

Survey on Appropriateness of Drug Administration in Elderly Patients at The Internal Medicine Ward dr. Cipto Mangunkusumo Hospital

Isabela Huliselan*, Purwastyastuti**, Nafrialdi**, Siti Setiati***

ABSTRACT

Aim: to evaluate the appropriateness of drug administration in elderly patients hospitalized at the Internal Medicine Ward dr. Cipto Mangunkusumo Hospital based on indication, dosage, duration of treatment, potential adverse events, contraindication, and potential drug interactions.

Methods: a cross sectional observational study was performed in patients aged over ≥ 60 years old staying at the Internal Medicine Ward. Appropriateness of drug administration was evaluated based on the support from literature. The supporting references being used were guidelines at the Internal Medicine Department, reference textbooks, and drug brochures for newly approved drugs but had not been listed in references nor guidelines.

Results: from 347 drug administrations in 43 patients, 228 of the drug administrations (67.71%) were considered appropriate for indication, 15.85% slightly inappropriate for indication, and 18.44% with inappropriate indication. From 228 drug administrations, 206 (90.35%) were administered with adequate dosage, 2.63% subtherapeutic dosage, 3.95% overdosage, and 3.07% undefined dosage. From 126 drug administration evaluated for duration of therapy, there were 77.78% administered with appropriate duration of therapy, 18.25% with inappropriate duration, and 3.97% undefined duration. Out of 347 drug administration there were 2 possibilities of adverse drug events, 5 drugs were actually contraindicated and 25 potential drug interaction.

Conclusion: there were 67% of drugs appropriately administered for indication. From this number, 90% were using accurate dosage, of all drug administration there were 2 possibilities of adverse drug events, 5 drugs were contraindicated and 25 potentially interacted drugs. From 126 drugs evaluated for duration of therapy, 77.78% received the right duration of therapy.

Key words: elderly, appropriate drug administration, indication, adverse effect, contraindication, drug interaction.

INTRODUCTION

Drug administration in the elderly should be administered continuously due to deterioration of physiologic. Compromised organ functions have caused changes of drug kinetic, drug interactions, and organ responses.¹ The main pharmacologic change in the elderly is the altered drug excretion. A decrease in creatinine clearance in the elderly could be found in approximately two-third of the population.² In patients with decreased creatinine clearance there are decreased clearance of drugs that are mainly excreted through the kidney, prolongation of drug half life ($T_{1/2}$), drug accumulation, and toxic effects when drug dosage is not properly adjusted. This condition is often found, for example with aminoglycoside, digoxin, lithium, allopurinol, amantadine, procainamide, and chlorpropamide use.³

The elderly are so sensitive to drugs that suppress the central nervous system (such as benzodiazepine), so that they are prone to experience side effects such as delirium, confusion, and agitation. Increased sensitivity to drugs could also increase incidence of other adverse effects such as risk of bleeding due to anticoagulant use, orthostatic hypotension due to antihypertensive and β -blocking agents, and delirium due to the use of psychoactive and anticholinergic agents.⁴

On the contrary, there is a decreased sensitivity to several drugs, such as bronchodilatation response to β agonist associated with decreased number of β receptors due to increased level of noradrenaline, and decreased cAMP response to stimulation of β receptor.⁵

Elderly patients generally show multipathologic conditions, therefore larger amount of drug is needed. Moreover, elderly patients also have a lot of symptoms which could encourage doctors to prescribe more drugs.

Based on the above explanation, therapy for the elderly requires careful and serious consideration from the doctor before prescribing.

The aim of this study is to observe the appropriateness of drug administration based on indication,

* Clinical Pharmacology Resident, ** Department of Pharmacology & Therapeutics, *** Division of Geriatric, Department of Internal Medicine Faculty of Medicine, University of Indonesia-dr. Cipto Mangunkusumo Hospital, Jakarta

dosage, duration of therapy, possibility of adverse event, contraindication, and potential drug interaction in elderly patients. This study is expected to be a source of information on drug usage in elderly patients and could encourage the establishment of a drug administration guidelines according to the clinical need of elderly patients in the Department of Internal Medicine, Faculty of Medicine University of Indonesia-dr. Cipto Mangunkusumo Hospital (FMUI/CMH).

METHODS

This is a cross-sectional study in patients aged 60 years and over, hospitalized at the internal medicine ward FMUI/CMH. Data collection was done from November 2005 to March 2006. Inclusion criterion was patients aged ≥ 60 years staying at 4th, 5th, and 6th floor of the Inpatient Building (IRNA B) at CMH. The drugs being evaluated were all systemically administered drugs (oral and parenteral), except cytostatic drugs.

Data were collected from patient medical records. The therapy received by patients was reviewed for appropriateness between data from medical record, nurse drug administration record, and medical instruction from the physician. Data on possibilities of adverse event were collected through anamnesis and objective information on patient's medical record.

Appropriateness of drug administration was determined according to references. The literature being used was from The Department of Internal Medicine Consensus and standard reference books. Drug leaflets could be used for new drugs that had obtained approval but had not been listed in the reference nor in consensus. Supporting literature being used were DM consensus according to Perkeni 2002, Consensus on Hypertension according to JNC VII 2003, Consensus on CHF according to ACC/AHA 2001, Consensus on Tuberculosis by the Indonesian Pulmonologist Association 2006, Consensus on Pneumonia according to ATS 2001, and some others. References being used were Harrison's Internal Medicine 16th edition (2005), Principles of Geriatric Medicine and Gerontology, 5th edition (2003), Geriatric medicine. An Evidence-Based Approach 4th edition (2003), Current Geriatric Diagnosis & Treatment (2004), Geriatric Dose Handbook 6th edition (2001), Goodman and Gilman's The Pharmacological Basis of Therapeutic 11th edition (2006), Martindale The Complete Drug Reference 34th edition (2005), Avery's Drug Treatment 4th edition (1997), Drug Interaction 5th edition (1999), Internal Medicine Textbook 4th edition (2006).

Drug administration was considered appropriate when it was supported by the literature. It is considered

not quite appropriate when there is no literature supporting the practice, but there are strong reasons for the administration, and considered inappropriate when drug administration is not supported by the literature and does not have clear purpose. Data were descriptively displayed in tabulated form.

Sample size was calculated using formula for single group proportion.

$$n = \frac{Z\alpha^2 \cdot P \cdot Q}{d^2}$$

By determining P value of 45% based on other studies, and 15% absolute accuracy level, and 5% significance, we got the required sample size in 43 patients.

RESULTS

Data was collected from November 2005 through March 2006 by obtaining 43 patients, 26 males and 17 females, most of them (41.86%) aged between 65 to 69 years old. Table 1 shows the patient demographic data in this study.

Table 1. Patient Sex and Age Distribution

Demographic data	Number of patients	Proportion (%)
Sex		
• Male	26	60.47
• Female	17	39.53
Patient age		
• 60-64	13	30.23
• 65-69	18	41.86
• 70-74	6	13.95
• 75-79	3	6.98
• ≥ 80	3	6.98

The number of diagnose ranged between 1 to 9 diseases. The highest frequency were 4 and 5 diseases, and the proportion was 20.93% each (Table 2), and the most frequent disease was on the cardiovascular system.

Total drug uses from all 43 patients were 347, with highest frequency of patients using 8 types of drugs, around 37,21% (Table 3). From 347 drug administrations there were 228 right-for-indication drugs (Table 4), and from this number there were 206 drugs given with adequate dosage (Table 5). From 126 drugs that could be evaluated for duration of therapy, there were 98 drugs administered with appropriate therapeutic period. (Table 6).

Table 2. Patient Frequency Based on The Number of Diagnose

Number of diagnose	Patient frequency	Patient proportion (%)	Patient cumulative proportion (%)	Total diagnose
9	1	2.33	2.33	9
8	-	-	-	-
7	4	9.3	11.63	28
6	5	11.63	23.26	30
5	9	20.93	44.19	45
4	9	20.93	65.12	36
3	8	18.6	83.72	24
2	5	11.63	95.35	10
1	2	4.65	100	2
Total	43	100		184

Table 3. Table of Frequency Based on The Number of Drugs Administered

Number of drug type	Patient frequency	Patient proportion (%)	Cumulative proportion (%)	Total number of drug administration
13	2	4.65	4.65	26
11	4	9.3	13.95	44
10	4	9.3	23.25	40
9	4	9.3	32.55	36
8	16	37.21	69.76	128
7	4	9.3	78.06	28
6	3	6.98	86.04	18
5	4	9.3	95.34	20
4	1	2.33	97.67	4
3	1	2.33	100	3
Total	43	100		347

From 347 drug uses there were 228 right-for-indication drug administration, 206 with adequate dosage, and 98 with appropriate duration of therapy. (Table 4).

Out of 347 drug administrations there were two drugs with possible side effects and 5 contraindicated drugs. Possibility of adverse events were hematemesis melena after a 10-day heparin usage in patients with right dorsalis pedis artery and the use of captopril in CHF fc II patients with history of cough when consuming captopril.

From all drugs being used, there were 25 potentially interacted drugs. (Table 6)

Table 5. Use of Contraindicated Drugs

Name of drug	Contraindicated conditions	Number of administration
Aspirin	Gastrointestinal bleeding	1
Heparin	Gastrointestinal bleeding	1
Simvastatin	Hepatoma with ALT/AST:178/256	1
Ticlopidine	Decreased liver function with ALT/AST: 166/636	1
Moxifloxacin	Decreased liver function with ALT/AST: 166/636	1
Total		5

DISCUSSION

In this study we evaluated drug administration in 43 patients over 60 years of age hospitalized at the Geriatric Division, Department of Internal Medicine FMUI/CMH. From all patients we found 347 types of drugs being administered. The number of diagnose ranged between 4 to 9 diseases, with the mean of 4 diseases (65.12%). Cardiovascular disease was most common (32.61%), followed by problems on the respiratory tract (17.93%), and gastrointestinal tract (14.67%). All these three could be found altogether in one patient. Pramantara and colleagues. (2005) reported the mean number of diagnosis around 4.5 ± 2.18 in 30 geriatric patients at Dr. Sarjito Hospital.⁶

Elderly patients tended to have more than one disease. This was due to the decrease in physiologic function, decreased immunity, homeostatic degradation, and degeneration process.

Slightly Inappropriate Indication of Drug Administration

From 347 types of drugs being used, there were 55 (15.85%) drugs administered with slightly inappropriate indication. The indication was considered slightly appropriate because there were no literature supporting the administration, while the goal of drug administration was relatively clear. Some drugs being administered

Table 4. Appropriateness of Drug Administration Based on Indication, Dosage, and Duration of Therapy

Indication	Number of drugs	(%)	Drug dosage	Number of drugs	(%)	Duration of therapy	Number of drugs	(%)
Appropriate	228	65.71	Adequate	206	90.35	Appropriate	98	77.78
Not quite appropriate	55	15.85	Subtherapeutic	6	2.63	Inappropriate	23	18.25
Inappropriate	64	18.44	Overdosage	9	3.95	Unable to define	5	3.97
			Unable to define	7	3.07			
Total	347	100.01	Total	228	100	Total	126	100

slightly inappropriately were proton pump inhibitor drugs (PPI) and histamin 2 antagonist (AH2) in small dose aspirin administration. The administration of PPI or AH2 is meant to prevent the onset of gastric or duodenum ulcer due to long-term use of aspirin in patients with the history of coronary heart disease. The motive of drug administration is quite clear, because there is no literature supporting routine administration of PPI or AH2 in patients without gastrointestinal symptoms.

The use of laxatives for constipation prophylaxis in patients with congestive heart failure and cor pulmonale is often found in clinics. However, various literature on the treatment of congestive heart failure does not mention the routine use of laxatives.

Other drugs also being used without literature support are lactulosa for prophylaxis in hepatic encephalopathy in patients with hematemesis melena due to hepatic cirrhosis; hepatoprotector for disturbance in liver function, vitamin B for treatment of diabetic neuropathy; use of mucolytic for lower respiratory tract infection, and Echinacea as immunostimulator.

Inappropriate Indication for Drug Administration

There were 64 out of 347 (15,85%) types of drugs being used without clear indication, because they are classified as inappropriate administration. As an example, the use of sucralphate and AH2 for diabetic gastropathy, the use of isorbid mononitrate (ISMO) to

minimize hematemesis melena due to hepatic cirrhosis, use of piracetam in ischemic stroke, and allupurinol for asymptomatic hyperuricemia, pentoxifyllin to treat peripheral drug diseases.

In bleeding such as esophageal varices, there are currently no literature supporting the use of tranexamate acid. Although this drug is indicated to treat acute bleeding, in esophageal varices there were no literature mentioning the use of this drug. Esophageal varices commonly based on hepatic cirrhosis is usually found in the refrigerating system, therefore the logical treatment would consist of vitamin K administration. In contrary, in this survey vitamin K was given for hematemesis-melena due to stress ulcer, erosive gastritis, and hematoschezia in colon ulcer, rectal ulcer, and proctitis. Actually in these cases there are no coagulation factor deficiency, therefore the administration of vitamin K is not really the right treatment. Some literatures and publications have shown the benefit of tranexamic acid in erosive gastritis and hemorrhoid.

Drug Administration Without Appropriate Indications

Antibiotic administration without appropriate indication was a common practice in both outpatient and inpatient settings. In this study we evaluated ceftriaxone administration for more than 10 days in patients

Table 6. Use of Interacting Drugs

Drug I	Drug II	Drug III	Interaction	Number of usage
Aspirin	Heparin	-	Risk of bleeding	1
Cilostazol	Pantoprazole	-	Inhibition of cilostazol metabolism	1
Sucralphate	Levofloxacin	-	Inhibition of levofloxacin absorption	3
Captopril	KSR	-	Hyperkalemia	2
Furosemide	Digoxin	-	Risk of arrhythmia	4
Captopril	KSR	Spironolactone	Hyperkalemia	2
Clopidogrel	Enoxaparin	-	Risk of bleeding	1
Aspirin	Enoxaparin	-	Risk of bleeding	2
Aspirin	Captopril	-	Decreasing the antihypertensive effect of captopril	1
Chlorpromazine	Nifedipine	-	Orthostatic hypotension	1
KSR	Spironolactone	-	Hyperkalemia	1
Captopril	Enoxaparin	-	Hyperkalemia	1
Captopril	Allopurinol	-	Risk of hypersensitivity	1
Diazepam	Omeprazole	-	Inhibition of diazepam metabolism	1
Total				25

diagnosed with extensive anterior NSTEMI post heparinization, CHF, II ec CAD, normoresponse AF with escape rhythm episodes, grade-II hypertension, dyslipidemia, and uncontrolled DM2, NW, and GD. Here we did not observe any diagnosis associated with infection, although we could predict that the patient's health condition was quite compromised.

Administration of drugs without indication sometimes happened due to miscommunication between the physician and the nurse. One example is the finding of a patient treated with bicarbonate, folic acid, and vitamin B12. This patient was hospitalized due to hepatoma, ascites, long term pulmonary tuberculosis with drug-induced hepatitis (DIH), antero-septal CAD, and hypoalbuminemia. There was no medical instruction written by the physician in the medical record, but it was found in the patient's card (drug administration record).

Excessive Drug Administration

In patients with renal function disorder, with creatinine clearance test (CCT) below 50 ml/minute, dosage of drugs that is mainly eliminated through the kidney in original form has to be adjusted. Usual dosage administration will cause accumulation.

In this study, there was a patient receiving levofloxacin 1 x 500 mg daily, while the patient's CCT was actually less than 50 mL/minute. According to the literature,⁷ the initial dose for patients with 20-49 ml/minute CCT is 500 mg and maintenance dose is 1 x 250 mg (initial dose 1 x 500 mg). For patients with CCT of 10-19 mL/minute, the maintenance dose is 250 mg/48 hours (initial dose 1 x 500 mg).

Dosage of cilostazol when given together with pantoprazole should be reduced to 2 x 50 mg because pantoprazole inhibits cilostazol metabolism, so that the plasma cilostazol level increases.⁸ In this study, the patient was given 2 x 100 mg cilostazol.

Ceftazidime for community-acquired pneumonia is given 1 gram three times daily in patients with Clcr of 11,9 mL/minute. This patient is supposed to receive ceftazidime 24 hourly. In patients with decreased renal function with CCT 30-50 mL/minute, ceftazidime is recommended to be given 12 hourly.⁹ For CCT 10-30 mL/minute, the drug is given every 24 hours, and when the CCT is less than 10 mL/minute, the drug is given every 48 hours.

Subtherapeutic Dose of Drug

Beside, excessive administration of drug dosage, in this study we also found the opposite condition, the subtherapeutic dosage administration, such as: Propranolol 2 x 5 mg for grade II-III esophageal varices with moderate portal hypertension gastropathy. Although

the most current data doubt the effectivity of beta receptor blocker in esophageal varices bleeding,¹⁰ however, the dosage listed on the reference is still 2 x 20 mg.¹¹

One patient weighed 42 kg received antituberculous drug rifampicin 300 mg, pyrazinamide 750 mg, and ethambutol 750 mg. It is said in the literature that for a 40 to 60 kg man, the dosage should be 450 mg, 1000 mg, and 1000 mg, respectively.¹² Chlorpromazine 1 x 25 mg for long term CVD with the history of chronic hiccups. During hospitalization, the hiccup is in this patient could not be eliminated. The chlorpromazine dose should actually be gradually increased, because the dosage of chlorpromazine for hiccups may be given 3-4 x 25-50 mg daily.¹³

Administration of Drugs with Undefined Dosage

Administration of drugs with undefined dosage is the administration of drugs where the dosage is not listed in the reference books, making it difficult to determine whether the patient is receiving adequate, subtherapeutic, or excessive dosage. These drugs are KSR tablet for hypokalemia, NaCl in hyponatremia, and intravenous ciprofloxacin for infection prophylaxis in esophageal variceal bleeding.

Administration of Drug Longer Than Patient's Clinical Need

Some drugs have been still administered although the patient's clinical condition has improved, such as: antiemetic drugs domperidone, metoclopramide, and ondansetron. Gastric acid suppressor drugs pantoprazole in dyspepsia patients were still administered although the patient's clinical condition has improved. The use of laxatives in constipated patients was continued although the patient no longer complaining for constipation. Inhalation drugs in pneumonia were still administered although clinically the patient no longer need the drugs, and the prolonged administration of suppository tramadol in renal colic patients although the patient did not clinically need the drug anymore.

Suboptimal Use of Drug

Use of octreotides in PVO patients was only for 1 day, while actually according to the literature it is supposed to be given for 2 to 5 days.¹⁵ In this patient, octreotide was only given for 1 day due to financial problem. There was also antibiotic administration in patients with pneumonia less than the recommended duration of therapy written in the ATS 2001.

Excessive Drug Administration (Overtreatment)

A patient was admitted with the diagnosis of fifth grade chronic renal disease due to diabetic nephropathy (Clcr 9,36 ml/min, serum creatinine level

6,5 mg/dl), first grade hypertension (150/80 mmHg), and hypercholesterolemia received antihypertensive therapy that consisted of captopril 2 x 25 mg, bisoprolol 1 x 5 mg, terazosin 1x2 mg, and furosemide 2 x 40 mg. Baseline blood pressure on admission was 160/90 mmHg, and received captopril 2 x 25 mg and furosemide 1 x 20 mg. According to JNC VII, patients with first grade hypertension should receive single drug.¹⁶

Less Drugs were Administered for The Patients' Clinical Requirements (Undertreatment)

- a. No corticosteroid was given in an acute attack in severe persistent asthma.

Patient was admitted to the hospital with acute attack in severe persistent asthma, and was treated with combivent inhalation (ipratropium br and salbutamol sulphate): bisolvon (bromhexin):NaCl= 1:1:1/6 hours.

Treatment for severe persistent asthma according to the *Global Initiative for Asthma* 2004 is as follows: as a reliever short-acting β_2 agonist inhalation should not be more than 3 to 4 times daily. For controller high dose glucocorticoid inhalation should be given together with long-acting β_2 agonist inhalation, and whenever needed one of the following drugs could be administered: slow - release teophylline, leukotrien modifier, long acting oral β_2 agonist, or oral glucocorticoid. When asthma has been controlled and maintained for over 3 months, maintenance therapy to control asthma could be started.¹⁷

- b. No diuretic was given to patient with CHF fc III ec CAD.

Patient was admitted to the hospital with the diagnosis of CHF fc III ec CAD and was given captopril 2 x 12,5 mg, aspirin 1 x 80 mg, and famotidine 1x20 mg. Pasien was only given diuretic (furosemide 1x40 mg iv) on the fourth day of hospitalization. The patient was supposed to receive diuretics from the first day of hospitalization according to the *Guideline for management of patients with CHF* according to ACC/AHA 2005.(Ref)

CONCLUSION

We have found 67% appropriate administrations of drug. From this number, 90% dose-appropriate, of all drug administrations there were 2 possibilities of adverse drug events, 5 drugs were contraindicated and 25 potentially interacted drugs. From 126 drug uses with measured duration of administration, there were 77.78% proper duration of drug administration.

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