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Undesirable events in the use of high-alert medicine geriatric patients at RSUPN Dr. Cipto Mangunkusumo

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ABSTRACT

High-Alert Medications (HAM) are drugs that have a high risk of causing significant harm to patients if misused. It is estimated that one in ten geriatric patients experiences undesirable events during hospitalization related to medication use. Detect undesirable events due to the use of high-alert insulin and high-alert heparin drugs in geriatric patients at Rumah Sakit Umum Pusat Nasional (RSUPN) Dr Cipto Mangunkusumo using the trigger tool method based on positive predictive value (PPV) and determine the effect of using high-alert insulin and high alert heparin drugs on undesirable events. A retrospective cohort study will review secondary data from patient medical records (MR). The sample used was from 300 geriatric patients, 82 patients used insulin and 79 patients used heparin which met the inclusion criteria. Data were analyzed in the form of frequencies and percentages (%), calculation of PPV values, and the effect of using high-alert insulin and high-alert heparin on undesirable events using the Chi-Square test. There were 8 trigger-positive patients with undesirable events in the form of hypoglycemia from 82 insulin patients and 4 trigger-positive patients with undesirable events in the form of extended activated partial thromboplastin time (aPTT) values from 79 heparin patients. Based on the PPV value, both insulin (9.75%) and heparin (5.33%), the trigger tool has not been able to detect undesirable events when using high-alert insulin and high-alert heparin. Based on statistical tests, the p-value= 0.033 ($p<0.05$) for insulin and heparin p-value= 0.043 ($p<0.05$) meaning that there is an influence of the use of high-alert insulin and high-alert heparin on undesirable events when using both drugs. The trigger tool method cannot detect undesirable events when using high-alert insulin and high-alert heparin drugs based on laboratory triggers

Keywords: geriatrics, high alert medication, Undesirable Events (UE), trigger tool

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INTRODUCTION

Cases of events related to insulin use in the form of hypoglycemia in general and bleeding due to heparin use are often found based on reports conducted by several studies (Geller et al., 2014; Ruiz et al., 2022). Around 13.7% of patients visited the emergency department (ED) due to bleeding in the gastrointestinal tract due to heparin use (Ruiz et al., 2022). Based on the National Electronic Injury Surveillance System-Cooperative Adverse Drug Event Surveillance, every year around 95% of patients visit the ED due to errors in insulin use (Geller et al., 2014). Errors related to insulin preparation and administration are frequently reported both outside and inside the hospital such as severe hypoglycemia, seizures, coma, and even death, but these errors are preventable (Staff, 2014).

Medication errors are real evidence that we often find in the environment where drugs are prescribed, used, and given to patients (Chakraborty et al, 2022). High-alert medications have the potential to increase the risk of patient harm ranging from 0.24 to 89.6 errors per 100 prescriptions (Aradhya et al., 2023). The Institute for Safe Medication Practice (ISMP) defines high-alert medicine (HAM) as a group of drugs that have the potential to cause significant harm to patients or even death if used inappropriately (He et al., 2022). Although errors in the use of HAM may not be more common than with other drugs, the consequences of errors with these drugs can be very serious (Chakraborty et al, 2022). Based on the 2024 ISMP, there are several types of high-alert drugs including insulin such as novorapid flexpen, lantus solostar, and anticoagulant groups such as warfarin, low molecular weight heparin (LMWH), unfractionated heparin (Institute for Safe Medication Practices., 2024).

Medications are the most frequent cause of side effects and undesirable events (Bailey et al., 2016). In 2006, 82% of the population in the United States (US) reported taking at least one prescription drug (hard drug), over-the-counter drug, or dietary supplement and 29% reported using five or more prescription drugs. Among adult patients aged 65 years or older, 57-59% reported taking five to nine medications and 17-19% reported taking 10 or more (Koh, 2014). Polypharmacy is the use of five or more different prescription drugs simultaneously for the treatment of one or more comorbidities (Ahmed et al., 2014). Polypharmacy is associated with an increase in undesirable events (Thorell et al., 2020).

Geriatric patients are elderly patients who are often associated with multiple diseases and or disorders due to decreased organ function, and psychological, social, economic, and environmental conditions that require integrated health services. The elderly are residents aged 60 years or more (Permenkes, 2014). Results from several studies show that polypharmacy is more common in geriatric patients than in other adults. This is because geriatric patients experience decreased organ function and various types of diseases which cause increased drug use, inappropriate drug use, and the risk of adverse drug reactions increases threefold (Lau et al., 2019; Soejono & Rizka., 2021; Khairunnisa & Ananda., 2023). It is estimated that one in ten geriatric patients experiences an adverse drug reaction that can lead to hospital admission or experiences undesirable events during hospitalization (Alhawassi. 2014).

The trigger tool is a method that can be used to identify and monitor undesirable events and provide information about these undesirable events to determine improvements (Parrinello et al., 2019). Using the trigger tool method and determining the positive predictive value (PPV) is one way to identify undesirable events in high-alert drugs at RSUPN Dr. Cipto Mangunkusumo Jakarta, especially in the geriatric inpatient room because research using the trigger tool method has never been carried out at this hospital. This study aims to detect undesirable events due to the use of high-alert insulin and high-alert heparin drugs in geriatric patients at RSUPN Dr. Cipto Mangunkusumo Jakarta using the trigger tool method based on positive predictive value (PPV) and determine the effect of using high-alert insulin and high alert heparin drugs on undesirable events.

MATERIALS AND METHOD

Materials

The material used in this research is data contained in the electronic medical records (EMR) of geriatric patients who are hospitalized in geriatric patients at RSUPN Dr. Cipto Mangunkusumo Jakarta for the period 1 January to 31 December 2023. The reason for selecting inpatients is because the risk of an increase in undesirable events is greater when compared to outpatients, where this can be seen as the patient's treatment progresses.

Methods

The method used in this research is a retrospective cohort study by reviewing secondary data from the patient's medical records (MR). The sample used was from 300 geriatric patients, obtained from 82 patients using insulin and 79 patients using heparin who met the inclusion criteria, including patients undergoing inpatient treatment for the period 1 January to 31 December 2023, patients in building A who had received treatment for more than 7 days, patients who receive high-alert insulin and high-alert heparin drug therapy based on ISMP and the use of high-alert drugs used at RSUPN Dr. Cipto Mangunkusumo and the patient had repeated admissions, so the first admission was taken.

Ethical Clearance This study has received ethical approval from Ahmad Dahlan University with number 012309216 and RSUPN Dr Cipto Mangunkusumo Jakarta with number KET-1770/UN2.F1/ETIK/PPM.00.02/2023.

Data Analysis

Data were analyzed in the form of frequencies and percentages (%), calculation of PPV values , and the effect of using high-alert insulin and high-alert heparin drugs on undesirable events using the Chi-Square test. Fisher's exact test is used when the chi-square test does not meet the requirements for testing

RESULT AND DISCUSSION

This research began in January to March 2024 at RSUPN Dr. Cipto Mangunkusumo Jakarta. The data used in the study is data from geriatric patients who used high-alert drugs from January to December 2023 with a total of 300 patients. However, the research samples are patients who use high-alert insulin and high-alert heparin drugs. The reason for taking the sample was because the use of these two groups of medicines dominated more than other high-alert groups. The number of patients used in this study was 161 geriatric patients in two types of high-alert drug classes, namely high-alert insulin and high-alert heparin who met the inclusion criteria.

Patient characteristics in this study included gender, age, diagnosis, length of stay (LOS), payment status, and type of high-alert medication used. Patients who received the high-alert insulin (n=82) and patients who received the high-alert heparin (n=79). Characteristics of geriatric patients who use high-alert insulin and high-alert heparin drugs at RSUPN Dr. Cipto Mangunkusumo Jakarta for the period January to December 2023 in Table 1. 161 geriatric patients used high-alert drugs using insulin and heparin, with details of 32 male patients (39%) and 50 female patients (61%) using insulin while 44 male patients (56%) used heparin and 35 female patients (44%). In Table 1, it can be seen that especially with high-alert insulin drugs, more women experience diabetes than men. A study shows that diabetes mellitus has some gender characteristics and some data shows that women suffer from the disease longer on average than men and have a higher body mass index (BMI). This seems to be related to the fact that sex hormones have a major influence on energy metabolism, body composition, vascular function, and inflammatory responses (Ciarambino et al., 2022).

In geriatric patients who use high-alert heparin, there are 44 men with a percentage of 56% while there are 35 women with a percentage of 44%. There is no specific research that states with certainty

regarding the use of high-alert heparin in geriatrics which dominates its use based on gender and the reasons for the increase in the use of this drug. However, some literature states that the use of anticoagulant drugs namely heparin can cause bleeding in the gastrointestinal tract in geriatric patients (Ruiz et al., 2022). The use of heparin is mostly used by men (58.1%) compared to other adults with the patient age range being 26 years (60%) to 66 years (40%) (Budyastiti, 2021).

Table 1. Characteristics of geriatric patients at Dr. National Central General Hospital. Cipto Mangunkusumo Jakarta

Patient Characteristics	Insulin (n=82)		Heparin (n=79)	
	Total	Percentage (%)	Total	Percentage (%)
Gender				
Male	32	39	44	56
Female	50	61	35	44
Age (Years)				
60–69	48	59	39	49
70-79	25	30	32	41
>80	9	11	8	10
Diagnosis				
Hypertension	38	46	35	44
Pneumonia	35	43	32	41
Sepsis	6	7	11	14
CHF *(congestive heart failure)*	3	4	1	1
Length of stay **(LOS)**				
8-12 days	44	54	30	38
> 12 days	38	46	49	62
Payment status				
JKN (Jaminan Kesehatan Nasional)	82	100	79	100

Another characteristic of data is age. The age most frequently confirmed as using high-alert drugs in this study was 60–69 years old with as many as 48 people, both patients who used high-alert insulin with a percentage of 59% and used high-alert heparin as many as 39 patients with a percentage of 49%. As many as 63.59% of the elderly are classified as young elderly (60-69 years), 27.76% are middle elderly (70-79 years), and 8.65% are old elderly (80 years and over) (Badan Pusat Statistik, 2023). This is in line with the patient data obtained in this study. The prevalence of diabetes is twice as high in elderly people as in middle-aged or young adults (Corriere, 2014). Another study shows that the prevalence of diabetes is highest among the adult age group namely the age group 60 years or more which is caused by health problems, lifestyle behavior, and lack of physical activity (Das & Kar, 2023). Meanwhile, in the age group of 60 years or more, geriatric patients regarding the increase in use of the high-alert drug heparin based on age there is no specific research that states with certainty regarding this matter. Research conducted by Torn involved patients aged <60 years, 60-70 years, 71-80 years and >80 years. The conclusion of this study states that the incidence of bleeding and thromboembolic events increases sharply with increasing age. Due to the higher risk of thromboembolism with increasing age, oral anticoagulants are often considered (Torn, 2015).

Characteristics based on diagnosis, hypertension has a higher prevalence than others both patients using high-alert insulin (46%) and patients using high-alert heparin (44%). A study states that the incidence of hypertension will increase with age. There are one in three geriatric patients who are not aware that they have hypertension (Fotouhi et al., 2022). Other research also states that insulin

resistance and diabetes are not only metabolic disorders but also predispose to hypertension and blood vessel stiffness (Jia & Sowers, 2021). A large body of evidence obtained in clinical and experimental studies suggests that insulin resistance is casually involved in some forms of hypertension. This is associated with the impact of insulin on sodium and water transport in the kidney. Strong evidence shows that insulin can cause sodium and water retention which can cause an increase in blood pressure (Brosolo et al., 2022). The use of heparin in patients suffering from hypertension can cause a decrease in blood pressure because besides its anticoagulation properties, heparin also has a vasodilation effect, it can reduce blood viscosity which affects lowering blood pressure (Kotoda et al., 2019).

Table 2. Characteristics of high-alert drugs use and laboratory results of trigger insulin and heparin in geriatric patients at RSUPN Dr. Cipto Mangunkusumo Jakarta

Tigger Drugs	Total (Patients)	Trigger Positive (Patients)	Trigger Negative (Patients)
Insulin	**82**	**8**	**74**
Novorapid flexpen 3 mL solution, injection 100 iu/ 1mL		5	47
Lantus solostar 3 mL solution, injection 100 iu/1 mL		3	22
Novomix 30 flexpen 3 ml suspension, injection 30 %ww; 70 %ww		0	1
Humalog kwikpen 3 mL suspension, injection 100 iu/1 mL		0	1
Levemir flexpen 3 mL solution, injection 300 iu/3 mL		0	1
Apidra solostar solution, injection 300 iu/3 mL		0	1
Humalog mix 25 kwikpen 3 mL suspension, injection 25 %wv; 75 %ww		0	1
TL (Trigger Laboratory)			
Hypoglycemia (< 70 mg/dL)	**8**		
Anticoagulant	**79**	**4**	**75**
Heparin sodium 5 mL solution, injection 5000 unt/1mL		4	75
TL (Trigger Laboratory)			
There was a prolonged aPTT (> 117,5 seconds)	**4**		

Patient characteristics are based on the length of stay (LOS) or the length of the patient's hospitalization. LOS is an indicator that can be used to evaluate hospital performance (Khosravizadeh et al., 2016). The ideal LOS is 3 to 12 days, if the LOS is more than 12 days then the possible causes include chronic patients being treated in hospitals intended for acute patients and there is no progress in treatment results (Ramadhan et al., 2022). Based on Table I, the length of stay (LOS) characteristics of patients using high-alert insulin (54%) with an LOS of 8 to 12 days is much more dominant than those with an LOS of more than 12 days (38%). However, in patients using the high-alert drug heparin, the LOS of 3 to 12 days (38%) was much lower than those with LOS of more than 12 days (62%).

Characteristics are based on payment rates with a percentage of 100% using Jaminan Kesehatan Nasional (JKN), both for patients using high-alert insulin and patients using high-alert heparin. The Jaminan Kesehatan Nasional (JKN) developed in Indonesia is part of the Sistem Jaminan Sosial Nasional (SJSN) which is implemented through a social insurance mechanism that aims to ensure that the entire Indonesian population is protected by the insurance system so that they can fulfill their basic health needs. This protection is given to everyone who has paid contributions or whose contributions are paid by the government (Permenkes RI., 2014).

The analyst's description of the calculation of positive predictive value (PPV) for geriatric patients using high-alert insulin or high-alert heparin can be seen in Table 2. The use of the high-alert drug

insulin with 8 positive trigger patients out of 82 patients and the use of the high-alert anticoagulant drug namely heparin with 4 positive trigger patients out of 79 patients. Some parameters that can indicate the occurrence of hypoglycemia and bleeding based on research are the category of patients who experience hypoglycemia characterized by the results of checking blood glucose < 70 mg/dL and also accompanied by other symptoms such as weakness, decreased consciousness, and respiratory distress. The category of patients who experience bleeding is characterized by the results of checking aPTT >117.5 seconds also accompanied by other symptoms such as microscopic hematuria, excessive bleeding in wounds, and black feces.

Based on Table 2, the positive predictive value (PPV) for both insulin and heparin high-alert drugs can be obtained as listed in Tables 3 and 4.

Table 3. Calculation of the Positive Predictive Value (PPV) of high-alert insulin

	Laboratory Trigger Hypoglycemia (+)	Laboratory Trigger Hypoglycemia (-)	Total	The calculation results PPV value
	(A)	(B)		
Insulin (+)	8	74	82	9,75%

Table 4. Calculation of the Positive Predictive Value (PPV) of the high-alert heparin

	Laboratory Trigger aPTT > 117,5 seconds (+)	Laboratory Trigger aPTT > 117,5 seconds (-)	Total	The calculation results PPV Value
	(A)	(B)		
Heparin (+)	4	75	79	5,33%

In Tables 3 and 4, it can be seen that there are differences in PPV values for each group both geriatric patients who use high-alert insulin drugs and geriatric patients who use heparin. Geriatric patients who used the high-alert drug insulin obtained a PPV value of 9.75%, as did geriatric patients who used the high-alert drug heparin obtained a PPV value of 5.33%. As is known the positive predictive value is the probability that a disease will exist if the test result is positive (Molinaro., 2015). whereas according to Trevethan, the positive predictive value is the probability that a person with a positive screening test result has that condition (Trevethan., 2017). As explained above, the PPV value for geriatric patients who use high-alert insulin medication with a PPV of 9.75% means that of the 82 geriatric patients who use high-alert insulin medication only 9.75% of people whose test results are positive experience an undesirable event desired in the form of hypoglycemia due to the use of high-alert insulin drugs. In Table 2, it is known that the high-alert insulin drugs that caused undesirable events were Novorapid Flexpen 3 mL solution, injection 100 iu/1 mL with a total of 5 patients and Lantus Solostar 3 ml solution, injection 100 iu/1 mL with a total of 3 patients. According to Rostami et al's research, there was no significant difference between patients who used Novorapid Flexpen and patients who used Lantus Solostar these two types of insulin are often combined to lower blood sugar levels (Rostami et al., 2014). Several factors influence the occurrence of hypoglycemia one of which is gender. According to research by Putri, women are more at risk of developing hypoglycemia compared to men. Women experience menopause which will cause a decrease in the amount of estrogen and progesterone so that insulin levels in the body will increase. Increased insulin levels will also increase glucose uptake to be converted into glycogen, thereby increasing the risk of hypoglycemia (Putri et al., 2023). This is in line with the data presented where of the total of 8 patients who experienced hypoglycemia 5 of them were female and 3 of them were male. The incidence of hypoglycemia in geriatric patients in this study was very small because daily therapy monitoring was carried out well by health workers including doctors in charge of patients, nurses, and pharmacists.

One of the pharmacist's roles is to make recommendations and monitor the use of drugs given by doctors to patients. This can be seen from the patient progress notes integrated into the medical record where monitoring parameters during drug use are measured. For insulin use, daily blood sugar levels are measured before insulin use.

Geriatric patients who used the high-alert heparin drug obtained a PPV value of 5.33% meaning that of the 79 geriatric patients who used the high-alert heparin drug only 5.33% of people whose test results were positive experienced an undesirable event in the form of an extension of the aPTT value due to use the drug. As with the case of using the high-alert insulin drug above, the incidence of bleeding in geriatric patients in this study was very small compared to the total used because daily therapy monitoring was carried out well by health workers including doctors in charge of patients, nurses, and pharmacists. This can be seen from the patient progress notes integrated into the medical record where monitoring parameters during drug use are measured aPTT. One of the complications of using heparin in geriatric patients is arterial bleeding (Niemann et al., 2022). According to Warnock, common side effects when administering heparin include bleeding, pain at the injection site, and thrombocytopenia. Bleeding is the main complication often associated with heparin use (Warnock & Huang, 2023). Several parameters determine the risk of bleeding, including dose, anemia, age factors, and duration of heparin use (Shoeb, 2014). What was stated by Fanikos et al was that heparin is a group of anticoagulants that causes the most undesirable events in the form of bleeding when compared with other groups of anticoagulants (Fanikos et al., 2023).

Based on the PPV calculation above, both insulin PPV values (9.72%) and heparin PPV (5.33%) mean that the trigger tool has not been able to detect undesirable events when using these two high alert drugs both insulin high alert drugs and heparin high alert drugs. If the PPV value is higher (as close as possible to 100) then this indicates that the use of a trigger tool can be applied to identifying undesirable events caused by high-alert drugs.

Table 5. Effect of using high-alert insulin and high alert heparin on undesirable events

Drugs Use		Trigger Events (n=300 patients)		
		Positive Trigger	**Negative Trigger**	**Sig Value (P-value)**
Insulin	Insulin (82 patients)	8 patients	74 patients	0,033 < 0,05 (There is influence)
	Without Insulin (218 patients)	7 patients	211 patients	
Heparin	Heparin (79 pasien)	4 patients	75 patients	0,043 < 0,05 (There is influence)
	Without Heparin (221 patients)	2 patients	219 patients	

Based on Table 5 namely the effect of using high-alert insulin and high-alert heparin drugs on undesirable events both geriatric patients who use high-alert insulin drugs with a total of 82 patients and 8 positive trigger patients and those who use anticoagulants namely heparin with a total of 79 patients and 4 trigger positive patients who were tested statistically showed that there was an influence of undesirable events between the use of high alert drugs both insulin with a p-value of 0.033 ($p<0.05$) and the anticoagulant group namely heparin with a p-value of 0.043 ($p< 0.05$) with undesirable events due to the use of these two types of drugs. This is to the literature which states that the use of insulin aspart and insulin glargine in geriatrics risks causing hypoglycemia with a very small incidence of hypoglycemia (Jin & Zhang, 2022; Rostami et al., 2014) and giving heparin to geriatric patients can increase risk of bleeding because elderly patients have much higher anti-Xa levels than elderly non-elderly adult patients (Lemke , 2020; Ruiz et al., 2022).

Some limitations in the study include the subjects in the geriatric patients used in this study being considered the same and not classifying the severity of the disease they experience. In addition, this study uses a retrospective method so that all data presented is data that cannot be checked back to the patient regarding what is found in the patient's medical record.

CONCLUSION

This study concludes that the trigger tool method has not been able to detect undesirable events when using high-alert insulin and high-alert heparin drugs based on laboratory triggers. However, statistically there is an effect of undesirable events on inpatient geriatric patients who use the two high-alert drugs with a p-value of insulin ($p<0.05$) and heparin ($p<0.05$).

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