Tittle of Manuscript: **Evaluation of Rationality in Prescribing Metformin (Biguanide Group) at Dr. Mohammad Hoesin General Hospital Palembang**

1.Proofread document received (February 1st, 2022)
-Document from proofreading service
2.Submitted to the journal "Bioscientia Medicina: Journal of Biomedicine and Translational Research (February 7th, 2022)
3.Peer Reviewer results: Revision Required (February 13th, 2022)
4.Revised version received by journal (February 21th, 2022)
5.Paper Accepted for publication (February 26th, 2022)
6.Galley proof (February 28th, 2022)
7.Paper published (March 1st, 2022)

-Document from proofreading service

February 1st, 2022

HM Publisher
Jl Sirnaraga No 99, 8 Ilir, Ilir Timur 3, Palembang, South Sumatra, Indonesia

CONFIDENTIAL
February 1st, 2022

Certificate Service Confirmation

To whom it may concern,
HM Publisher provided comprehensive editing services for manuscript entitled Evaluation of Rationality in Prescribing Metformin (Biguanide Group) at Dr. Mohammad Hoesin General Hospital Palembang. The edit has achieved Grade A: priority publishing; no language polishing required after editing. Should you require any additional information, please do not hesitate to contact me.

Regards,

Khrishna Murti, PhD
Head of Language Institute-HM Publisher
Email: khrishnamurti@gmail.com

Submitted to the journal "Bioscientia Medicina: Journal of Biomedicine and Translational Research (February 7th, 2022)

Evaluation of Rationality in Prescribing Metformin (Biguanide Group) at Dr. Mohammad Hoesin General Hospital Palembang

Nita Parisa[1*], Dwi Tantri Marylin[2], Theodorus[1]

[1]Department of Pharmacology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

[2]Medical Education Study Program, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

*Email: nitaparisa@unsri.ac.id

Abstract

Background. Evaluation and assessment of the rationality of the use of antidiabetic drugs, especially the biguanid group (metformin) is very important to be carried out in order to maintain the quality and quality of diabetes mellitus drug administration so that Diabetes mellitus control targets can be optimized. This study aims to evaluate the rationality of oral antidiabetic meformin prescribing at Dr Mohammad Hoesin General Hospital Palembang

Methods. The research design was a descriptive study using secondary data of medical records in the medical record section of RSUP Dr. Moh Hoesin Palembang. The object of the study was all medical records of patients with type 2 diabetes mellitus who used metformin drugs at RSMH Palembang in the period July 1 , 2019-July 31, 2020, with complete medical record data and without severe comorbidities. The rationality of the use of metformin drugs assessed in this study is the frequency of use, drug dosage, mode of administration , duration of administration and drug interactions. The frequency of use of the drug is assessed how many times the drug is consumed in one day.

Results. Thehighest age of patients who received metformin prescriptions were aged 51-60 years and 61-70 years with a total of 17 patients (35.4%). The majority of patients were female as much as 60.4%. Drug interactions from metformin are still quite common, although the majority are synergistic and potentiating interactions. There were still 2 cases or 4.2 percent who experienced antagonistic interactions.

Conclusion. The rationality of using metformin drugs in type 2 diabetes mellitus patients is based on the right dose criteria (100%), the right frequency of drug administration (100%), the right length of drug administration (100%), the right way of drug administration (100%), and the right drug interaction (95.8%).

Keywords. Metformin, Biguanide, Oral Antidiabetic, Pharmacology, Descriptive Study.

Introduction

Indonesia is ranked fourth largest of all those who experience diabetes mellitus, which is 8.6% of the total population while the ranks above are India, China, and the United States (WHO, 2018). WHO predicts an increase in the number of people experiencing Diabetes Mellitus in Indonesia, amounting to 8.4 million people in 2000, increasing to reach 21.3 million in 2030. *The International Diabetes Foundation* (IDF) estimates that there will be an increase in the number of people suffering from Diabetes Mellitus in 2009 from 7 million will increase in 2030 to reach 12 million people. From this information, it shows a 2-3 fold increase in the population experiencing Diabetes Mellitus in 2030. [1] Diabetes Mellitus management generally consists of four indicators, namely education, nutritional therapy, exercise, and pharmacological interventions. Pharmacological therapy is given to patients who do not respond or respond at least during a carbohydrate diet, exercise is recommended to change a healthy lifestyle for three months to keep blood glucose levels above 200 mg / dL and HbA1c above 6.5%. [2-4]

Pharmacological interventions include oral and injectable antidiabetic drugs. Oral drugs include the group of biguanids, sulfunilureas. Oral antidiabetic drugs are the more commonly used drugs. The first drug selection in these patients was metformin. In order to achieve effective therapy, the administration of rational oral antidiabetic drugs, namely the right dose, the right diagnosis of the patient, right in the selection and administration of drugs, and there are no contra indications, needs good attention. Evaluation and assessment of the rationality of the use of antidiabetic drugs, especially the biguanid group (metformin) is very important to be carried out in order to maintain the quality and quality of diabetes mellitus drug administration So that the target of controlling diabetes mellitus can be optimized.

Methods

The research design was a descriptive study using secondary data of medical records in the medical record section of RSUP Dr. Moh Hoesin Palembang. The object of the study was all medical records of patients with type 2 diabetes mellitus who used metformin drugs at RSMH Palembang in the period July 1, 2019-July 31, 2020, with medical record data that complete and without severe comorbidities. The rationality of the use of metformin drugs assessed in this study is the frequency of use, drug dosage, mode of administration , duration of administration and drug interactions. The frequency of use of the drug is assessed how many times the drug is consumed in one day. The dose of metformin used is 500 mg or 850 mg. The method of drug administration is the method of consumption of metformin drugs and the duration of drug administration is the length of drug administration written on the prescription. Drug interaction is a reaction that arises between two or more drugs in concurrent use, in the form of sinergis, namely the administration of one drug can strengthen the effect of the other drug, antagonis, ie the administration of one drug can reduce the effect of the other drug and p Authentication, namely the administration of one drug can strengthen the effect of another drug by increasing the concentration of the other drug by the body.

The data used is secondary data through medical records obtained from the Medical Record Installation Section of RSMH Palembang. In data collection, the researcher does not take data directly, but by parties who are not researchers. The data collected in this study will be processed using SPSS descriptive statistical method based on the number of cases recorded in the medical record of diabetes mellitus patients in accordance with the variables studied. The results of the research will be analyzed and presented in the form of tables and will be explained in the form of narratives. The type of statistical analysis that will be used in this study is univariate analysis which aims to describe the characteristics of each variable studied.

Results

Table 1, from48 patients saw the number of patients with type 2 DM with the drug Metformin, the youngest age suffering from type 2 DM was 42 years, while the oldest age was 77 years. Where these results obtained the highest average age group were 51-60 years old and 61-70 years with 17 patients (35.4%). The majority of patients were female as much as 60.4%. The majority of patients get as many as 3-4 drugs per prescription.

Table 1. Baseline Characteristics

Variable	Number of Cases (n)	Percentage (%)
Age		
40-50 years	12	25,0
51-60 years	17	35,4
61-70 years old	17	35,4
71-80 years	2	4,2
Gender		
Man	19	39,6
Woman	29	60,4
Number of Drugs Per Prescription		
1	8	16,7
2	9	18,8
3	13	27,1
4	10	20,8
5	8	16,7

Table 2 shows that drug interactions of metformin are still quite common, although the majority are synergistic and potentiating interactions. There are still 2 cases or 4.2 percent who experience antagonistic interactions.

Table 2. Distribution of respondents based on drug interactions

Drug Interactions	Number of Cases (n)	Percentage (%)
Synergistic Interaction	17	35,4
Potentiation	29	60,4
Interactions	2	4,2
Antagonistic Interactions		

Table 3. Synergistic distribution of drug interactions

Synergistic Interaction	Number of Cases (n)	Percentage (%)
Metformin + Glimepirid	9	18,8
Metformin + Glucobay	2	4,2
Metformin + Gliclazide	3	6,2
Metformin + Glibenclamid	3	6,2

Table 4. Distribution of potentiating drug interactions

Potentiation Interactions	Number of Cases (n)	Percentage (%)
Metformin + Aspilet	2	4,2
Metformin + Amlodipine	10	20,8
Metformin + Captopril	6	12,5
Metformin + Ranitidine	5	10,4
Metformin + Furosemide	4	8,3
Metformin + Valsartan	2	4,2

Table 5. Distribution of antagonistic drug interactions

Antagonistic Interactions	Number of Cases (n)	Percentage (%)
Metformin + Spironolactone	1	2,1
Metformin + Methylprednisolone	1	2,1

Table 6 shows patients with the right dose set at 47 patients with a percentage of 97.9%, the right frequency of drug administration is 48 patients with a percentage of 100%, the right time period of drug administration is 48 people (100%), the right way of drug administration is 48

people (100%), the right drug interaction is 17 patients with a percentage of 35.4%, and the right drug interaction is potentiating 29 patients with a percentage of 60.4%.

Table 6. Rationality of use of the drug Metformin

Variable	True			
	Yes	(%)	Not	(%)
Dose	47	97,9	1	2,1
Frequency of administration	48	100	0	0
Duration of Administration	48	100	0	0
How to Give	48	100	0	0
Synergistic Interaction	17	35,4	0	0
Potentiation Interactions	29	60,4	0	0
Antagonistic Interactions	0	0	2	4,2

Discussion

Glimepiride is a third-generation sulfonylurea drug with a longer processing time and faster onset. The use of a mixture of other antidiabetic drugs creates a synergistic relationship, where the activity of each drug reinforces each other to achieve the same goal, with the aim of lowering glucose more. Glimepiride stimulates beta cells tosecrete insulin, while ethformin reduces hepatic glucose production, decreases intestinal glucose absorption, and improves insulin sensitivity by increasing peripheral glucose absorption and utilization. Glimepiride canminimize cardiovascular complexity and convert insulin levels released into glucose levels, especially in postprandial conditions, with the aim that glimepiride hypoglycemia occurs smaller than glibenclamide. With the profile they have, the combination of Metformin and Glimepirid is more viable and safe. [5-7] metformin given along with glucobay can lower metformin AUC levels. The alpha-glucosidase inhibitor, Glucobay, decreases the bioavailability of Metformin and reduces the normal peak plasma centralization of Metformin, but the chances of achieving that top fixation do

not change. The patient should be informed about the need to regularly observe blood glucose levels and know about the indications of hypoglycemia. [8-10]

The mostwidely given drug and has po tensiation interactions is antihypertensive drugs. Metformin given together with calcium chanel blocker drugs such as amlodipine can reduce the effects of metformin and has a pharmacodynamic interaction system with moderate levels. [11,12] Metformin given along with Ranitidine may increase plasma concentrations by slowing the excretion of metformin in the renal tubules. [13-15] metformin given along with captopril may increase the risk of hypoglycemia. Moreover, simultaneous use of captopril will cause blood glucose levels to increase by 2.2 mmol / L after 24 hours and increase to 2.9 mmol / L after 48 hours. For this situation, the use of the drug Captopril can be replaced with Valsartan class ARB (angiotensin receptor blocker), since Valsartan can lower circulatory pressure through the main enemy of the skeleton renin-angiotensin aldosterone. Likewise, Valsartan can also reduce the release of albumin in serum, if excess albumin lost from the blood shows high blood glucose levels for a long time, so that it can be overcome with Valsartan in expanding albumin secretion. [16-18] Metformin given along with furosemide will increase metformin levels in the blood causing hypoglycemia, while metformin can reduce furosemide levels. Furosemide and metformin are secreted in the tubular part of the kidney in order to interact with each other in the tubular system which causes metformin levels to increase. Furosemide can increase plasma metformin concentrations by 22% and metformin can reduce peak concentrations and elimination half-lives of furosemide by 31% and 32%, respectively. [19]

Spironolactone is a diuretic drug. Metformin given along with Spironolactone will induce kidney impairment and dehydration which may increase the risk of lactic acidosis in patients concomitantly taking Metformin. Methylprednisolone is a class of corticosteroids, Metformin given together with Methylprednisolone can inhibit glucose levels resulting in hyperglycemia, glucose intolerance, changes in glucose levels with new onset and exacerbation of diabetes mellitus. [20]

Conclusion

The rationality of using Metformin in Type 2 Diabetes Mellitus patients is based on the right dose criteria (100%), the right frequency of drug administration (100%), the right duration of

drug administration (100%), the right way of drug administration (100%), and the right drug interaction (95.8%).

References

1.Ministry of Health of the Republic of Indonesia. In 2030, the prevalence of diabetes mellitus in Indonesia will reach 21.3 million people. 2009. (http://www.depkes.go.id/index.php/berita/pressrelease/414-tahun-2030-prevalensidiabetes-melitusdi-indonesia-mencapai-213-juta-orang.html. Retrieved 12 December 2014).

2. PERKENI. Consensus on Management and Prevention of Type 2 Diabetes Mellitus in Indonesia. Jakarta: PERKENI.2011

3. Vickova V, Cornelius V, Kasliwal R, Wilton L, Shakir SA. Hypoglycaemia with oral antidiabetic drugs: results from prescription-event monitoring cohorts of rosiglitazone, pioglitazone, nateglinide and repaglinide. Drug Saf. 2009;32:409–18

4. Istiqomatunnisa. Rationality of the Use of Anti-Diabetes Drugs and Evaluation of the Cost Burden of Pharmaceutical Supplies on Healthy Jakarta Card Inpatients at Dr. Mintohardjo Navy Hospital. Thesis. Unpublished, Faculty of Medicine and Health Sciences, State Islamic University, Jakarta. 2014.

5. Khasanah M. Lifestyle in Diabetes Mellitus Sufferers. Thesis. Unpublished, Faculty of Da'wah Sunan Ampel State Islamic Institute, Surabaya. 2012.

6. Widya D. Relationship between Nutritional Status and Physical Activity on Diabetes Mellitus in the Elderly in West Kalimantan Province. Thesis. Unpublished, Faculty of Health Sciences, Esa Unggul University, Jakarta. 2015.

7. Naranjo, CA, Busto U., Sellers, E.M., Sandor, P., Ruiz, I., Robert, E.A., et al., A Method For Estimating the Probability od Adverse Drug Reactions, Clinical Pharmacology and therapeutics. 1981; 30:2:239 -45.

8. BPOM RI. Guidelines for Monitoring Drug Side Effects (MESO) for Health Workers. Jakarta: Badan POM RI. 2012.

9. Alomar MJ. Factors Affecting The Development of Adverse Drug Reactions. Saudi Pharmaceutical Journal. Feb 2013:22:83 -94.

10. Arifin AL. Current Type 2 Diabetes Mellitus Therapy Guide. Sub Section Endocrinology &; Metabolism Section / UPF. Internal Medicine. Faculty of Medicine. UNPAD / RSUP dr. Hasan Sadikin Bandung. 2011.

11. Malin SK, Kashyap SR. Effects of metformin on weight loss: potential mechanisms. Curr Opin Endocrinol Diabetes Obese. 2014 Oct;21(5):323 -9.

12. Drugs.com. Metformin Side Effects. 2015. (http://www.drugs.com/sfx/metformin -side -effects.html. Retrieved 3 July 2015).

13. Bouchoucha M, Uzzan B, Cohen R. Metformin and digestive disorders. Diabetes Metab 2011;37:90 -6. 14. Stoppler, M.C., Glucophage Side Effects Center. http://www.rxlist.com/glucophage -side -effects -drug - center.htm. Retrieved 1 August 2015.

15. Al Abri SA, S. Hayashi, K.L. Thoren, K.R. Olson. Metformin Ovedose -induced in the absence of other diabetic drugs. June 2013:51(5)(444 -447).

16. U.S. National Library of Medicine. Metformin. 2015. (https://www.nlm.nih.gov/medlineplus/druginfo/meds/a696005.html. Retrieved 20 August 2015).

17. Cunha, J.P., 2015. Glumetza Side Effects Center. (Online). (http://www.rxlist.com/glumetza -side - effects -drug -center.htm, accessed June 30, 2015).

18. Ting RZ, Szeto CC, Chan MH, Ma KK, Chow KM. Risk factors of vitamin B(12) deficiency in patients receiving metformin. Arch Intern Med. 2006; 166(18):1975 -9.

19. Drugs.com. Glimepiride Side Effects. 2015. (http://www.drugs.com/sfx/glimepirideside -effects.html. Retrieved 28 June 2015).

20. Ogbru, O., Williams, E., Marks, J.W. Insulin: Drug Facts, Side Effects and Dosing. 2015. (http://www.medicinenet.com/insulin/article.htm. Retrieved 23 July 2015).

Submitted to the journal “Bioscientia Medicina: Journal of Biomedicine and Translational Research (February 7th, 2022)

Bioscientia Medicina

Journal of Biomedicine and Translational Research

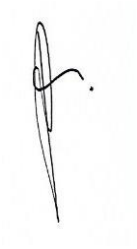
HM Publisher

Submission acknowledgement

Dear author(s),

Nita Parisa*, Dwi Tantri Marylin, Theodorus has submitted the manuscript “Evaluation of Rationality in Prescribing Metformin (Biguanide Group) at Dr. Mohammad Hoesin General Hospital Palembang“ to Bioscientia Medicina: Journal of Biomedicine and Translational Research. The paper will be screened by editor and reviewed by peer review.

Cordially,



Prof. Paula Magnano, PhD

Editor HM Publisher

(*) Corresponding author

Bioscientia Medicina

Journal of Biomedicine and Translational Research

HM Publisher

Peer Review Results

Dear author(s),

Nita Parisa*, Dwi Tantri Marylin, Theodorus has submitted the manuscript “Evaluation of Rationality in Prescribing Metformin (Biguanide Group) at Dr. Mohammad Hoesin General Hospital Palembang“ to Bioscientia Medicina: Journal of Biomedicine & Translational Research.

The decision : Revision Required.

Cordially,

Prof. Paula Magnano, PhD

Editor HM Publisher

(*) Corresponding author

Reviewer 1: Revision required

Evaluation of Rationality in Prescribing Metformin (Biguanide Group) at Dr. Mohammad Hoesin General Hospital Palembang→1

Nita Parisa[1*], Dwi Tantri Marylin[2], Theodorus[1]

[1]Department of Pharmacology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

[2]Medical Education Study Program, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

*Email: nitaparisa@unsri.ac.id

Abstract→3

Background. Evaluation and assessment of the rationality of the use of antidiabetic drugs, especially the biguanid group (metformin) is very important to be carried out in order to maintain the quality and quality of diabetes mellitus drug administration so that Diabetes mellitus control targets can be optimized. This study aims to evaluate the rationality of oral antidiabetic meformin prescribing at Dr Mohammad Hoesin General Hospital Palembang

Methods. The research design was a descriptive study using secondary data of medical records in the medical record section of RSUP Dr. Moh Hoesin Palembang. The object of the study was all medical records of patients with type 2 diabetes mellitus who used metformin drugs at RSMH Palembang in the period July 1 , 2019-July 31, 2020, with complete medical record data and without severe comorbidities. The rationality of the use of metformin drugs assessed in this study is the frequency of use, drug dosage, mode of administration , duration of administration and drug interactions. The frequency of use of the drug is assessed how many times the drug is consumed in one day.

Results. Thehighest age of patients who received metformin prescriptions were aged 51-60 years and 61-70 years with a total of 17 patients (35.4%). The majority of patients were female as much as 60.4%. Drug interactions from metformin are still quite common, although the majority are synergistic and potentiating interactions. There were still 2 cases or 4.2 percent who experienced antagonistic interactions.

Conclusion. The rationality of using metformin drugs in type 2 diabetes mellitus patients is based on the right dose criteria (100%), the right frequency of drug administration (100%), the right length of drug administration (100%), the right way of drug administration (100%), and the right drug interaction (95.8%).

Keywords. Metformin, Biguanide, Oral Antidiabetic, Pharmacology, Descriptive Study. →2

Introduction→4

Indonesia is ranked fourth largest of all those who experience diabetes mellitus, which is 8.6% of the total population while the ranks above are India, China, and the United States (WHO, 2018). WHO predicts an increase in the number of people experiencing Diabetes Mellitus in Indonesia, amounting to 8.4 million people in 2000, increasing to reach 21.3 million in 2030. *The International Diabetes Foundation* (IDF) estimates that there will be an increase in the number of people suffering from Diabetes Mellitus in 2009 from 7 million will increase in 2030 to reach 12 million people. From this information, it shows a 2-3 fold increase in the population experiencing Diabetes Mellitus in 2030. [1] Diabetes Mellitus management generally consists of four indicators, namely education, nutritional therapy, exercise, and pharmacological interventions. Pharmacological therapy is given to patients who do not respond or respond at least during a carbohydrate diet, exercise is recommended to change a healthy lifestyle for three months to keep blood glucose levels above 200 mg / dL and HbA1c above 6.5%. [2-4]

Pharmacological interventions include oral and injectable antidiabetic drugs. Oral drugs include the group of biguanids, sulfunilureas. Oral antidiabetic drugs are the more commonly used drugs. The first drug selection in these patients was metformin. In order to achieve effective therapy, the administration of rational oral antidiabetic drugs, namely the right dose, the right diagnosis of the patient, right in the selection and administration of drugs, and there are no contra indications, needs good attention. Evaluation and assessment of the rationality of the use of antidiabetic drugs, especially the biguanid group (metformin) is very important to be carried out in order to maintain the quality and quality of diabetes mellitus drug administration So that the target of controlling diabetes mellitus can be optimized.

Methods→5

The research design was a descriptive study using secondary data of medical records in the medical record section of RSUP Dr. Moh Hoesin Palembang. The object of the study was all medical records of patients with type 2 diabetes mellitus who used metformin drugs at RSMH Palembang in the period July 1, 2019-July 31, 2020, with medical record data that complete and without severe comorbidities. The rationality of the use of metformin drugs assessed in this study is the frequency of use, drug dosage, mode of administration , duration of administration and drug interactions. The frequency of use of the drug is assessed how many times the drug is consumed in one day. The dose of metformin used is 500 mg or 850 mg. The method of drug administration is the method of consumption of metformin drugs and the duration of drug administration is the length of drug administration written on the prescription. Drug interaction is a reaction that arises between two or more drugs in concurrent use, in the form of sinergis, namely the administration of one drug can strengthen the effect of the other drug, antagonis, ie the administration of one drug can reduce the effect of the other drug and p Authentication, namely the administration of one drug can strengthen the effect of another drug by increasing the concentration of the other drug by the body.

The data used is secondary data through medical records obtained from the Medical Record Installation Section of RSMH Palembang. In data collection, the researcher does not take data directly, but by parties who are not researchers. The data collected in this study will be processed using SPSS descriptive statistical method based on the number of cases recorded in the medical record of diabetes mellitus patients in accordance with the variables studied. The results of the research will be analyzed and presented in the form of tables and will be explained in the form of narratives. The type of statistical analysis that will be used in this study is univariate analysis which aims to describe the characteristics of each variable studied.

Results→6

Table 1, from48 patients saw the number of patients with type 2 DM with the drug Metformin, the youngest age suffering from type 2 DM was 42 years, while the oldest age was 77 years. Where these results obtained the highest average age group were 51-60 years old and 61-70 years with 17 patients (35.4%). The majority of patients were female as much as 60.4%. The majority of patients get as many as 3-4 drugs per prescription.

Table 1. Baseline Characteristics

Variable	Number of Cases (n)	Percentage (%)
Age		
40-50 years	12	25,0
51-60 years	17	35,4
61-70 years old	17	35,4
71-80 years	2	4,2
Gender		
Man	19	39,6
Woman	29	60,4
Number of Drugs Per Prescription		
1	8	16,7
2	9	18,8
3	13	27,1
4	10	20,8
5	8	16,7

Table 2 shows that drug interactions of metformin are still quite common, although the majority are synergistic and potentiating interactions. There are still 2 cases or 4.2 percent who experience antagonistic interactions.

Table 2. Distribution of respondents based on drug interactions

Drug Interactions	Number of Cases (n)	Percentage (%)
Synergistic Interaction	17	35,4
Potentiation	29	60,4
Interactions	2	4,2
Antagonistic Interactions		

Table 3. Synergistic distribution of drug interactions

Synergistic Interaction	Number of Cases (n)	Percentage (%)
Metformin + Glimepirid	9	18,8
Metformin + Glucobay	2	4,2
Metformin + Gliclazide	3	6,2
Metformin + Glibenclamid	3	6,2

Table 4. Distribution of potentiating drug interactions

Potentiation Interactions	Number of Cases (n)	Percentage (%)
Metformin + Aspilet	2	4,2
Metformin + Amlodipine	10	20,8
Metformin + Captopril	6	12,5
Metformin + Ranitidine	5	10,4
Metformin + Furosemide	4	8,3
Metformin + Valsartan	2	4,2

Table 5. Distribution of antagonistic drug interactions

Antagonistic Interactions	Number of Cases (n)	Percentage (%)
Metformin + Spironolactone	1	2,1
Metformin + Methylprednisolone	1	2,1

Table 6 shows patients with the right dose set at 47 patients with a percentage of 97.9%, the right frequency of drug administration is 48 patients with a percentage of 100%, the right time period of drug administration is 48 people (100%), the right way of drug administration is 48

people (100%), the right drug interaction is 17 patients with a percentage of 35.4%, and the right drug interaction is potentiating 29 patients with a percentage of 60.4%.

Table 6. Rationality of use of the drug Metformin

Variable	True			
	Yes	(%)	Not	(%)
Dose	47	97,9	1	2,1
Frequency of administration	48	100	0	0
Duration of Administration	48	100	0	0
How to Give	48	100	0	0
Synergistic Interaction	17	35,4	0	0
Potentiation Interactions	29	60,4	0	0
Antagonistic Interactions	0	0	2	4,2

Discussion→7

Glimepiride is a third-generation sulfonylurea drug with a longer processing time and faster onset. The use of a mixture of other antidiabetic drugs creates a synergistic relationship, where the activity of each drug reinforces each other to achieve the same goal, with the aim of lowering glucose more. Glimepiride stimulates beta cells tosecrete insulin, while ethformin reduces hepatic glucose production, decreases intestinal glucose absorption, and improves insulin sensitivity by increasing peripheral glucose absorption and utilization. Glimepiride canminimize cardiovascular complexity and convert insulin levels released into glucose levels, especially in postprandial conditions, with the aim that glimepiride hypoglycemia occurs smaller than glibenclamide. With the profile they have, the combination of Metformin and Glimepirid is more viable and safe. [5-7] metformin given along with glucobay can lower metformin AUC levels. The alpha-glucosidase inhibitor, Glucobay, decreases the bioavailability of Metformin and reduces the normal peak plasma centralization of Metformin, but the chances of achieving that top fixation do

not change. The patient should be informed about the need to regularly observe blood glucose levels and know about the indications of hypoglycemia. [8-10]

The mostwidely given drug and has po tensiation interactions is antihypertensive drugs. Metformin given together with calcium chanel blocker drugs such as amlodipine can reduce the effects of metformin and has a pharmacodynamic interaction system with moderate levels. [11,12] Metformin given along with Ranitidine may increase plasma concentrations by slowing the excretion of metformin in the renal tubules. [13-15] metformin given along with captopril may increase the risk of hypoglycemia. Moreover, simultaneous use of captopril will cause blood glucose levels to increase by 2.2 mmol / L after 24 hours and increase to 2.9 mmol / L after 48 hours. For this situation, the use of the drug Captopril can be replaced with Valsartan class ARB (angiotensin receptor blocker), since Valsartan can lower circulatory pressure through the main enemy of the skeleton renin-angiotensin aldosterone. Likewise, Valsartan can also reduce the release of albumin in serum, if excess albumin lost from the blood shows high blood glucose levels for a long time, so that it can be overcome with Valsartan in expanding albumin secretion. [16-18] Metformin given along with furosemide will increase metformin levels in the blood causing hypoglycemia, while metformin can reduce furosemide levels. Furosemide and metformin are secreted in the tubular part of the kidney in order to interact with each other in the tubular system which causes metformin levels to increase. Furosemide can increase plasma metformin concentrations by 22% and metformin can reduce peak concentrations and elimination half-lives of furosemide by 31% and 32%, respectively. [19]

Spironolactone is a diuretic drug. Metformin given along with Spironolactone will induce kidney impairment and dehydration which may increase the risk of lactic acidosis in patients concomitantly taking Metformin. Methylprednisolone is a class of corticosteroids, Metformin given together with Methylprednisolone can inhibit glucose levels resulting in hyperglycemia, glucose intolerance, changes in glucose levels with new onset and exacerbation of diabetes mellitus. [20]

Conclusion→8

The rationality of using Metformin in Type 2 Diabetes Mellitus patients is based on the right dose criteria (100%), the right frequency of drug administration (100%), the right duration of

drug administration (100%), the right way of drug administration (100%), and the right drug interaction (95.8%).

References→9

1.Ministry of Health of the Republic of Indonesia. In 2030, the prevalence of diabetes mellitus in Indonesia will reach 21.3 million people. 2009. (http://www.depkes.go.id/index.php/berita/pressrelease/414-tahun-2030-prevalensidiabetes-melitusdi-indonesia-mencapai-213-juta-orang.html. Retrieved 12 December 2014).

2. PERKENI. Consensus on Management and Prevention of Type 2 Diabetes Mellitus in Indonesia. Jakarta: PERKENI.2011

3. Vickova V, Cornelius V, Kasliwal R, Wilton L, Shakir SA. Hypoglycaemia with oral antidiabetic drugs: results from prescription-event monitoring cohorts of rosiglitazone, pioglitazone, nateglinide and repaglinide. Drug Saf. 2009;32:409–18

4. Istiqomatunnisa. Rationality of the Use of Anti-Diabetes Drugs and Evaluation of the Cost Burden of Pharmaceutical Supplies on Healthy Jakarta Card Inpatients at Dr. Mintohardjo Navy Hospital. Thesis. Unpublished, Faculty of Medicine and Health Sciences, State Islamic University, Jakarta. 2014.

5. Khasanah M. Lifestyle in Diabetes Mellitus Sufferers. Thesis. Unpublished, Faculty of Da'wah Sunan Ampel State Islamic Institute, Surabaya. 2012.

6. Widya D. Relationship between Nutritional Status and Physical Activity on Diabetes Mellitus in the Elderly in West Kalimantan Province. Thesis. Unpublished, Faculty of Health Sciences, Esa Unggul University, Jakarta. 2015.

7. Naranjo, CA, Busto U., Sellers, E.M., Sandor, P., Ruiz, I., Robert, E.A., et al., A Method For Estimating the Probability od Adverse Drug Reactions, Clinical Pharmacology and therapeutics. 1981; 30:2:239 -45.

8. BPOM RI. Guidelines for Monitoring Drug Side Effects (MESO) for Health Workers. Jakarta: Badan POM RI. 2012.

9. Alomar MJ. Factors Affecting The Development of Adverse Drug Reactions. Saudi Pharmaceutical Journal. Feb 2013:22:83 -94.

10. Arifin AL. Current Type 2 Diabetes Mellitus Therapy Guide. Sub Section Endocrinology &; Metabolism Section / UPF. Internal Medicine. Faculty of Medicine. UNPAD / RSUP dr. Hasan Sadikin Bandung. 2011.

11. Malin SK, Kashyap SR. Effects of metformin on weight loss: potential mechanisms. Curr Opin Endocrinol Diabetes Obese. 2014 Oct;21(5):323 -9.

12. Drugs.com. Metformin Side Effects. 2015. (http://www.drugs.com/sfx/metformin -side -effects.html. Retrieved 3 July 2015).

13. Bouchoucha M, Uzzan B, Cohen R. Metformin and digestive disorders. Diabetes Metab 2011;37:90 -6. 14. Stoppler, M.C., Glucophage Side Effects Center. http://www.rxlist.com/glucophage -side -effects -drug - center.htm. Retrieved 1 August 2015.

15. Al Abri SA, S. Hayashi, K.L. Thoren, K.R. Olson. Metformin Ovedose -induced in the absence of other diabetic drugs. June 2013:51(5)(444 -447).

16. U.S. National Library of Medicine. Metformin. 2015. (https://www.nlm.nih.gov/medlineplus/druginfo/meds/a696005.html. Retrieved 20 August 2015).

17. Cunha, J.P., 2015. Glumetza Side Effects Center. (Online). (http://www.rxlist.com/glumetza -side - effects -drug -center.htm, accessed June 30, 2015).

18. Ting RZ, Szeto CC, Chan MH, Ma KK, Chow KM. Risk factors of vitamin B(12) deficiency in patients receiving metformin. Arch Intern Med. 2006; 166(18):1975 -9.

19. Drugs.com. Glimepiride Side Effects. 2015. (http://www.drugs.com/sfx/glimepirideside -effects.html. Retrieved 28 June 2015).

20. Ogbru, O., Williams, E., Marks, J.W. Insulin: Drug Facts, Side Effects and Dosing. 2015. (http://www.medicinenet.com/insulin/article.htm. Retrieved 23 July 2015).

Reviewer Comment:

1→ Title of Manuscripts should be explained independent variable and dependent variable also subject of study.

2→ Keywords should be showed the main words of the study, the authors can use MeSH to develop keywords.

3→ Abstract should be showed the main of background, methods, results and conclusion of study.

- Background abstract should be showed the urgency of study and why the study important, in simple way.
- Conclusion should be wrote in simple way, specific to the main results. Conclusion in abstract should not showed statistic results.

4→Introduction should be showed the urgency of study (epidemiology data), biological plausibility concept, and lack of knowledge in the study.

- Paragraph 1→ need improvement in urgency of study and explain more about epidemiology data. Authors do not only show the data, but try to elaborate and make comparison about the data from year to year.
- Paragraph 2 and 3 need improvement to focus in biological plausibility concept.

5→ Methods should be showed more about how the study develop. Methods should be showed the design of study; population, sample and sample size of study; inclusion criteria; place of study; ethical clearence steatment; independent and dependent variable; data analysis.

- Methods need to showed the design of study; population, sample and sample size of study; inclusion criteria; place of study; ethical clearence steatment; independent and dependent variable; data analysis, more specific but not to long.

6→ Results should be showed baseline characteristics subject of study, main results of study. Authors must be focused and try to make results no more table and figure.

7→ Discussion should be explored more biological plausibility, not only showed about statistical results.

8→ Conclusion should more specific and not more showed statistical results

9→ Authors must check the references for make update references. References should no more than 10 years.

Reviewer 2: Revision required

Evaluation of Rationality in Prescribing Metformin (Biguanide Group) at Dr. Mohammad Hoesin General Hospital Palembang→1

Nita Parisa[1*], Dwi Tantri Marylin[2], Theodorus[1]

[1]Department of Pharmacology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

[2]Medical Education Study Program, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

*Email: nitaparisa@unsri.ac.id

Abstract→3

Background. Evaluation and assessment of the rationality of the use of antidiabetic drugs, especially the biguanid group (metformin) is very important to be carried out in order to maintain the quality and quality of diabetes mellitus drug administration so that Diabetes mellitus control targets can be optimized. This study aims to evaluate the rationality of oral antidiabetic meformin prescribing at Dr Mohammad Hoesin General Hospital Palembang

Methods. The research design was a descriptive study using secondary data of medical records in the medical record section of RSUP Dr. Moh Hoesin Palembang. The object of the study was all medical records of patients with type 2 diabetes mellitus who used metformin drugs at RSMH Palembang in the period July 1 , 2019-July 31, 2020, with complete medical record data and without severe comorbidities. The rationality of the use of metformin drugs assessed in this study is the frequency of use, drug dosage, mode of administration , duration of administration and drug interactions. The frequency of use of the drug is assessed how many times the drug is consumed in one day.

Results. Thehighest age of patients who received metformin prescriptions were aged 51-60 years and 61-70 years with a total of 17 patients (35.4%). The majority of patients were female as much as 60.4%. Drug interactions from metformin are still quite common, although the majority are synergistic and potentiating interactions. There were still 2 cases or 4.2 percent who experienced antagonistic interactions.

Conclusion. The rationality of using metformin drugs in type 2 diabetes mellitus patients is based on the right dose criteria (100%), the right frequency of drug administration (100%), the right length of drug administration (100%), the right way of drug administration (100%), and the right drug interaction (95.8%).

Keywords. Metformin, Biguanide, Oral Antidiabetic, Pharmacology, Descriptive Study. →2

Introduction→4

Indonesia is ranked fourth largest of all those who experience diabetes mellitus, which is 8.6% of the total population while the ranks above are India, China, and the United States (WHO, 2018). WHO predicts an increase in the number of people experiencing Diabetes Mellitus in Indonesia, amounting to 8.4 million people in 2000, increasing to reach 21.3 million in 2030. *The International Diabetes Foundation* (IDF) estimates that there will be an increase in the number of people suffering from Diabetes Mellitus in 2009 from 7 million will increase in 2030 to reach 12 million people. From this information, it shows a 2-3 fold increase in the population experiencing Diabetes Mellitus in 2030. [1] Diabetes Mellitus management generally consists of four indicators, namely education, nutritional therapy, exercise, and pharmacological interventions. Pharmacological therapy is given to patients who do not respond or respond at least during a carbohydrate diet, exercise is recommended to change a healthy lifestyle for three months to keep blood glucose levels above 200 mg / dL and HbA1c above 6.5%. [2-4]

Pharmacological interventions include oral and injectable antidiabetic drugs. Oral drugs include the group of biguanids, sulfunilureas. Oral antidiabetic drugs are the more commonly used drugs. The first drug selection in these patients was metformin. In order to achieve effective therapy, the administration of rational oral antidiabetic drugs, namely the right dose, the right diagnosis of the patient, right in the selection and administration of drugs, and there are no contra indications, needs good attention. Evaluation and assessment of the rationality of the use of antidiabetic drugs, especially the biguanid group (metformin) is very important to be carried out in order to maintain the quality and quality of diabetes mellitus drug administration So that the target of controlling diabetes mellitus can be optimized.

Methods→5

The research design was a descriptive study using secondary data of medical records in the medical record section of RSUP Dr. Moh Hoesin Palembang. The object of the study was all medical records of patients with type 2 diabetes mellitus who used metformin drugs at RSMH Palembang in the period July 1, 2019-July 31, 2020, with medical record data that complete and without severe comorbidities. The rationality of the use of metformin drugs assessed in this study is the frequency of use, drug dosage, mode of administration , duration of administration and drug interactions. The frequency of use of the drug is assessed how many times the drug is consumed in one day. The dose of metformin used is 500 mg or 850 mg. The method of drug administration is the method of consumption of metformin drugs and the duration of drug administration is the length of drug administration written on the prescription. Drug interaction is a reaction that arises between two or more drugs in concurrent use, in the form of sinergis, namely the administration of one drug can strengthen the effect of the other drug, antagonis, ie the administration of one drug can reduce the effect of the other drug and p Authentication, namely the administration of one drug can strengthen the effect of another drug by increasing the concentration of the other drug by the body.

The data used is secondary data through medical records obtained from the Medical Record Installation Section of RSMH Palembang. In data collection, the researcher does not take data directly, but by parties who are not researchers. The data collected in this study will be processed using SPSS descriptive statistical method based on the number of cases recorded in the medical record of diabetes mellitus patients in accordance with the variables studied. The results of the research will be analyzed and presented in the form of tables and will be explained in the form of narratives. The type of statistical analysis that will be used in this study is univariate analysis which aims to describe the characteristics of each variable studied.

Results→6

Table 1, from48 patients saw the number of patients with type 2 DM with the drug Metformin, the youngest age suffering from type 2 DM was 42 years, while the oldest age was 77 years. Where these results obtained the highest average age group were 51-60 years old and 61-70 years with 17 patients (35.4%). The majority of patients were female as much as 60.4%. The majority of patients get as many as 3-4 drugs per prescription.

Table 1. Baseline Characteristics

Variable	Number of Cases (n)	Percentage (%)
Age		
40-50 years	12	25,0
51-60 years	17	35,4
61-70 years old	17	35,4
71-80 years	2	4,2
Gender		
Man	19	39,6
Woman	29	60,4
Number of Drugs Per Prescription		
1	8	16,7
2	9	18,8
3	13	27,1
4	10	20,8
5	8	16,7

Table 2 shows that drug interactions of metformin are still quite common, although the majority are synergistic and potentiating interactions. There are still 2 cases or 4.2 percent who experience antagonistic interactions.

Table 2. Distribution of respondents based on drug interactions

Drug Interactions	Number of Cases (n)	Percentage (%)
Synergistic Interaction	17	35,4
Potentiation	29	60,4
Interactions	2	4,2
Antagonistic Interactions		

Table 3. Synergistic distribution of drug interactions

Synergistic Interaction	Number of Cases (n)	Percentage (%)
Metformin + Glimepirid	9	18,8
Metformin + Glucobay	2	4,2
Metformin + Gliclazide	3	6,2
Metformin + Glibenclamid	3	6,2

Table 4. Distribution of potentiating drug interactions

Potentiation Interactions	Number of Cases (n)	Percentage (%)
Metformin + Aspilet	2	4,2
Metformin + Amlodipine	10	20,8
Metformin + Captopril	6	12,5
Metformin + Ranitidine	5	10,4
Metformin + Furosemide	4	8,3
Metformin + Valsartan	2	4,2

Table 5. Distribution of antagonistic drug interactions

Antagonistic Interactions	Number of Cases (n)	Percentage (%)
Metformin + Spironolactone	1	2,1
Metformin + Methylprednisolone	1	2,1

Table 6 shows patients with the right dose set at 47 patients with a percentage of 97.9%, the right frequency of drug administration is 48 patients with a percentage of 100%, the right time period of drug administration is 48 people (100%), the right way of drug administration is 48

people (100%), the right drug interaction is 17 patients with a percentage of 35.4%, and the right drug interaction is potentiating 29 patients with a percentage of 60.4%.

Table 6. Rationality of use of the drug Metformin

Variable	True			
	Yes	(%)	Not	(%)
Dose	47	97,9	1	2,1
Frequency of administration	48	100	0	0
Duration of Administration	48	100	0	0
How to Give	48	100	0	0
Synergistic Interaction	17	35,4	0	0
Potentiation Interactions	29	60,4	0	0
Antagonistic Interactions	0	0	2	4,2

Discussion→7

Glimepiride is a third-generation sulfonylurea drug with a longer processing time and faster onset. The use of a mixture of other antidiabetic drugs creates a synergistic relationship, where the activity of each drug reinforces each other to achieve the same goal, with the aim of lowering glucose more. Glimepiride stimulates beta cells tosecrete insulin, while ethformin reduces hepatic glucose production, decreases intestinal glucose absorption, and improves insulin sensitivity by increasing peripheral glucose absorption and utilization. Glimepiride canminimize cardiovascular complexity and convert insulin levels released into glucose levels, especially in postprandial conditions, with the aim that glimepiride hypoglycemia occurs smaller than glibenclamide. With the profile they have, the combination of Metformin and Glimepirid is more viable and safe. [5-7] metformin given along with glucobay can lower metformin AUC levels. The alpha-glucosidase inhibitor, Glucobay, decreases the bioavailability of Metformin and reduces the normal peak plasma centralization of Metformin, but the chances of achieving that top fixation do

not change. The patient should be informed about the need to regularly observe blood glucose levels and know about the indications of hypoglycemia. [8-10]

The mostwidely given drug and has po tensiation interactions is antihypertensive drugs. Metformin given together with calcium chanel blocker drugs such as amlodipine can reduce the effects of metformin and has a pharmacodynamic interaction system with moderate levels. [11,12] Metformin given along with Ranitidine may increase plasma concentrations by slowing the excretion of metformin in the renal tubules. [13-15] metformin given along with captopril may increase the risk of hypoglycemia. Moreover, simultaneous use of captopril will cause blood glucose levels to increase by 2.2 mmol / L after 24 hours and increase to 2.9 mmol / L after 48 hours. For this situation, the use of the drug Captopril can be replaced with Valsartan class ARB (angiotensin receptor blocker), since Valsartan can lower circulatory pressure through the main enemy of the skeleton renin-angiotensin aldosterone. Likewise, Valsartan can also reduce the release of albumin in serum, if excess albumin lost from the blood shows high blood glucose levels for a long time, so that it can be overcome with Valsartan in expanding albumin secretion. [16-18] Metformin given along with furosemide will increase metformin levels in the blood causing hypoglycemia, while metformin can reduce furosemide levels. Furosemide and metformin are secreted in the tubular part of the kidney in order to interact with each other in the tubular system which causes metformin levels to increase. Furosemide can increase plasma metformin concentrations by 22% and metformin can reduce peak concentrations and elimination half-lives of furosemide by 31% and 32%, respectively. [19]

Spironolactone is a diuretic drug. Metformin given along with Spironolactone will induce kidney impairment and dehydration which may increase the risk of lactic acidosis in patients concomitantly taking Metformin. Methylprednisolone is a class of corticosteroids, Metformin given together with Methylprednisolone can inhibit glucose levels resulting in hyperglycemia, glucose intolerance, changes in glucose levels with new onset and exacerbation of diabetes mellitus. [20]

Conclusion→8

The rationality of using Metformin in Type 2 Diabetes Mellitus patients is based on the right dose criteria (100%), the right frequency of drug administration (100%), the right duration of

drug administration (100%), the right way of drug administration (100%), and the right drug interaction (95.8%).

References→9

1.Ministry of Health of the Republic of Indonesia. In 2030, the prevalence of diabetes mellitus in Indonesia will reach 21.3 million people. 2009. (http://www.depkes.go.id/index.php/berita/pressrelease/414-tahun-2030-prevalensidiabetes-melitusdi-indonesia-mencapai-213-juta-orang.html. Retrieved 12 December 2014).

2. PERKENI. Consensus on Management and Prevention of Type 2 Diabetes Mellitus in Indonesia. Jakarta: PERKENI.2011

3. Vickova V, Cornelius V, Kasliwal R, Wilton L, Shakir SA. Hypoglycaemia with oral antidiabetic drugs: results from prescription-event monitoring cohorts of rosiglitazone, pioglitazone, nateglinide and repaglinide. Drug Saf. 2009;32:409–18

4. Istiqomatunnisa. Rationality of the Use of Anti-Diabetes Drugs and Evaluation of the Cost Burden of Pharmaceutical Supplies on Healthy Jakarta Card Inpatients at Dr. Mintohardjo Navy Hospital. Thesis. Unpublished, Faculty of Medicine and Health Sciences, State Islamic University, Jakarta. 2014.

5. Khasanah M. Lifestyle in Diabetes Mellitus Sufferers. Thesis. Unpublished, Faculty of Da'wah Sunan Ampel State Islamic Institute, Surabaya. 2012.

6. Widya D. Relationship between Nutritional Status and Physical Activity on Diabetes Mellitus in the Elderly in West Kalimantan Province. Thesis. Unpublished, Faculty of Health Sciences, Esa Unggul University, Jakarta. 2015.

7. Naranjo, CA, Busto U., Sellers, E.M., Sandor, P., Ruiz, I., Robert, E.A., et al., A Method For Estimating the Probability od Adverse Drug Reactions, Clinical Pharmacology and therapeutics. 1981; 30:2:239 -45.

8. BPOM RI. Guidelines for Monitoring Drug Side Effects (MESO) for Health Workers. Jakarta: Badan POM RI. 2012.

9. Alomar MJ. Factors Affecting The Development of Adverse Drug Reactions. Saudi Pharmaceutical Journal. Feb 2013:22:83 -94.

10. Arifin AL. Current Type 2 Diabetes Mellitus Therapy Guide. Sub Section Endocrinology &; Metabolism Section / UPF. Internal Medicine. Faculty of Medicine. UNPAD / RSUP dr. Hasan Sadikin Bandung. 2011.

11. Malin SK, Kashyap SR. Effects of metformin on weight loss: potential mechanisms. Curr Opin Endocrinol Diabetes Obese. 2014 Oct;21(5):323 -9.

12. Drugs.com. Metformin Side Effects. 2015. (http://www.drugs.com/sfx/metformin -side -effects.html. Retrieved 3 July 2015).

13. Bouchoucha M, Uzzan B, Cohen R. Metformin and digestive disorders. Diabetes Metab 2011;37:90 -6. 14. Stoppler, M.C., Glucophage Side Effects Center. http://www.rxlist.com/glucophage -side -effects -drug - center.htm. Retrieved 1 August 2015.

15. Al Abri SA, S. Hayashi, K.L. Thoren, K.R. Olson. Metformin Ovedose -induced in the absence of other diabetic drugs. June 2013:51(5)(444 -447).

16. U.S. National Library of Medicine. Metformin. 2015. (https://www.nlm.nih.gov/medlineplus/druginfo/meds/a696005.html. Retrieved 20 August 2015).

17. Cunha, J.P., 2015. Glumetza Side Effects Center. (Online). (http://www.rxlist.com/glumetza -side - effects -drug -center.htm, accessed June 30, 2015).

18. Ting RZ, Szeto CC, Chan MH, Ma KK, Chow KM. Risk factors of vitamin B(12) deficiency in patients receiving metformin. Arch Intern Med. 2006; 166(18):1975 -9.

19. Drugs.com. Glimepiride Side Effects. 2015. (http://www.drugs.com/sfx/glimepirideside -effects.html. Retrieved 28 June 2015).

20. Ogbru, O., Williams, E., Marks, J.W. Insulin: Drug Facts, Side Effects and Dosing. 2015. (http://www.medicinenet.com/insulin/article.htm. Retrieved 23 July 2015).

Reviewer Comment:

1→ Title of Manuscripts should be explained independent variable and dependent variable also subject of study.

2→ Keywords should be showed the main words of the study, the authors can use MeSH to develop keywords.

3→ Abstract should be showed the main of background, methods, results and conclusion of study.

- Background abstract should be showed the urgency of study and why the study important, in simple way.
- Conclusion should be wrote in simple way, specific to the main results. Conclusion in abstract should not showed statistic results.

4→Introduction should be showed the urgency of study (epidemiology data), biological plausibility concept, and lack of knowledge in the study.

- Paragraph 1→ need improvement in urgency of study and explain more about epidemiology data. Authors do not only show the data, but try to elaborate and make comparison about the data from year to year.
- Paragraph 2 and 3 need improvement to focus in biological plausibility concept.

5→ Methods should be showed more about how the study develop. Methods should be showed the design of study; population, sample and sample size of study; inclusion criteria; place of study; ethical clearence steatment; independent and dependent variable; data analysis.

- Methods need to showed the design of study; population, sample and sample size of study; inclusion criteria; place of study; ethical clearence steatment; independent and dependent variable; data analysis, more specific but not to long.

6→ Results should be showed baseline characteristics subject of study, main results of study. Authors must be focused and try to make results no more table and figure.

7→ Discussion should be explored more biological plausibility, not only showed about statistical results.

8→ Conclusion should more specific and not more showed statistical results

9→ Authors must check the references for make update references. References should no more than 10 years.

Revised version received by journal (February 21th, 2022)

Bioscientia Medicina: Journal Of Biomedicine & Translational Research

eISSN (Online): 2598-0580

Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Evaluation of Rationality in Prescribing Metformin (Biguanide Group) at Dr. Mohammad Hoesin General Hospital Palembang

Nita Parisa[1*], Dwi Tantri Marylin[2], Theodorus[1]

[1] Department of Pharmacology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
[2] Medical Education Study Program, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

ARTICLE INFO

Keywords:
Metformin
Biguanide
Oral antidiabetic
Pharmacology
Descriptive study

***Corresponding author:**
Nita Parisa

E-mail address:
nitaparisa@unsri.ac.id

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v6i3.471

ABSTRACT

Backgrounds. It is very important to evaluate and assess the rationality of the use of antidiabetic drugs, especially the biguanide (metformin) group to maintain the quality and quality of diabetes mellitus drug administration so that the target of diabetes mellitus control can be optimized. This study aims to evaluate the rationality of prescribing metformin oral antidiabetic at Dr. Mohammad Hoesin General Hospital Palembang. **Methods:** The research design is a descriptive study using secondary data from medical records in the medical records section of Dr. Moh Hoesin Hospital Palembang. The object of research is all medical records of patients with type 2 diabetes mellitus who used metformin at RSMH Palembang in the period July 1st, 2019-July 31st, 2020, with complete medical record data and without serious comorbidities. The rationality for using metformin that was assessed in this study was the frequency of use, drug dose, route of administration, duration of administration, and drug interactions. The frequency of drug use is assessed by how many times the drug is taken in one day. **Results:** The most age group of patients who received a prescription for metformin were 51-60 years old and 61-70 years old with a total of 17 patients (35.4%). The majority of patients were female as much as 60.4%. Drug interactions with metformin are still quite common, although the majority are synergistic and potentiating interactions. There are still 2 cases or 4.2 percent who experience antagonistic interactions. **Conclusion:** The rationality for using metformin in patients with type 2 diabetes mellitus is based on the criteria for the right dose (100%), the right frequency of drug administration (100%), the right time for giving the drug (100%), the right way of giving the drug (100%), and the right drug interaction. (95.8%).

1. Introduction

Indonesia is ranked the fourth largest of all those with diabetes mellitus, which is 8.6% of the total population, while the top rankings are India, China, and the United States (WHO, 2018). WHO predicts that there will be an increase in the number of people with diabetes mellitus in Indonesia, which was 8.4 million people in 2000, increasing to 21.3 million in 2030. The International Diabetes Foundation (IDF) estimates that there will be an increase in the number of people suffering from Diabetes Mellitus in 2009 from 7 million and will increase in 2030 to reach 12 million people. This information, it shows that there will be a 2-3 times increase in the population experiencing Diabetes Mellitus in 2030.[1] Management of Diabetes Mellitus

generally consists of four indicators, namely education, nutritional therapy, exercise, and pharmacological intervention. Pharmacological therapy is given to patients who do not respond or respond at least during a carbohydrate diet, exercise is recommended to change a healthy lifestyle for three months to maintain blood glucose levels to remain above 200 mg/dL and HbA1c above 6.5 %.[2-4]

Pharmacological interventions include oral and injectable antidiabetic drugs. Oral drugs include the biguanide group, sulfunilureas. Oral antidiabetic drugs are the drugs that are used more often. The first choice of drug in this patient is metformin. To achieve effective therapy, the rational administration of oral antidiabetic drugs, namely the right dose, the right patient diagnosis, the right choice and administration of drugs, and there are no contraindications, needs good attention. It is very important to evaluate and assess the rationality of the use of antidiabetic drugs, especially the biguanide (metformin) group to maintain the quality and quality of diabetes mellitus drug administration so that the target of diabetes mellitus control can be optimized.

2. Methods

The research design is a descriptive study using secondary data from medical records in the medical records section of Dr. Moh Hoesin Hospital Palembang. The object of the study was all medical records of patients with type 2 diabetes mellitus who used metformin at RSMH Palembang in the period July 1st, 2019-July 31st, 2020, with complete medical record data and without serious comorbidities. The rationality for using metformin that was assessed in this study was the frequency of use, drug dose, route of administration, duration of administration, and drug interactions. The frequency of drug use is assessed by how many times the drug is taken in one day. The dose of metformin used is 500 mg or 850 mg. The method of administration of the drug is the method of consumption of the drug metformin and the duration of drug administration is the duration of administration of the drug written on the prescription. Drug interactions are reactions that arise between two or more drugs in the same use, in the form of synergism, namely the administration of one drug can strengthen the effects of other drugs, antagonists, namely the administration of one drug can reduce the effects of other drugs and potentiation, namely the administration of one drug can strengthen the effect of another drug by increasing the concentration of that other drug by the body.

The data used is secondary data through medical records obtained from the Medical Record Installation Section of RSMH Palembang. In data collection, the researcher does not take data directly, but by parties who are not researchers. The data collected in this study will be processed using the SPSS descriptive statistical method based on the number of cases recorded in the medical records of patients with diabetes mellitus according to the variables studied. The research results will be analyzed and presented in tabular form and will be explained in narrative form. The type of statistical analysis that will be used in this research is a univariate analysis which aims to describe the characteristics of each variable being studied.

3. Results

Table 1 shows the number of patients with type 2 DM with Metformin, the youngest age suffering from type 2 DM is 42 years, while the oldest age is 77 years. Where these results were obtained the average age group is 51-60 years old and 61-70 years old with a total of 17 patients (35.4%). The majority of patients were female as much as 60.4%. The majority of patients received 3-4 drugs per prescription.

Table 1. Baseline characteristic

Variable	Number of Cases (n)	Percentage (%)
Age		
40-50 years old	12	25.0
51-60 years old	17	35.4
61-70 years old	17	35.4
71-80 years old	2	4.2
Gender		
Male	19	39.6
Female	29	60.4
Number of Drugs Per Prescription		
1	8	16.7
2	9	18.8
3	13	27.1
4	10	20.8
5	8	16.7

Table 2 shows that drug interactions with metformin are still quite often encountered, although the majority are synergistic and potentiating interactions. There are still 2 cases or 4.2 percent who experience antagonistic interactions.

Table 2. Distribution of respondents based on drug Interactions

Drug Interactions	Number of Cases (n)	Percentage (%)
Synergistic Interactions	17	35.4
Potentializing Interactions	29	60.4
Antagonist Interactions	2	4.2

Table 3. Distribution of synergistic drug Interactions

Synergistic interactions	Number of cases (n)	Percentage (%)
Metformin + Glimepiride	9	18.8
Metformin + Glucobay	12	4.2
Metformin + Gliclazid	3	6.2
Metformin + Glibenclamid	3	6.2

Table 4. Distribution of potentiating drug Interactions

Potentiating interactions	Number of cases (n))	Percentage (%)
Metformin + Aspilet	2	4,2
Metformin + Amlodipine	10	20,8
Metformin + Captopril	6	12,5
Metformin + Ranitidine	5	10,4
Metformin + Furosemide	4	8,3
Metformin + Valsartan	2	4,2

Table 5. Distribution of antagonistic drug Interactions

Antagonist interactions	Number of cases (n)	Percentage (%)
Metformin + Spironolactone	1	2.1
Metformin + Methylprednisolone	1	2.1

Table 6 shows that the patients with the right dose set amounted to 47 patients with a percentage of 97.9%, exact frequency of delivery There were 48 patients with a percentage of 100% of drugs, 48 people (100%) on the right time to administer the drugs, 48 people on the right way of administering drugs (100%), 17 patients with the right drug interactions with a percentage of 35.4%, and the right drug interactions. potentiating drug interactions 29 patients with a percentage of 60.4%.

Table 6. The rationality for using Metformin

Variable	Appropriate			
	Yes	(%)	No	(%)
Dosage	47	97.9	1	2.1
Frequency of administration	48	100	0	0
Duration of administration	48	100	0	0
Method of administration	48	100	0	0
Synergistic interactions	17	35.4	0	0
Potentiating Interaction	29	60.4	0	0
Antagonist Interaction	0	0	2	4.2

4. Discussion

Glimepiride is a third-generation sulfonylurea drug with a longer duration of action and a faster onset of action. The use of a mixture of other antidiabetic drugs creates a synergistic relationship, where the activities of each drug reinforce each other to achieve the same goal, to lower glucose more. Glimepiride stimulates beta cells to secrete insulin, while metformin reduces hepatic glucose production, decreasing intestinal glucose absorption, and increase insulin sensitivity by increasing peripheral glucose uptake and utilization. Glimepiride can reduce cardiovascular complications and convert insulin released into glucose levels, especially in the postprandial state, with the aim that glimepiride is less hypoglycemic than glibenclamide. With the profile they have, the combination of Metformin and Glimepirid is more feasible and safe.[5-7] Metformin given concurrently with Glucobay can decrease metformin AUC levels. The alpha-glucosidase inhibitor Glucobay decreases the bioavailability of Metformin and reduces the normal peak plasma centralization of Metformin, but the chances of achieving that top fixation are unchanged. Patients should be informed of the need to monitor blood glucose levels regularly and be aware of indications for hypoglycemia.[8-10]

The most widely administered drugs and have potentiating interactions are antihypertensive drugs. Metformin given together with calcium channel blocker drugs such as amlodipine can reduce the effects of metformin and has a moderate level of pharmacodynamic interaction.[11,12] Metformin given concurrently with Ranitidine can increase plasma concentrations by slowing the renal tubular excretion of metformin.[13-15] Metformin given concurrently with captopril may increase the risk of hypoglycemia. Moreover, the simultaneous use of captopril will cause blood glucose levels to increase by 2.2 mmol/L after 24 hours and increase to 2.9 mmol/L after 48 hours. For this situation, the use of the drug Captopril can be replaced with Valsartan class ARB (angiotensin receptor blocker), because Valsartan can lower blood pressure through the main enemy of the renin-angiotensin-aldosterone framework. Likewise,

Valsartan can also reduce the release of albumin in the serum, if the excess albumin lost from the blood shows high blood glucose levels for a long time, so Valsartan can be overcome by slowing albumin secretion.[16-18] Metformin given together with furosemide will increase metformin levels in the blood, causing hypoglycemia, while metformin can reduce furosemide levels. Furosemide and metformin are secreted in the tubular portion of the kidney so that they can interact with each other in the tubular system, resulting in increased metformin levels. Furosemide can increase the plasma metformin concentration by 22% and metformin can reduce the peak concentration and elimination half-life of furosemide by 31% and 32%, respectively.[19]

Spironolactone is a diuretic drug. Metformin given concurrently with Spironolactone will induce renal impairment and dehydration which can increase the risk of lactic acidosis in patients concurrently using Metformin. Methylprednisolone is a corticosteroid class, Metformin which is given together with Methylprednisolone can inhibit glucose levels resulting in hyperglycemia, glucose intolerance, changes in glucose levels with new-onset, and exacerbation of diabetes mellitus.[20]

5. Conclusion

The rationality for the use of Metformin in Patients with Type 2 Diabetes Mellitus is based on the criteria for the right dose (100%), the right frequency of administration (100%), the right time for giving the drug (100%), the right way of giving the drug (100%), and the right way. drug interactions (95.8%).

6. References

1. Ministry of Health of the Republic of Indonesia. In 2030, the prevalence of diabetes mellitus in Indonesia reaches 21.3 million people. 2009.
2. PERKENI. Consensus on the Management and Prevention of Type 2 Diabetes Mellitus in Indonesia. Jakarta: PERKENI.2011
3. Vicckova V, Cornelius V, Kasliwal R, Wilton L, Shakir SA. Hypoglycaemia with oral antidiabetic drugs: results from the prescription-event monitoring cohorts of rosiglitazone, pioglitazone, nateglinide and repaglinide. Drug Saf. 2009; 32: 409–18
4. Istiqomatunnisa. The Rationality of the Use of Anti-Diabetes Drugs and Evaluation of the Cost of Pharmaceutical Supplies for Inpatients with the Healthy Jakarta Card at the Dr. Navy Hospital. Mintohardjo. Essay. Unpublished, Faculty of Medicine and Health Sciences, State Islamic University, Jakarta. 2014.
5. Khasanah M. Lifestyle in Diabetes Mellitus Patients. Essay. Unpublished, Faculty of Da'wah State Islamic Institute of Sunan Ampel, Surabaya. 2012.
6. Widya D. The Relationship between Nutritional Status and Physical Activity on Diabetes Mellitus in the Elderly in West Kalimantan Province. Essay. Unpublished, Faculty of Health Sciences, Esa Unggul University, Jakarta. 2015.
7. Naranjo, CA, Busto U., Sellers, EM, Sandor, P., Ruiz, I., Robert, EA, et al., A method for estimating the probability of adverse drug reactions, clinical pharmacology and therapeutics. 1981; 30:2:239 -45.
8. BPOM RI. Guidelines for Monitoring Drug Side Effects (MESO) for Health Workers. Jakarta: POM RI Agency. 2012.
9. Alomar MJ. Factors affecting the development of adverse drug reactions. Saudi Pharmaceutical Journal. Feb 2013: 22: 83 -94.
10. Arifin AL. The latest type 2 diabetes mellitus therapy guide. endocrinology & metabolism sub division / UPF. Internal Medicine. Medical School. UNPAD / RSUP dr. Hasan Sadikin Bandung. 2011.
11. Malin SK, Kashyap SR. Effects of metformin on weight loss: potential mechanisms. Curr Opin Endocrinol Diabetes Obes. 2014 Oct; 21(5): 323 -9.
12. Drugs.com. Metformin Side Effects. 2015. (http://www.drugs.com/sfx/metformin -side -effects.html. Accessed July 3, 2015).
13. Bouchoucha M, Uzzan B, Cohen R. Metformin and digestive disorders. Diabetes Metab 2011;

37: 90 -6.

14. Stoppler, MC, Glucophage Side Effects Center. http://www.rxlist.com/glucophage -side -effects -drug -center.htm. Accessed August 1, 2015.
15. Al Abri SA, S. Hayashi, KL Thoren, KR Olson. Metformin Ovedose -induced in the absence of other diabetic drugs. June 2013: 51(5): 444 -447.
16. US National Library of Medicine. metformin. 2015. (https://www.nlm.nih.gov/medlineplus/druginfo/meds/a696005.html. Accessed August 20, 2015).
17. Cunha, JP, 2015. Glumetza Side Effects Center. (On line). (http://www.rxlist.com/glumetza -side -effects -drug -center.htm, Accessed June 30, 2015).
18. Ting RZ, Szeto CC, Chan MH, Ma KK, Chow KM. Risk factors of vitamin B(12) deficiency in patients receiving metformin. Arch Intern Med. 2006; 166(18): 1975-9.
19. Drugs.com. Glimepiride Side Effects. 2015. (http://www.drugs.com/sfx/glimepirideside -effects.html. Accessed June 28, 2015).
20. Ogbru, O., Williams, E., Marks, JW Insulin: Drug Facts, Side Effects and Dosing. 2015. (http://www.medicinenet.com/insulin/article .htm. Accessed July 23, 2015).

Paper Accepted for publication (February 26th, 2022)

Bioscientia Medicina

Journal of Biomedicine and Translational Research

HM Publisher

Letter of Acceptance

Manuscript “Evaluation of Rationality in Prescribing Metformin (Biguanide Group) at Dr. Mohammad Hoesin General Hospital Palembang“ by Nita Parisa*, Dwi Tantri Marylin, Theodorus, has been accepted to publish in Bioscientia Medicina: Journal of Biomedicine and Translational Research (Bioscmed) Vol 6 issue 3 in March 2022.

Cordially,

Prof. Paula Magnano, PhD

Editor HM Publisher

(*) Corresponding author

The Coresponding Author can access the acount in website :

https://bioscmed.com/index.php/bsm/login

User: nita_parisa

Password: 210587

eISSN (Online): 2598-0580

Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Evaluation of Rationality in Prescribing Metformin (Biguanide Group) at Dr. Mohammad Hoesin General Hospital Palembang

Nita Parisa[1*], Dwi Tantri Marylin[2], Theodorus[1]

[1] Department of Pharmacology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
[2] Medical Education Study Program, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

ARTICLE INFO

Keywords:
Metformin
Biguanide
Oral antidiabetic
Pharmacology
Descriptive study

***Corresponding author:**
Nita Parisa

E-mail address:
nitaparisa@unsri.ac.id

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v6i3.471

ABSTRACT

Backgrounds. It is very important to evaluate and assess the rationality of the use of antidiabetic drugs, especially the biguanide (metformin) group to maintain the quality and quality of diabetes mellitus drug administration so that the target of diabetes mellitus control can be optimized. This study aims to evaluate the rationality of prescribing metformin oral antidiabetic at Dr. Mohammad Hoesin General Hospital Palembang. **Methods:** The research design is a descriptive study using secondary data from medical records in the medical records section of Dr. Moh Hoesin Hospital Palembang. The object of research is all medical records of patients with type 2 diabetes mellitus who used metformin at RSMH Palembang in the period July 1st, 2019-July 31st, 2020, with complete medical record data and without serious comorbidities. The rationality for using metformin that was assessed in this study was the frequency of use, drug dose, route of administration, duration of administration, and drug interactions. The frequency of drug use is assessed by how many times the drug is taken in one day. **Results:** The most age group of patients who received a prescription for metformin were 51-60 years old and 61-70 years old with a total of 17 patients (35.4%). The majority of patients were female as much as 60.4%. Drug interactions with metformin are still quite common, although the majority are synergistic and potentiating interactions. There are still 2 cases or 4.2 percent who experience antagonistic interactions. **Conclusion:** The rationality for using metformin in patients with type 2 diabetes mellitus is based on the criteria for the right dose (100%), the right frequency of drug administration (100%), the right time for giving the drug (100%), the right way of giving the drug (100%), and the right drug interaction. (95.8%).

1. Introduction

Indonesia is ranked the fourth largest of all those with diabetes mellitus, which is 8.6% of the total population, while the top rankings are India, China, and the United States (WHO, 2018). WHO predicts that there will be an increase in the number of people with diabetes mellitus in Indonesia, which was 8.4 million people in 2000, increasing to 21.3 million in 2030. The International Diabetes Foundation (IDF) estimates that there will be an increase in the number of people suffering from Diabetes Mellitus in 2009 from 7 million and will increase in 2030 to reach 12 million people. This information, it shows that there will be a 2-3 times increase in the population experiencing Diabetes Mellitus in 2030.[1] Management of Diabetes Mellitus

generally consists of four indicators, namely education, nutritional therapy, exercise, and pharmacological intervention. Pharmacological therapy is given to patients who do not respond or respond at least during a carbohydrate diet, exercise is recommended to change a healthy lifestyle for three months to maintain blood glucose levels to remain above 200 mg/dL and HbA1c above 6.5 %.[2-4]

Pharmacological interventions include oral and injectable antidiabetic drugs. Oral drugs include the biguanide group, sulfunilureas. Oral antidiabetic drugs are the drugs that are used more often. The first choice of drug in this patient is metformin. To achieve effective therapy, the rational administration of oral antidiabetic drugs, namely the right dose, the right patient diagnosis, the right choice and administration of drugs, and there are no contraindications, needs good attention. It is very important to evaluate and assess the rationality of the use of antidiabetic drugs, especially the biguanide (metformin) group to maintain the quality and quality of diabetes mellitus drug administration so that the target of diabetes mellitus control can be optimized.

2. Methods

The research design is a descriptive study using secondary data from medical records in the medical records section of Dr. Moh Hoesin Hospital Palembang. The object of the study was all medical records of patients with type 2 diabetes mellitus who used metformin at RSMH Palembang in the period July 1st, 2019-July 31st, 2020, with complete medical record data and without serious comorbidities. The rationality for using metformin that was assessed in this study was the frequency of use, drug dose, route of administration, duration of administration, and drug interactions. The frequency of drug use is assessed by how many times the drug is taken in one day. The dose of metformin used is 500 mg or 850 mg. The method of administration of the drug is the method of consumption of the drug metformin and the duration of drug administration is the duration of administration of the drug written on the prescription. Drug interactions are reactions that arise between two or more drugs in the same use, in the form of synergism, namely the administration of one drug can strengthen the effects of other drugs, antagonists, namely the administration of one drug can reduce the effects of other drugs and potentiation, namely the administration of one drug can strengthen the effect of another drug by increasing the concentration of that other drug by the body.

The data used is secondary data through medical records obtained from the Medical Record Installation Section of RSMH Palembang. In data collection, the researcher does not take data directly, but by parties who are not researchers. The data collected in this study will be processed using the SPSS descriptive statistical method based on the number of cases recorded in the medical records of patients with diabetes mellitus according to the variables studied. The research results will be analyzed and presented in tabular form and will be explained in narrative form. The type of statistical analysis that will be used in this research is a univariate analysis which aims to describe the characteristics of each variable being studied.

3. Results

Table 1 shows the number of patients with type 2 DM with Metformin, the youngest age suffering from type 2 DM is 42 years, while the oldest age is 77 years. Where these results were obtained the average age group is 51-60 years old and 61-70 years old with a total of 17 patients (35.4%). The majority of patients were female as much as 60.4%. The majority of patients received 3-4 drugs per prescription.

Table 1. Baseline characteristic

Variable	Number of Cases (n)	Percentage (%)
Age		
40-50 years old	12	25.0
51-60 years old	17	35.4
61-70 years old	17	35.4
71-80 years old	2	4.2
Gender		
Male	19	39.6
Female	29	60.4
Number of Drugs Per Prescription		
1	8	16.7
2	9	18.8
3	13	27.1
4	10	20.8
5	8	16.7

Table 2 shows that drug interactions with metformin are still quite often encountered, although the majority are synergistic and potentiating interactions. There are still 2 cases or 4.2 percent who experience antagonistic interactions.

Table 2. Distribution of respondents based on drug Interactions

Drug Interactions	Number of Cases (n)	Percentage (%)
Synergistic Interactions	17	35.4
Potentializing Interactions	29	60.4
Antagonist Interactions	2	4.2

Table 3. Distribution of synergistic drug Interactions

Synergistic interactions	Number of cases (n)	Percentage (%)
Metformin + Glimepiride	9	18.8
Metformin + Glucobay	12	4.2
Metformin + Gliclazid	3	6.2
Metformin + Glibenclamid	3	6.2

Table 4. Distribution of potentiating drug Interactions

Potentiating interactions	Number of cases (n))	Percentage (%)
Metformin + Aspilet	2	4,2
Metformin + Amlodipine	10	20,8
Metformin + Captopril	6	12,5
Metformin + Ranitidine	5	10,4
Metformin + Furosemide	4	8,3
Metformin + Valsartan	2	4,2

Table 5. Distribution of antagonistic drug Interactions

Antagonist interactions	Number of cases (n)	Percentage (%)
Metformin + Spironolactone	1	2.1
Metformin + Methylprednisolone	1	2.1

Table 6 shows that the patients with the right dose set amounted to 47 patients with a percentage of 97.9%, exact frequency of delivery There were 48 patients with a percentage of 100% of drugs, 48 people (100%) on the right time to administer the drugs, 48 people on the right way of administering drugs (100%), 17 patients with the right drug interactions with a percentage of 35.4%, and the right drug interactions. potentiating drug interactions 29 patients with a percentage of 60.4%.

Table 6. The rationality for using Metformin

Variable	Appropriate			
	Yes	(%)	No	(%)
Dosage	47	97.9	1	2.1
Frequency of administration	48	100	0	0
Duration of administration	48	100	0	0
Method of administration	48	100	0	0
Synergistic interactions	17	35.4	0	0
Potentiating Interaction	29	60.4	0	0
Antagonist Interaction	0	0	2	4.2

4. Discussion

Glimepiride is a third-generation sulfonylurea drug with a longer duration of action and a faster onset of action. The use of a mixture of other antidiabetic drugs creates a synergistic relationship, where the activities of each drug reinforce each other to achieve the same goal, to lower glucose more. Glimepiride stimulates beta cells to secrete insulin, while metformin reduces hepatic glucose production, decreasing intestinal glucose absorption, and increase insulin sensitivity by increasing peripheral glucose uptake and utilization. Glimepiride can reduce cardiovascular complications and convert insulin released into glucose levels, especially in the postprandial state, with the aim that glimepiride is less hypoglycemic than glibenclamide. With the profile they have, the combination of Metformin and Glimepirid is more feasible and safe.[5-7] Metformin given concurrently with Glucobay can decrease metformin AUC levels. The alpha-glucosidase inhibitor Glucobay decreases the bioavailability of Metformin and reduces the normal peak plasma centralization of Metformin, but the chances of achieving that top fixation are unchanged. Patients should be informed of the need to monitor blood glucose levels regularly and be aware of indications for hypoglycemia.[8-10]

The most widely administered drugs and have potentiating interactions are antihypertensive drugs. Metformin given together with calcium channel blocker drugs such as amlodipine can reduce the effects of metformin and has a moderate level of pharmacodynamic interaction.[11,12] Metformin given concurrently with Ranitidine can increase plasma concentrations by slowing the renal tubular excretion of metformin.[13-15] Metformin given concurrently with captopril may increase the risk of hypoglycemia. Moreover, the simultaneous use of captopril will cause blood glucose levels to increase by 2.2 mmol/L after 24 hours and increase to 2.9 mmol/L after 48 hours. For this situation, the use of the drug Captopril can be

replaced with Valsartan class ARB (angiotensin receptor blocker), because Valsartan can lower blood pressure through the main enemy of the renin-angiotensin-aldosterone framework. Likewise, Valsartan can also reduce the release of albumin in the serum, if the excess albumin lost from the blood shows high blood glucose levels for a long time, so Valsartan can be overcome by slowing albumin secretion.[16-18] Metformin given together with furosemide will increase metformin levels in the blood, causing hypoglycemia, while metformin can reduce furosemide levels. Furosemide and metformin are secreted in the tubular portion of the kidney so that they can interact with each other in the tubular system, resulting in increased metformin levels. Furosemide can increase the plasma metformin concentration by 22% and metformin can reduce the peak concentration and elimination half-life of furosemide by 31% and 32%, respectively.[19]

Spironolactone is a diuretic drug. Metformin given concurrently with Spironolactone will induce renal impairment and dehydration which can increase the risk of lactic acidosis in patients concurrently using Metformin. Methylprednisolone is a corticosteroid class, Metformin which is given together with Methylprednisolone can inhibit glucose levels resulting in hyperglycemia, glucose intolerance, changes in glucose levels with new-onset, and exacerbation of diabetes mellitus.[20]

5. Conclusion

The rationality for the use of Metformin in Patients with Type 2 Diabetes Mellitus is based on the criteria for the right dose (100%), the right frequency of administration (100%), the right time for giving the drug (100%), the right way of giving the drug (100%), and the right way. drug interactions (95.8%).

6. References

1. Ministry of Health of the Republic of Indonesia. In 2030, the prevalence of diabetes mellitus in Indonesia reaches 21.3 million people. 2009.
2. PERKENI. Consensus on the Management and Prevention of Type 2 Diabetes Mellitus in Indonesia. Jakarta: PERKENI.2011
3. Vicckova V, Cornelius V, Kasliwal R, Wilton L, Shakir SA. Hypoglycaemia with oral antidiabetic drugs: results from the prescription-event monitoring cohorts of rosiglitazone, pioglitazone, nateglinide and repaglinide. Drug Saf. 2009; 32: 409–18
4. Istiqomatunnisa. The Rationality of the Use of Anti-Diabetes Drugs and Evaluation of the Cost of Pharmaceutical Supplies for Inpatients with the Healthy Jakarta Card at the Dr. Navy Hospital. Mintohardjo. Essay. Unpublished, Faculty of Medicine and Health Sciences, State Islamic University, Jakarta. 2014.
5. Khasanah M. Lifestyle in Diabetes Mellitus Patients. Essay. Unpublished, Faculty of Da'wah State Islamic Institute of Sunan Ampel, Surabaya. 2012.
6. Widya D. The Relationship between Nutritional Status and Physical Activity on Diabetes Mellitus in the Elderly in West Kalimantan Province. Essay. Unpublished, Faculty of Health Sciences, Esa Unggul University, Jakarta. 2015.
7. Naranjo, CA, Busto U., Sellers, EM, Sandor, P., Ruiz, I., Robert, EA, et al., A method for estimating the probability of adverse drug reactions, clinical pharmacology and therapeutics. 1981; 30:2:239 -45.
8. BPOM RI. Guidelines for Monitoring Drug Side Effects (MESO) for Health Workers. Jakarta: POM RI Agency. 2012.
9. Alomar MJ. Factors affecting the development of adverse drug reactions. Saudi Pharmaceutical Journal. Feb 2013: 22: 83 -94.
10. Arifin AL. The latest type 2 diabetes mellitus therapy guide. endocrinology & metabolism sub division / UPF. Internal Medicine. Medical School. UNPAD / RSUP dr. Hasan Sadikin Bandung. 2011.
11. Malin SK, Kashyap SR. Effects of metformin on weight loss: potential mechanisms. Curr Opin Endocrinol Diabetes Obes. 2014 Oct; 21(5): 323 -9.

12. Drugs.com. Metformin Side Effects. 2015. (http://www.drugs.com/sfx/metformin -side -effects.html. Accessed July 3, 2015).
13. Bouchoucha M, Uzzan B, Cohen R. Metformin and digestive disorders. Diabetes Metab 2011; 37: 90 -6.
14. Stoppler, MC, Glucophage Side Effects Center. http://www.rxlist.com/glucophage -side -effects -drug -center.htm. Accessed August 1, 2015.
15. Al Abri SA, S. Hayashi, KL Thoren, KR Olson. Metformin Ovedose -induced in the absence of other diabetic drugs. June 2013: 51(5): 444 -447.
16. US National Library of Medicine. metformin. 2015. (https://www.nlm.nih.gov/medlineplus/druginfo/meds/a696005.html. Accessed August 20, 2015).
17. Cunha, JP, 2015. Glumetza Side Effects Center. (On line). (http://www.rxlist.com/glumetza -side -effects -drug -center.htm, Accessed June 30, 2015).
18. Ting RZ, Szeto CC, Chan MH, Ma KK, Chow KM. Risk factors of vitamin B(12) deficiency in patients receiving metformin. Arch Intern Med. 2006; 166(18): 1975-9.
19. Drugs.com. Glimepiride Side Effects. 2015. (http://www.drugs.com/sfx/glimepirideside -effects.html. Accessed June 28, 2015).
20. Ogbru, O., Williams, E., Marks, JW Insulin: Drug Facts, Side Effects and Dosing. 2015. (http://www.medicinenet.com/insulin/article.htm. Accessed July 23, 2015).

CERTIFICATE

OF PUBLICATION

For the article titled:

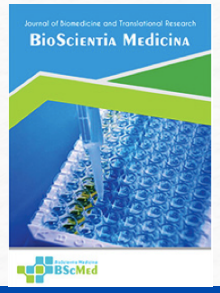
Evaluation of Rationality in Prescribing Metformin (Biguanide Group) at Dr. Mohammad Hoesin General Hospital Palembang

Authored by;

Nita Parisa, Dwi Tantri Marylin, Theodorus

Published in

Bioscientia Medicina Volume 6 Issue 3 2022



Accredited in:

Bioscientia Medicina S3 sinta Science and Technology Index

Indexed in:

CABI

INDEX COPERNICUS INTERNATIONAL

Dimensions