement with similar studies^{2,6,9}. But, the effect of potential drug-drug interaction on inappropriate dosage were not studied by similar studies reviewed by the current study since other studies considered drug-drug interactions as one class of DRPs. Non of the variables studied by the current study were found to affect compliance of hospitalized patients.

CONCLUSION

The prevalence of unnecessary drug therapy or inappropriate dosage was significantly high. Invalid indication for the drug therapy was the most frequent reason for unnecessary drug therapy. The presence of low dose prescribing and drug interaction which might decrease the concentration of a drug were more common reasons for low dosage. Short dosing frequency and high dose prescribing were common reasons for high dosage. Polypharmacy was the only associated factor for unnecessary drug therapy. Polypharmacy, not considering organ function test and clinically significant potential drug-drug interaction were independent factors associated with inappropriate dosage.

ACKNOWLEDGEMENTS

We would like to acknowledge Jimma University which supported this research financially and Addis Ababa University School of Pharmacy Drug Information Center for the co-operation given to use drug interaction software.

Table 1. Reasons which made drug therapy to be considered as problem for the individual class of problems for hospital admitted patients in internal medicine ward, Jimma University Specialized Hospital, from February 5, 2011- March 21, 2011.

Class of drug-related problems	Reasons	Frequency(%)
Unnecessary drug therapy	Invalid indication for the drug therapy	29(61.7)
	Multiple drug products used for a condition that need asingle drug therapy	18(38.3)
Low dosage	The dose given was low	20(41.7)
	There was drug interaction which decreases the concentration a drug	19(39.6)
	The dosing frequency was too infrequent to produce the desired response	8(16.7)
	The duration of drug therapy was short to produce the desired response	1(2.0)
High dosage	The dosing frequency was too short	25(48.1)
	The dose given was high	22(42.3)
	The duration of drug therapy was long for a given condition	5(9.6)

Table 2. Drugs involved with individual drug-related problems among hospital admitted patients in internal medicine ward, Jimma University Specialized Hospital, from February 5, 2011- March 21, 2011.

Drug class or drug name	Unnecessary drug therapy No_(%)	Low dosage No_(%)	High dosage No_(%)
Antimicrobials	24(9.3)	22(8.5)	14(5.5)
ACE inhibitors	2(0.8)	9(3.5)	-
FeSO ₄ and/or folic acid	1(0.4)	3(1.2)	-
Beta blockers	4(1.6)	-	-
Corticosteroids	2(0.8)	3(1.2)	9(3.5)
Diuretics	-	1(0.4)	2(0.8)
Salbutamol	8(3.1)	-	-
Amlodipine	-	1(0.4)	6(2.3)
Laxatives	1(0.4)	1(0.4)	11(4.3)

Digoxin	-	2(0.4)	4(1.6)
Pethidine	1(0.4)	-	2(0.8)
Acid secretion inhibitors	4(1.6)	-	-
Diclofenac	-	-	1(0.4)
Oral hypoglycemic agents	-	1(0.4)	-
Anticoagulants	-	1(0.4)	-

Table 3. Determinants for unnecessary drug therapy among hospital admitted patients in internal medicine ward, Jimma University Specialized Hospital from February 5,2011- March 21,2011.

		Unnecessary drug therapy		COR	AOR
		Yes	No	95%CI	95%CI
Sex	Male	27(10.5%)	109(42.4%)	1	1
	Female	20(7.8%)	101(39.3%)	0.799	0.763
				0.422-1.514	0.379-1.535
Age				0.994	0.990
				0.976-1.014	0.967-1.013
Length of hospital stay	≤ 7 days	30(11.7%)	139(54.1%)	1	1
	> 7 days	17(6.6%)	71(27.6%)	1.109	0.691
				0.573-2.147	0.325-1.468
Number of diagnosed disease	One	12(4.7%)	53(20.6%)	1.016	1.513
	Two or more	35(13.6%)	157(61.1%)	0.491-2.099	0.659-3.475
Organ function test done	Yes	38(14.8%)	156(60.7%)	1	1
	No	9(3.5%)	54(21.0%)	0.684	0.629
				0.311-1.507	0.264-1.495
Average number of drugs/day	< 5	27(10.8%)	177(70.8%)	1	1
	≥ 5	20(8.0%)	26(10.4%)	5.043	5.963
				2.480-10.255*	2.611-13.621*
Clinically significant	Yes	14(5.6%)	28(11.2%)	2.652	1.718
	No	33(13.2%)	175(70.0%)	1.263-5.566*	0.704-4.193
Potential drug-drug interaction	No	33(13.2%)	175(70.0%)	1	1

- COR-crude odds ratio,AOR-adjusted odds ratio, CI-confidence interval, *statistically significant

Table 4. Determinants for inappropriate dosage among hospital admitted patients in internal medicine ward, Jimma University Specialized Hospital, from February 5, 2011- March 21, 2011.

		Inappropriate dosage		COR	AOR
		Yes	No	95%CI	95%CI
Length of hospital stay	≤ 7 days	44(17.1%)	125(48.6%)	1	1
	> 7 days	41(16.0%)	47(18.3%)	2.478	1.504
				1.442-4.260*	0.685-3.304
Number of diagnosed disease	One	11(4.3%)	54(21.0%)	0.325	0.466
	Two or more	74(28.8%)	118(45.9%)	0.160-0.661*	0.164-1.322
Organ function test done	Yes	69(26.8%)	125(48.6%)	1	1
	No	16(6.3%)	47(18.3%)	0.617	0.742
				0.326-1.168	0.351-1.570
Organ function tests considered for drug prescribing	Yes	53(27.3%)	122(62.9%)	1	1
	No	16(8.2%)	3(1.6%)	12.277	8.498
				3.432-43.916*	1.632-44.250*
Average number of drugs/day	< 5	54(21.6%)	150(60.0%)	1	1
	≥ 5	31(12.4%)	15(6.0%)	5.741	2.708
				2.878-11.451*	1.004-7.303*
Clinically significant potential drug-drug interaction	Yes	31(12.4%)	11(4.4%)	8.037	4.403
	No	54(21.6%)	154(61.6%)	3.779-17.091*	1.556-12.456*

- COR-crude odds ratio,AOR-adjusted odds ratio, CI-confidence interval, *statistically significant

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