

Drug-related problems in elderly patients with diabetes: A study in primary health care setting

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ABSTRACT

This study's aim was to investigate the prevalence of drug-related problems (DRPs) in the treatment of elderly patients with type 2 diabetic mellitus (T2DM) in a primary care environment. This study used cross-sectional, non-experimental research methods. The sampling method included total sampling with 90 medical records of elderly patients with T2DM at one of Yogyakarta's key healthcare facilities in the 2018 period. This study's classification of DRPs was based on PCNE V5.01. The American Diabetes Association (ADA), JNC 8, Beers Criteria, STOPP/START Criteria, Geriatric Dosage Handbook, Indonesian Endocrinology Association 2015, Indonesian Endocrinology Association 2019, and Drug Interaction Fact 2009 were used to analyze the data. Descriptive data were supplied. According to the findings, 263 DRP episodes occurred in 70 patients, or 77.78%, of the 90 patients who were evaluated. The category of adverse drug reactions saw 2 incidences (0.76%), the category of drug choice problems saw 118 incidences (44.87%), the category of dosing problems saw 41 incidences (15.59%), the category of drug use problems saw 3 incidences (1.14%), and the category of drug interactions saw 99 incidences (37.64%). The result implies that type 2 DM treatment for senior individuals needs to take into account the possibility of DRP incidence. To increase the safety of treating the elderly, health professionals must pay greater attention.

Keywords: Type 2 diabetes mellitus, Drug related problems, Geriatric, PCNE V5.01

Introduction

Patients with diabetes mellitus (DM) worldwide increase every year. Indonesia itself ranked sixth with the number of DM sufferers around 10.3 million people [1]. Numerous degenerative diseases, including diabetes mellitus (DM), are brought on by the reduction in organ function that occurs with geriatric aging, and it is predicted that as the population of the old rises, so will the prevalence of DM [2]. The most prevalent form of diabetes in older people is type 2 diabetes mellitus (T2DM). The geriatric population is susceptible to many co-

morbidities and complications of DM that can affect morbidity and mortality [3] making it possible to experience polypharmacy associated with drug-related problems (DRPs) [4]. Medicine interactions, polypharmacy, and incorrect drug prescriptions in the elderly can all have a negative impact on their quality of life, necessitating extra care [5].

Drug related problems is a problem caused by the use of drugs [6]. Several articles have been published regarding the potential incidence of DRPs in T2DM patients, especially the elderly [7, 8]. Few people have, however, identified the prevalence of DRPs at the level of basic healthcare facilities as a primary healthcare service that can be crucial in the management of T2DM patients. This study intends to describe the prevalence of DRP in an Indonesian primary healthcare facility.

Materials and Methods

Research design and sampling technique

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Cross-sectional research methods were used in the execution of this study. Data collection was carried out retrospectively from the medical records of geriatric patients with T2DM with or without complication who had undergone treatment at one of primary health care centers of Yogyakarta in 2018. The sampling technique used a total sampling of 257 patients from the total population, and 90 patients met the inclusion criteria.

Data analysis

The kind and number of each type of DRP used in the treatment of geriatric patients with T2DM were identified using qualitative and quantitative data analysis. The qualitative data is described as the outcomes of data analysis in comparison to the Indonesian Endocrinology Association in 2015, the American Diabetes Association (ADA) in 2019, JNC 8, the Beers Criteria in 2019, the STOPP/START Criteria in 2019, the Geriatric Dosage Handbook in 2004, the Drug Interaction Fact in 2009, and other relevant journals. Quantitative information was reported as percentages of DRP occurrence, which were derived by contrasting each type of DRP with the total proportion of DRP occurrence. The PCNE (Pharmaceutical Care Network Europe) V5.01 2006 category of adverse drug reactions (ADR), drug choice problems, drug dose problems, drug use problems, drug interactions, and other problems served as the basis for grouping the DRPs category.

Results and Discussion

Patient characteristics

The majority of the patients ($n = 54$; 60%) were female, and the remaining patients ($n = 36$; 40%) were male. A total of 90 patients matched the inclusion criteria (**Table 1**). This is in accordance with Basic Health Research (2018) stating that DM sufferers in Indonesia are more female, which is 1.8% compared to 1.2% of men out of 1.2 million people [9]. A study stated that women have a higher risk of DM compared to men related to advanced age, high LDL level and physical activity [10]. The second patient characteristic was age related. The majority of patients belonged to the elderly group, namely 60-74 years ($n = 87$; 97%), while the elderly group, namely 75-90 years, only 3 patients and no patients in the very old age group or >90 years (**Table 1**). Basic health research 2018 showed that in the older age group, the prevalence of DM increases. These results are in accordance with the guidelines mentioning that the age group >45 years has a high risk of developing diabetes mellitus [11]. Because of the combined effects of increased insulin resistance and reduced activity of the pancreatic islets in making insulin, older individuals are more at risk for T2DM [12].

Based on comorbidities, there were 58 diseases experienced by 84 patients (93.33%) based on a doctor's diagnosis, and the remaining 6 patients (6.67%) had no comorbidities. The most common comorbidities experienced by geriatrics patients in this study were hypertension ($n = 56$; 22.86%), then dyslipidemia ($n = 52$; 21.22%), myalgia ($n = 13$; 5.31%) and osteoarthritis ($n =$

12; 4.9%) (**Table 1**). Previous studies have shown that people with T2DM have two or more comorbidities, even though the comorbidity profiles varies [13].

The regular use of five or more medicines is a common definition of polypharmacy [14]. As a result, polypharmacy patients are those who received an average of 5 medications during visits in 2018 at a rate of 17.7%. (16 patients). In geriatrics, polypharmacy can lead to DRPs [4], hospitalization and non-adherence to medications [15].

Table 1. Overview of patients' characteristics

Patient Characteristics	Number of patients n (%)
Gender	
Female	54 (60)
Male	36 (40)
Age	
Elderly (60-74 years)	87 (97)
Old age (75-90 years)	3 (3)
Comorbidities	
Hypertension	56 (22.86)
Dyslipidemia	52 (21.22)
Myalgia	13 (5.31)
Osteoarthritis	12 (4.90)
Hyperuricemia	11 (4.49)
Acute respiratory infection	9 (3.67)
Common cold	9 (3.67)
Acute pain	5 (2.04)
Dry eye syndrome	5 (2.04)
Dyspepsia	5 (2.04)
Others	68(27.79)
Average drug use	
< 5 drug	74 (82)
≥ 5 drug	16 (18)

Drug usage profile

A total of 3 types of antidiabetic drugs, namely metformin, glimepiride, and glibenclamide, were used by patients, either alone or in combination. Of the antidiabetic drugs that patients used, the combination of metformin and glimepiride was the most widely used ($n = 44$; 48.9%) followed by metformin alone ($n = 40$; 44.4%) (**Table 2**). Due to its effectiveness and safety, metformin is the first-line treatment for type 2 diabetes [16]. The combination of metformin and glimepiride is preferable to being the first-choice drug in the management of T2DM, and in terms of efficacy in glycemic control of T2DM and lower risk of hypoglycemia compared to the combination of metformin and glibenclamide [17, 18].

Table 2. Overview of patients' antidiabetic drugs

Antidiabetic drugs	Number of patients n (%)
Single	
Metformin	40 (44.4)

Glimepiride	4 (4.4)
Combinations	
Metformin +Glimepiride	44 (48.9)
Metformin +Glibenclamide	2 (2.2)

In the profile of drug use for the management of comorbidities, there are 47 types of oral drugs and 10 types of topical drugs. Of the 47 types of oral drugs used, amlodipine was the most widely used in 54 patients (Table 3). The amount of use of amlodipine corresponded to the most common comorbidity, namely hypertension. The aging process causes stiffness in the arteries and decreases their ability to dilate, resulting in an increase in blood pressure [19]. Amlodipine is a calcium channel blocker drug that causes smooth muscle relaxation and lowers blood pressure. If hypertension is present, amlodipine can be used as a first-line treatment due to its high efficacy [20, 21].

Table 3. Overview of drugs used for comorbidities

Drug	Frequency
Amlodipine	54
Vitamin B complex	48
Simvastatin	41
Meloxicam	30
Gemfibrozil	16
Na diclofenac	16
Paracetamol	14
Ibuprofen	13
Allopurinol	12
Methyl prednisolone	11
Cetirizine	9
Ambroxol	8
Glyceryl Guaiacolate	8
Hydrochlorothiazide	6
Kalium diclofenac	6
Others	88

Identification of DRPs

Adverse Medication Reactions (ADR), drug choice problems, dosing problems, drug use problems, and drug interactions were the categories that made up the Pharmaceutical Care Network Europe (PCNE) V5.01 DRPs categorization, which was the category that was recognized. The drug choice problem category consists of the incidence of indications without drugs, drugs without indications, and inappropriate drug selection. Drug doses that are too low and too high can be included in the dosing problem category. The category of drug use problem is a problem related to the use of drugs in patients who are not compliant in taking drugs.

Table 4. Identified drug related problems

DRPs category	Frequency	Percentage (%)
Adverse drug reactions	2	0.76

Drug choice problem		
Indications without drugs	80	30.42
Drugs without indication	18	6.84
Inappropriate drug selection	20	7.6
Dosing problem		
Dosage too low	26	9.89
Dosage too high	15	5.7
Drug use problem	3	1.14
Drug interaction	99	37.64
Total	263	100

Adverse drug reactions

The patient's complaint records in the medical record from each visit were used in this study to identify adverse medication responses. There were 2 cases of patients experiencing adverse drug reactions, namely nausea on the use of metformin and glibenclamide. Compared to the use of sulfonylureas, these adverse effects are more frequent with metformin use. Metformin has side effects of nausea and vomiting (26%), while glibenclamide is known to have side effects of hypoglycemia [22]. The mechanism of metformin induced gastrointestinal side effects is unclear. Serotonin (5-hydroxytryptamine (5-HT)) release from the intestine is anticipated to be connected to these outcomes, nevertheless [23]. Taking metformin with or after meals can be done with the aim of reducing nausea.

Drug choice problem

The category of drug choice problems was the most prevalent DRPs problem in this study, with 118 occurrences (44.87%) (Table 4).

Indications without drugs

Of the 80 events, as many as 35 incidents of pain complaints but not given medication were experienced by 32 patients. Paracetamol becomes a safe first-line therapy for the management of mild to moderate pain in geriatric patients unless contraindicated, whereas nonselective NSAIDs require special attention and avoid chronic use because of their associated gastrointestinal side effects [24]. The most common indication without medication after pain was hypertension with a total of 22 cases in 14 patients. There were 3 cases of patients with indications of hyperuricemia but not given the drug. No other drug indication occurred in 4 patients with hypercholesterolemia. In this study, the identification of DRPs regarding indications without drugs were limited to a review in the medical record including diagnoses, treatment data, laboratory test results, and symptoms reported by patients and this is one of the limitations of the study. Therefore, treatment recommendations needed to be communicated with other health workers to confirm the suitability of treatment.

Drugs without indication

Of the 18 events of DRPs in this category, the most common occurrences of drug without indication were patients receiving the non-selective NSAID meloxicam with 7 cases and 4 cases of patients receiving gemfibrozil without indication. Administration of NSAIDs for unclear indications should be avoided because geriatric patients are at high risk for gastrointestinal side effects [24]. Gemfibrozil became a therapy given for hypertriglyceridemia when the patient's triglyceride level reached >500 mg/dL. In addition to giving gemfibrozil without clear indications, patients also received statins which are not recommended in combination with fibrates because they can increase the risk of rhabdomyolysis or muscle tissue damage [25].

Inappropriate drug selection

Avoiding the use of inappropriate drugs is one of the interventions in geriatric patients to avoid DRPs. Of the 20 cases of inappropriate drug selection, 11 patients received glibenclamide, and 5 patients received diazepam. Glibenclamide is a long-acting sulfonylurea that should be avoided in geriatrics, because it can increase the risk of hypoglycemia by 83% compared to other sulfonylureas [24]. Glimepiride was not included in the incidence of DRPs in this study because its use was well tolerated under close monitoring. Geriatrics are known to have lower metabolism for long-acting drugs and greater susceptibility to benzodiazepines while using diazepam, which may extend the sedative effect of diazepam [24].

Dosing problem

The dosing problem category ranked the third highest incidence of DRPs, namely there were 41 cases (15.59%) (**Table 4**).

Dosage too low

Types of drugs included in the incidence of too low a dose were glyceryl guaiacolate (GG) as many as 8 cases and gemfibrozil as many as 18 cases. The dosage of GG drug recommended by the Geriatric Dosage Handbook is 200-400 mg every 4 hours and not more than 2.4 grams/day, while patients received a dose of 3x100 mg. The doses of gemfibrozil that the patient received were 1x300 mg, 2x300 mg, and 1x600 mg. In the treatment of hypertriglyceridemia, the recommended dose of gemfibrozil is 2x600 mg [22].

Dose too high

In this study, as many as 15 cases of overdose drug were found. Drugs with doses too high were cetirizine, amlodipine, and hydrochlorothiazide (HCTZ), while CTM, glimepiride, and omeprazole were not given the correct frequency of administration. The patient received cetirizine 2x10 mg, meaning that in a day the patient consumed 20 mg of cetirizine. The initial dose of cetirizine according to the literature is 5 mg then it can be increased to 10 mg/day and the maximum dose in

patients aged <77 years is 10 mg/day [22]. In addition, the dose of amlodipine 1x20 mg obtained by the patient exceeded the maximum dose of amlodipine, which was 10 mg/day [22]. Patients who received HCTZ 1x25 mg were also known to receive amlodipine 1x10 mg. The recommended dose of HCTZ is 12.5 mg once daily for the initial dose in geriatrics. The use of thiazide diuretics should be used with caution because they can cause hyponatremia in geriatrics [22].

CTM was given to the patient three times a day at a dose of 4 mg. The frequency of CTM administration exceeded the literature recommendation, which should be 4 mg 1 or 2 times a day for geriatrics [22]. The use of CTM in geriatrics should be avoided because of the risk of causing confusion, constipation, or significant urinary problems [22]. In addition, the frequency of administration of glimepiride should be once a day because it is a long-acting sulfonylurea, but the patient received a dose of glimepiride 2 mg with a frequency of 2 times a day. Another case was that the use of omeprazole for dyspepsia therapy recommended by the literature should be 1x20 mg, while the patient received omeprazole 20 mg with a frequency of 2 times a day. Doses and frequency of administration that exceed the recommendations are concerned to increase the risk of side effects.

Drug use problem

Problems related to drug use can occur in patients who are not compliant in taking medication. To determine the non-adherence to treatment of patients in this study was limited only from medical records. In this category, there were 3 incidents of patients not being compliant in treatment. Drugs that the patient did not comply with were metformin, glimepiride, glibenclamide, and amlodipine. This resulted in a lack of therapeutic doses of antidiabetic and antihypertensive drugs, so that the patient's blood sugar and blood pressure levels were still not controlled. A study showed that poor medication adherence was found in low and middle-income countries (LMICs) leading to poor quality of life [26].

Drug interaction

The sorts of drug interactions that were examined in this study were those that were anticipated to happen in patients receiving pharmacological therapy. Three categories—major, moderate, and mild interactions—are used in the literature to categorize the severity of medication interactions. Major interactions have the potential to be life-threatening or cause irreversible damage; moderate effects can lead to a decrease in the clinical status of the patient; whereas minor interactions should not significantly affect the outcome of therapy [27].

In this study, there were 99 drug interactions (37.64%) (**Table 4**) from minor to major severity. Minor interactions were 59 cases with 4 types of drug interactions; moderate cases were 31 events with 6 types of drug interactions, and major interactions were 9 events with 1 type of drug interaction. The most frequent minor interaction was between glimepiride and simvastatin,

which was 55 cases in 19 patients. This interaction may increase the effect of hypoglycemia. The most frequent moderate interactions were glimepiride and gemfibrozil, which were 16 cases in 10 patients. This interaction may enhance the hypoglycemic effect of glimepiride caused by inhibition of the sulfonylurea metabolic enzyme (CYP2C9) by gemfibrozil. The major interactions between simvastatin and gemfibrozil were 9 events in 7 patients. This interaction can lead to severe myopathy or rhabdomyolysis due to the synergistic effect of the two drugs [28]. Fenofibrate can be an alternative since it does not increase the rhabdomyolysis risk significantly because of minimum effect on statin metabolism [29].

This study has advantages such as involving patients with complete prescriptions during one year's visit so that a more comprehensive image can be obtained. On the other hand, because this study used a retrospective study design, the data obtained were only limited to the information contained in the medical record so that the DRPs analysis could only be based on existing data.

Conclusion

This study shows that treatment in elderly patients with T2DM needs to be considered in terms of the potential for the incidence of DRPs. Therefore, more attention from health workers is needed to improve the safety of treatment in the elderly.

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