Adverse drug reactions (ADRs) in geriatric hospitalized patients

Adverse drug reactions (ADRs) pada pasien rawat inap geriatri

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Abstract

Adverse drug reactions in elderly patients are major clinical problem. The aim of the study was to assess the incidence of adverse drug reactions (ADRs) in geriatric hospitalized patients.

The study was conducted in 100 geriatric patients hospitalized by prospectively. All admissions of patients aged 60 and over to internal department medical wards IRNA I RSUP Dr. Sardjito Yogyakarta from January-February and August-October 2006 were analyzed. Data collection was conducted base on the medical record then adverse drug reactions were identified by pharmacist-physician discussion. Evaluation of the data was carried out descriptively.

The result of the study showed that suspect of ADRs occurred in 25 patients. We identified the existence of 30 ADRs. The majority symptoms of ADRs were related with gastrointestinal (nausea, vomiting, dyspepsia, abdominal discomfort, constipation, diarrhea, and gastritis) 56.7 %, cardio-vascular (hypertension, and hypotension) 16.7 %. The finding of our study in adverse drug reactions (ADRs) identification supports pharmacists in building effective collaboration between health professional physician-pharmacist-nurse to identify and to prevent adverse drug reactions (ADRs) in geriatric patient.

Key word: Adverse drug reactions (ADRs), Geriatric, Inpatient.

Abstrak

Adverse drug reactions (ADRs) merupakan masalah yang sering terjadi pada pasien lanjut usia. Penelitian bertujuan mengetahui angka kejadian *adverse drug reactions* pada pasien rawat inap geriatri.

Penelitian dilakukan dengan mengambil data secara prospektif pada 100 pasien rawat inap geriatri dengan kriteria usia pasien 60 tahun atau lebih dan menjalani rawat inap di bagian Penyakit Dalam (IRNA1) RSUP Dr. Sardjito Yogyakarta pada dua periode waktu (Januari–Februari 2006 dan Agustus–Oktober 2006). Pengambilan data dilakukan melalui catatan medik kemudian identifikasi efek samping obat dilakukan melalui diskusi farmasis dengan klinisi konsultan geriatri. Evaluasi data dilakukan secara deskriptive

Hasil penelitian menunjukkan bahwa ADRs diduga kuat dialami oleh 25 pasien dengan total 30 kejadian ADRs. Sebagian besar ADRs yang ditemukan berhubungan dengan gangguan pada gastrointestinal (mual, muntah, dispepsia, konstipasi, diare dan gastritis) 56,7 % dan kardiovaskular (hipertensi dan hipotensi) 16,7 %. Farmasis dapat berperan dalam identifikasi ADRs melalui kolaborasi dengan tenaga kesehatan lain di rumah

sakit sehingga dapat dilakukan upaya pencegahan terhadap ADRs pada pasien geriatri
Kata kunci: *Adverse drug reactions (ADRs)*, Geriatri, Rawat inap.

Introduction

There are many problems which can be associated with the introduction of drugs into the human body, adverse drug reactions represent one of eight identified categories of drug related problems (Helper and Strand, 1990). The World Health Organization (WHO) describes an adverse drug reaction (ADR) as a drug-related event that is noxious and unintended and occurs at doses used employed in human for prophylaxis, diagnosis or therapy of disease (Wiffen, *et al.,* 2007). The Food and Drug Administration (FDA) defines an ADR as an undesirable effect, reasonably associated with the use of the drug that may occur as part of the pharmacological action of a drug or may be unpredictable in its occurrence. The FDA includes incidents of overdose and incidents due to drug dependence or withdrawal after cessation of drug administration (Gharaibeh, *et al.,* 1998).

Adverse drug reactions can be categorized into two general types, Type 1 and Type 2, respectively. Type 1 refers to ADRs which can be predicted from the known pharmacology of the drug and frequently may be dose-dependent. Type 2 ADRs are idiosyncratic and characteristically not dose-dependent (Gharaibeh, *et al.,* 1998). ADRs occur more frequently in the presence of one or more of the following factors: extremes of age (neonates and the elderly), gender, multiple medications, disease state (disease of liver, kidney and heart), past history of ADR or allergy, genetic factors, large dose (Wiffen, *et al.,* 2007).

Some condition in elderly such as pharmacokinetics and pharmacodynamics changes, cognitive dysfunction, poor vision, and hearing contribute to adverse drug events (Nair, 1999). Several studies have assessed the association between age and ADRs. The results have been variable, but a trend for a relationship between age and increased incidence of ADRs has been established (Walker and Wynne, 1994). The Harvard medical practice study found that adverse events were more common among elderly patients (Leape, *et al.,* 1991). In the United States, as many as 28 % of hospital admissions of elderly patients are the direct result of drug-related problems, with 70 % being attributable to adverse drug reactions (ADRs) (Col, *et al*, 1990).

Adverse drug reactions add an unnecessary cost to an already burdened heath care system and are usually preventable. In a prospective case-control study in hospitalized patients, ADRs complicated 2.3 % of cases, caused 3.5 % mortality, increased hospital stay by 17 %, and resulted in a doubling of mean costs of hospitalization from $5,335 to $ 10,010 (Classen, *et al.,* 1997). Bates et al, estimated that, for a 700-bed teaching hospital, the annual costs attributable to all ADRs is $ 5.6 million, of which $ 2.8 million, or 50 %, is preventable (Bates, *et al.,* 1997)

Report of adverse drug reactions occurred frequently among inpatients included elderly, but adverse drug reactions report in Indonesia especially in elderly still very limited. The study performed to asses the incidence of adverse drug reactions (ADRs) in geriatric hospitalized patients.

Methodology

Research type is descriptive. Data were taken prospectively in two time periods, January until February 2006 and August until October 2006. The study was conducted in 100 geriatric patients hospitalized at Bougainville ward IRNA 1 RSUP Dr. Sardjito Hospital, Yogyakarta, Indonesia. All the patients with inclusion criteria were involved in the study. The inclusion criteria are patient who were 60 years old and above, patient hospitalized in internal medicine department, and had complete document.

Data collection was conducted through review medical record and interview with the patients. First, the presence of an adverse drug reaction was assessed from the history, examination, laboratory tests and drug treatment. Then, the patients were asked whether they thought any of their medical problems were caused by their drugs. Patients gave their informed consent for this purpose. Possible adverse drug reactions were identified by clinical pharmacist & physician (geriatrician consultant) discussion. Adverse drug reaction defined as undesirable side effect/injuries

caused by drug at therapeutic dose (WHO definition). Analysis of the data was carried out descriptively.

Results And Discussion

Of the 100 selected hospitalized geriatric patients, 60 % were women and their ages ranged from 60 to 89 years. The majority of patient's ages were between 60-69 (51 %) and 70-79 (36 %) years old (Figure 1). This data can describe life expectancy for elderly in Yogyakarta, statistical data for life expectancy in Yogyakarta were 72 years old for women and 69 years old for men (Anonim, 2007).

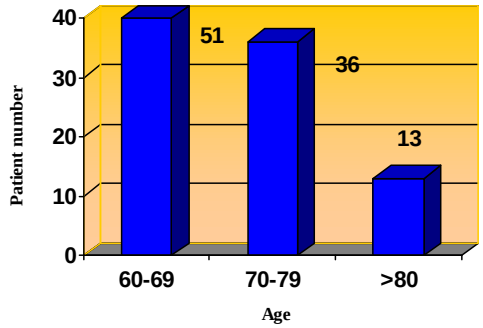

Figure 1. Distribution of geriatric patient age

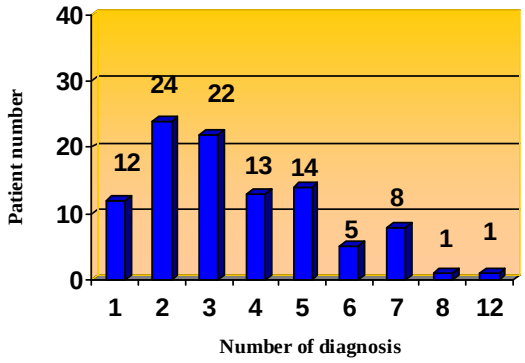

Figure 2. Number of diagnosis in geriatric patient

With increasing age comes an increasing vulnerability to develop diseases and, in the elderly, the tendency to acquire multiple and chronic diseases (Giron, et al, 1999). We found 46 % elderly patients have 2 to 3 diagnoses, 27 % have 4 to 5 and 15 % patients have 6 diagnoses and over (Figure 2).

The most common co morbid condition were cardiovascular (hypertension 43 % and congestive heart failure 21 %), endocrine (diabetes mellitus 26 %), infection (pneumonia 17 %, sepsis 20 %, and urinary track Infection 13 %), cancer 28 % , and renal disease (acute renal failure 6 % and chronic kidney disease 10 %).

In this study, medication use range during hospitalization was two (2) until twenty four (24) different medications. Seventeen patients received 2 to 5 medications, 57 patients received 6 to 10 medications, 20 patients received 11 to 15 medications, and 6 patients received more than 15 medications during hospitalization. A patient received 24 different medications; the diagnosis of this patient is chronic kidney disease, effusion pleura sinister, congestive heart failure, hernia Inguinalis laterals, and bronchopneumonia. A lot of medication used might cause of symptom and patient's diagnosis often changes during hospitalization and also large of diagnosis in elderly patients.

Polypharmacy, duration of hospital stay and number of medical problems, variables often associated with ageing, were found to be the independent predictors of ADRs. Hohl et al assed the degree of polypharmacy and frequency of potential adverse drug interactions (PADIs) in medication regimen of elderly patients in the emergency department (ED). He found 257 (90.8 %) patient were taking 1 or more medications (prescribed or over the counter). The number of medications consumed range from 0 to 17 and averaged 4.2 drugs per patient. Adverse drug-related events accounted for 10.6 %, and thirty one percent of all patients in the research had at least 1 PADI in their medication list (Hohl, *et al.,* 2001). Similar research, Larson found the potential of ADR occurrence equal 6 % among patient who got two kinds of drug, 50 % among the patient accepting five kinds of drug, 50 % among the patient accepting five kinds of drug and 100 % at the patient accepting eight or more kinds of drug (Larsen and Martin, 1999).

The result of the study showed that suspect of ADRs occurred in 25 patients (25 %). We identified the existence of 30 events of ADRs. It is higher than another research

Table I. List of Symptom and the drug that caused of ADRs

N0.	ADRs	Medication	Number of cases
1	Dyspepsia	Methylprednisolone	1
		Tramadol	1
2	Increased blood pressure	Methylprednisolone	1
3	Nausea and vomiting	Cisplatin	2
		Tramadol	1
		Carboplatin	2
		Metronidazole	3
4	Increased creatinin serum	Captopril	1
5	Abdominal discomfort	Propranolol	1
6	Diarrhea	Lactulose	1
		Ceftriaxon	1
		Ciprofloxacin	1
7	Hypoglycemia	Insulin	3
8	Hypotension	Diazepam	1
		Furosemid	1
		Combine of spironolacton, captopril and furosemid	1
		Combine of furosemid and lisinopril	1
9	Fever	Albumin	1
10	Cough	Captopril	1
11	Thrombocytopenia	Ceftriaxon	1
12	Gastritis	Aspirin	2
13	Constipation	Attapulgit	1
14	Hypokalaemia	Furosemid	1
		Total	30

done by Williamson and Chopin, in a multi-centre study of geriatric units in the UK based upon questionnaire replies, reported an ADR rate of 15.3 % (Williamson and Chopin, 1980). Hurwitz reported the 15.4 % reaction ADR rate in the over-65s. (Hurwitz, 1969). Table I showed name of drug and symptom of ADRs.

Why are adverse drug reactions so frequent in older people, with old age there are changes in both pharmacokinetics and pharmacodynamics. Age-associated alterations in drug absorption, distribution, and protein-binding are of limited clinical importance and have not been clearly shown to have a large influence upon an elderly patient's risk of an ADR. Renal excretion diminished with advancing age and this is of particular relevance to drugs dependent on renal excretion with a narrow therapeutic index and serious adverse effects. The hepatic clearance of drugs can be reduced in elderly people owing to age-associated declines in liver size and blood flow. This increases the risk of dose-dependent ADRs with hepatically cleared drugs such as the benzodiazepines (Walker and Wynne, 1994).

The agents most commonly associated with suspect of adverse reactions from this study were antibiotics, antihypertensives, anticancers, corticosteroid, and analgesics (Table I). This is similar with report from the pharmaceutical journal that analgesics, antibiotics, antihypertensives, psychiatric drugs, drugs with narrow therapeutic indices, and illegal drugs were the agents associated with adverse reactions (Bednall, 2003).

The type of ADRs in the study is type 1 reaction with the following characteristics: largely predictable, usually dose dependent, incidence and morbidity high and mortality low (Wiffen *et al,* 2007). There were 56,7 % types of ADRs in this study were related with gastrointestinal problem, such as nausea and vomiting 8 cases. Four cases caused by anticancer drug (cisplatin and carboplatin). Nausea and vomiting symptoms still appeared although patients received premedication for these symptom. National Comprehensive

Cancer Network (NCCN) report adverse drug event of cisplatin and carboplatin on gastrointestinal are nausea vomiting (60 % - 90 %) (Anonim, 2005).

We found four cases ADRs hypotension and one case electrolyte disturbance hypokalaemia (3.29 mmol/L on day one, then 2.41 mmol/L on second day hospitalization) because of antihypertensive drug used. Among patients with ADRs, two patients identified as caused by drug interactions. One of these cases is combination of furosemid and lisinopril that caused hypotension in the patients. Previously patient's BP was 160/70, in few days hospitalization BP become 120/40. Other case was combination of spironolacton, captopril and furosemid. Semla et al documented combination of furosemid with ACEI may increase hypotension effect and/or renal effect are potentiated by hypovolemia (Semla, *et al.,* 2004).

In the era of modern clinical therapeutics, understanding the mechanism by which drugs produce adverse effects is also highlighted. In that way, health care providers may avoid ADRs in their patients and maximize the efficacy of their therapeutic regimens (Gharaibeh *et al.,* 1998). It was suggested that 50 % of ADRs were potentially preventable (Classen *et al.,* 1997).

Limitation of this study due to lack of laboratory data made us difficult to adjust ADRs. For examples, some parameters of laboratory data to evaluate ADRs of a drug only measured once, when patient admitted to hospital or once after few days of admission. One possibility was the clinicians did not pay attention to ADRs. The clinicians did inspection of laboratory data only as mean to know the progress of disease and did not aim for evaluating the ADRs. This is why report about ADRs in Indonesia is just a few.

On the other side, the detection of adverse effect in the elderly complicated by both the co-morbidity and the polypharmacy that are prevalent in geriatric medicine. Unwanted drug effects may add to the co-morbidity of age and co-existing disease may mask the presence of underlying drug-related clinical effects. Moreover, the tendency to over prescribe in the elderly may result in the inappropriate use of drug to treat the adverse effect another. In practice, expedients aimed at reducing the number of prescribed medication in an elderly population can reduce the number of ADRs (Hudson and Bouter, 1997).

Identification of ADR is a task, which involves important decision making at all level of health care system. The research of ADRs identification in geriatric patients in Indonesia has given description of the effect ADRs and the drugs that often caused ADRs. This information will help the doctors, pharmacists, and nurse to give special attention to the patients who give the drugs that often caused ADRs. Further more this action can prevent ADRs in geriatric patients.

Conclusion

Adverse drug reactions occur frequently among geriatric inpatients. The finding of our study in adverse drug reactions (ADRs) identification supports pharmacists in building effective collaboration between health professional physician-pharmacist-nurse to identify and to prevent adverse drug reactions (ADRs) in geriatric patient.

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