Polypharmacy and Drug Interactions in Geriatric Patients with Type 2 Diabetes Mellitus at the Internal Medicine Inpatient Installation at RSUP Dr. M. Djamil Padang

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Abstract:

One of the diseases commonly suffered by geriatric patients is diabetes mellitus, more than 95% of diabetics suffer from type 2 DM. Type 2 DM has a 2.28 times higher risk in the elderly and a greater risk of suffering from geriatric syndromes, one of them is polypharmacy which can increase the potential for drug interactions. The purpose of this study was to describe polypharmacy and drug interactions and to analyze the correlation between polypharmacy and drug interactions in geriatric patients with type 2 DM at the Internal Medicine Inpatient Installation at RSUP Dr. M. Djamil Padang in 2021. This type of research is non-experimental using a cross sectional method. Retrieval of data is retrospective originating from the patients medical records. A total of 39 samples included in the inclusion criteria showed that the incidence of drug interactions in patients prescribing polypharmacy was 79.49%, with the highest severity of drug interactions was moderate at 74.46%, and the most pattern of drug interaction mechanisms was pharmacodynamics at 78.72%. In this study it can be concluded that there is a strong and significant corelation between polypharmacy and the potential for drug interactions (p=0.000, r=0.570), which means that the more drugs used, the more potential drug-drug interactions.

Keywords: Polypharmacy; Drug Interaction; Type 2 Diabetes Mellitus; Geriatric

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1. Introduction

Geriatric patients are elderly patients with multiple diseases due to decreased organ, psychological, social, economic, and environmental functions that require integrated and multidisciplinary services, while the elderly are someone over 60 years of age (Ministry of Health, 2014). One of the diseases commonly suffered by geriatric patients is diabetes mellitus, which is a disease with a high prevalence in Indonesia.

Based on estimates from the International Diabetes Federation (2021), Indonesia occupies the 5th position as a country with diabetes mellitus aged 20-79 years with a total of 19.5 million people with diabetes mellitus. According to the Ministry of Health of the Republic of Indonesia (2018), 6.3% of elderly patients are diagnosed with diabetes mellitus. In West Sumatra alone, there are 1.6% of people with diabetes mellitus. Geriatric patients with diabetes mellitus have higher rates of early death, functional disability, coronary heart disease, and stroke than those who do not have diabetes mellitus (Prasetyo, 2019).

Diabetes mellitus is a chronic disease in which the body cannot produce insulin or insulin cannot be used effectively. There are several types of diabetes, including type 1 diabetes mellitus. 2 (Type 2 DM), which occurs because the body does not produce enough insulin or insulin is produced ineffectively (Rian, 2020), gestational diabetes caused by pregnancy, and other types of diabetes mellitus caused by chemicals or drugs (PERKENI, 2021). More than 95% of people with diabetes suffer from type 2 DM (WHO, 2021), and the incidence of type 2 DM has a 2.28 times higher risk in the elderly (Amalia, 2014). Geriatricians with diabetes mellitus are also at greater risk of suffering from several geriatric syndromes, such as polypharmacy, cognitive impairment, urinary incontinence, the risk of falling, and pain (Prasetyo, 2019).

In geriatric patients, the need to strictly control blood sugar and the presence of comorbidities or complications make the number of drug prescriptions in geriatric patients with diabetes mellitus increase, which of course requires polypharmacy drugs. The use of drugs in polypharmacy is the use of five or more types of drugs at the same time every day; this polypharmacy is most often used in health therapy in geriatric patients (Zulkarnaini & Martini, 2019).

The use of drugs in polypharmacy can cause various problems; the more drugs prescribed, the higher the percentage of interactions (Maulida & Puspitasari, 2021). Drug-drug interactions are changes in the effectiveness or toxicity of a drug caused by the presence of other drugs that are given simultaneously. The most common potential interactions are with drugs that are used daily in the clinical management of patients with chronic and geriatric diseases (Shetty et al., 2018).

In several polyclinics at RSUP, Dr. M. Djamil Padang found that geriatric patients who received 5-7 types of drugs received 59.55%, and 5.17% received more than 8 types of drugs (Zulkarnaini & Martini, 2019). Meanwhile, from the medical record cards of geriatric patients who have metabolic diseases with the use of polypharmacy drugs at the Outpatient Clinic of Haji Adam Malik General Hospital Medan, there are 78.96% of patients who experience drug interactions (Dasopang et al., 2015). Similar studies have shown that the incidence of drug interactions in geriatric patients at the Inpatient Ward of Internal Medicine at RSUP Dr. M. Djamil Padang in 2016 was 64.3% for patients aged 60–70 years (Adekurnia, 2016).

2. Methods

The research method is non-experimental with a retrospective design and uses a cross-sectional method. Data were taken from the medical records of geriatric patients with type 2 DM at the Internal Medicine Inpatient Installation of M. Djamil Hospital Padang in the period of January to December 2021.

The population in this study was all geriatric patients with type 2 DM at the Internal Medicine Inpatient Installation at Dr. M. Djamil Hospital Padang from January to December 2021. The samples in this study were geriatric patients with type 2 DM at the Internal Medicine Inpatient Installation at Dr. M. Djamil Padang who met the inclusion criteria with a purposive sampling method, namely a sampling method based on a consideration, not randomly to achieve a specific target or focus.

Data analysis is used in the selection of data that meets the inclusion criteria. The selected data is checked for interaction with the Medscape or Drugs.com applications. The analysis used IBM SPSS with the Spearman test to see the correlation between polypharmacy and drug interactions by including the total number of interactions and the number of drugs. If $p<0.05$ is obtained, there is a correlation between polypharmacy and drug interactions.

3. Research Clearance Ethics

This research ethical test was submitted to the research ethics committee team at RSUP Dr. M. Djamil Padang with number LB.02.02/5.7/370/2022.

4. Results

A total of 39 geriatric patients with type 2 DM at the Internal Medicine Inpatient Installation at RSUP Dr. M. Djamil Padang in 2021 had a fairly high incidence of drug interactions. From the 39 patients, 31 experienced drug interactions (79.49%). Based on gender, the incidence of drug interactions in men is higher (93.75%) compared to women (69.57%). Based on the number of drugs used, the potential for drug interactions is also higher.

The results of the correlation test using the Spearman test showed a positive and significant correlation where there was a strong correlation between the number of drug use events and the number of interaction events, in the sense that the greater the number of drug use events, the more drug-drug interactions that occurred.

Table 1. Description of Drug Interaction Events in Type 2 DM Patients in Internal Medicine Inpatient Installations

No	Subject	Total geriatric patient with type 2 diabetes (n=39)				
		Interact	Percentage (%)	No interaction	Percentage (%)	Total
1	**Gender**					
	Man	15	93,75	1	6,25	**16**
	Woman	16	69,57	7	30,43	**23**
2	**Age Classification**					
	Elderly (60 – 69 tahun)	25	86,20	4	13,80	**29**
	Middle lderly (70 – 79 tahun)	4	57,14	3	42,86	**7**
	Old Elderly (≥80 tahun)	2	66,65	1	33,35	**3**
3	**Total Drugs**					
	Five drugs	6	46,15	7	53,85	**13**
	Six drugs	21	87,5	3	12,5	**24**
	Seven drugs	28	87,5	4	12,5	**32**
	Eight drugs	36	100	0	0	**36**
	Nine drugs	15	100	0	0	**15**
	Ten drugs	8	100	0	0	**8**
	Eleven drugs	18	100	0	0	**18**
	Twelve drugs	9	100	0	0	**9**

5. Discussion

Based on gender, the most frequent were women, namely 23 patients and 16 male patients. This is in line with research conducted by the Ministry of Health of the Republic of Indonesia (2018), where the prevalence of diabetes mellitus is greater in women (1.8%) compared to men (1.2%).

Gender is one of the factors associated with the incidence of type 2 DM due to differences in daily lifestyles between men and women, and the cholesterol that women have is higher than that of men. The amount of fat in men is 15–20% of body weight, while women are 20–25% of body weight, so the increase in fat levels in women is higher and causes risk factors for developing diabetes mellitus that are 3–7 times higher than those in men (Imelda, 2019).

A geriatric patient with type 2 DM at the Internal Medicine Inpatient Unit at RSUP Dr. M. Djamil Padang in 2021 with an age of 60–69 years is the age group that has the highest prevalence of type 2 DM, namely 29 patients. This is in line with research conducted by Rosyada (2013), which found that as many as 83.3% of people with diabetes mellitus are in the age group of 60–74 years. Type 2 diabetes mellitus has a risk of 2.28 times higher in the elderly (Amalia, 2014). As we age, mitochondrial activity in muscle cells decreases by 35% due to an increase in fat levels in the muscles by 30%, which triggers insulin resistance (Samiyah, 2017).

For the incidence of polypharmacy and drug interaction cases, the patients with the most potential drug interactions had a total of 8 types of drug use, namely 36 interaction cases (100%), meaning that in patients who received 8 types of drugs, none of the patients did not have the potential for drug interactions. Then in patients who used 7 types of drugs, there were 28 cases of interactions (87.5%) and 4 cases that did not have potential interactions (12.5%), while in patients who used 5 types of drugs, there were more cases that did not interact, namely 7 cases (patients did not have the potential for drug interactions. Then in patients who used 7 types of drugs, there were 28 cases of interactions (87.5%) and 4 cases that did not have potential interactions (12.5%), while in patients who used 5 types of drugs, there were more cases that did not interact, namely 7 cases (53.85%), compared to interacting cases, namely 6 cases (46.15%).

According to research conducted by Dasopang et al. (2015) based on the number of drugs used, the greater the number of drugs used, the higher the incidence or potential for drug interactions. The use of many drugs that occurs can be caused by the patient suffering from several diseases or getting a diagnosis of more than one. Patients who receive therapy or medication for more than one type of drug are certainly at risk for polypharmacy. Research at Prof. Hospital Dr. Margono Soekarjo Purwokerto also mentioned that the incidence of drug-drug interactions increased with the use of many prescription drugs (Andriana, 2012).

Table 2. Correlation Between Number of Drugs and Number of Interactions

Number Of Interactions	r	P
Number of drugs	0,570**	0,000

The most dominant comorbid disease in this study was chronic kidney disease (CKD), in 24 patients. High blood sugar levels are a risk factor for kidney disease (Melia, 2020). This is in line with research conducted by Satria (2018), which found that out of 37 samples, 26 samples of type 2 DM patients at Dr. M. Djamil Padang had comorbid kidney disease.

In this study, treatment therapy using insulin was widely used, especially insulin novorapid. Novorapid insulin, also known as insulin aspart, belongs to the fast-acting insulin analog class (PERKENI, 2021). Rapid-acting insulin can be used either alone or in combination because it can lower glucose levels more quickly than regular insulin (Istiqomatunnisa, 2014).

The most widely used oral anti-diabetic drug for monotherapy is gliquidone. Gliquidone is a class of sulfonylurea drugs, in which this drug is metabolized in the liver; some are in the form of active metabolites and some are in an inactive form. This makes gliquidone safe for use in patients suffering from chronic kidney disease (CKD) and makes it the main drug of choice after metformin. can be given monotherapy (Dipiro et al. 2017). In this case, of the geriatric patients with type 2 DM at RSUP Dr. M. Djamil Padang in 2021, the majority have comorbid chronic kidney disease (CKD). It is also stated that monotherapy for type 2 DM patients in PERKENI (2021) with HbA1C 7.5% other than metformin is a sulfonylurea/glinid group.

The use of combination anti-diabetic drugs is intended to maximize the effect obtained because rapid-acting insulin only lowers blood glucose levels 20 minutes after injection; therefore, a combination with long-acting insulin is needed so that blood glucose is more stable and this combination therapy can control blood glucose. well with insulin doses that are not so high (Istiqomatunnisa, 2014).

Potential drug interactions in type 2 DM patients at the Internal Medicine Inpatient Unit at RSUP Dr. M. Djamil Padang in 2021 were 79.49%, or found in 31 patients out of a total of 39 patients. Potential drug interactions in geriatric patients with type 2 DM at the Internal Medicine Inpatient Installation at RSUP Dr. M. Djamil Padang in 2021 based on the level of severity obtained data that out of 141 drug interaction events, the highest interactions were moderate (74.46%), minor (19.86%), and major (5.68%). This is consistent with the study of Dasopang et al. (2015), where the highest severity of drug interactions in outpatients at Haji Adam Malik General Hospital Medan was moderate, namely 69.8%. In addition, research conducted at Hasanuddin Hospital also explained that the highest drug interaction based on the level of severity was moderate, with a percentage of 59.27% (Tonny, 2011).

Table 3. Severity of Drug Interactions in Geriatric Patients with Type 2 DM at RSUP Dr. M. Djamil Padang

Interaction Type	Cases	Percentage (%)
Mayor	8	5,68
Moderate	105	74,46
Minor	28	19,86
TOTAL	**141**	**100**

The most common interaction potential found in this study is the potential for moderate interaction, where the potential for moderate interaction is indeed more common in the elderly or geriatric group. Geriatric patients are more susceptible to drug interactions because they are related to age, physiology, increased risk of disease, and increased consequences of drug use (Ting Yeh, 2014).

Based on the pattern of interaction mechanisms obtained from 141 cases of drug interactions in geriatric patients with type 2 DM at RSUP Dr. M. Djamil Padang in 2021, it is known that the highest pattern of interaction mechanisms is pharmacodynamic interactions, namely 78.72%. Research conducted by Setyoningsih (2022) also states that the highest interaction mechanism is pharmacodynamics at 58.7%. One of the pharmacodynamic interactions found in this study is the interaction between candesartan and levemir, where the effect of the interaction is to increase the risk of hypoglycemia. In the pharmacodynamic interaction mechanism, the drugs taken bind to each other and interact with receptors or sites of action, causing synergistic, additive, and antagonistic effects (Setyoningsih, 2022).

Table 4. Mechanisms of drug interactions in geriatric patients with type 2 DM at RSUP Dr. M. Djamil Padang

Mechanisms of drug interactions	Cases	Percentage (%)
Pharmacokinetics	28	19,86
pharmacodynamics	111	78,72
Unknown	2	1,42
TOTAL	**141**	**100**

Furthermore, data obtained showed that the mechanism of pharmacokinetic interaction was 19.86%, and there were several types of drugs whose interaction mechanism was unknown (unknown) at 1.42. Pharmacokinetic interactions occur when one drug affects the absorption, distribution, metabolism, or excretion of another drug, so that the plasma levels of the two drugs can increase or decrease (Sa'adah, 2016).

As for other studies, the same thing was mentioned by Rahmiati and Supadmi (2016) at PKU Muhammadiyah Yogyakarta Hospital: the highest interaction mechanism was also found in pharmacodynamic interactions with a percentage of 62.71%. Decreased organ function, such as in the endocrine, digestive, urinary, neurological, musculoskeletal, and cardiopulmonary systems, can be a factor influencing the pharmacodynamic and pharmacokinetic processes of drugs in the body (Ekowati, 2006).

The results of this correlation test showed a positive and significant correlation with a value of $p = 0.000$, which means that there is a correlation between polypharmacy and drug interactions. For the value of the strength of the relationship, it was found that $r = 0.570$, which means that there is a strong correlation between the number of drugs used and the number of interactions, in the sense that the more drugs used, the more drug-drug interactions that occur. This is consistent with research conducted by Dasopang et al. (2015), where the correlation between the number of drugs and the number of interactions is very significant.

The research conducted by Raquel (2011) also stated that the higher the number of drugs, the higher the incidence of interactions. There are other factors that can affect the incidence of polypharmacy and drug interactions, such as the number of diagnoses or the number of comorbid diseases suffered by patients (Dasopang et al., 2015).

6. Conclusion

In this study, data were obtained showing that there was an incidence of drug interactions in patients prescribing polypharmacy of 79.49%, with the highest severity of drug interactions being moderate at 74.46% and the highest pattern of interaction mechanisms being pharmacodynamic interactions with a percentage of 78.72%. According to the results of the correlation test, there was a positive and significant correlation between polypharmacy and the potential for drug interactions, with a value of $p = 0.000$. The greater the number of drugs, the more potential drug-drug interactions occur.

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