Occurrence of Hypoglycemia, Hypokalemia and Hyperkalemia in Diabetic Hypertensive Patients Using Insulin and Diuretics (Research Conducted in Outpatient and Hospitalized Patient in Sanglah General Hospital Denpasar)

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Abstract

Diabetes Mellitus (DM) is a metabolic disease with characteristics of hyperglycemia that occurs due to insulin secretion abnormalities, insulin work or both. DM can cause macrovascular complications such as hypertension. Administration of therapy may lead to hypoglycemic and hypokalemia that may increase the risk of impaired brain and heart. Objective: The purpose of this study to analyze the incidence of hypoglycemia and hypokalemia side effects in patients with diabetic hypertension using antidiabetes and antihypertensives. Method: The study was conducted retrospectively with retrospective patient medical records from January to December 2016. Blood and potassium blood glucose levels were measured as long as the patient was treated. Random and potassium blood glucose levels prior to therapy were compared with after therapy using paired t-test. Result : From the results of the study found 27 patients suffering from diabetic hypertension and get therapy. The value of changes in the patient's random blood glucose level averaged 280.89 mg/dl to 189.15 mg/dl, which met the target of antidiabetic drug therapy, and no patients had hypoglycemia. From 27 patients, as many as 7 people did not get antihypertensive therapy. Three patients had hyperkalemia (serum potassium level > 5 mEq/L). The value of changes in blood potassium levels of patients averaged 4.74 mEq/L to 4.46 mEq/L, where no patients had hypokalemia. Conclusion : the occurrence of hypoglycemia and hyperkalemia were suspected due to side effect of insulin and antihypertensive drugs.

Keywords : **diabetes mellitus, hypertension, hypoglycemia, hypokalemia, hyperkalemia.**

I. INTRODUCTION

Today, Diabetes Mellitus (DM) has become a health problem in the world, especially in Indonesia. Based on estimations from the World Health Organization (WHO) and International Diabetes Federation (IDF), the prevalence of diabetes in Indonesia is 5.6 million people in 2000[1]. Even in 2030 it is estimated that the prevalence of diabetes mellitus will increase to 21.3 million population[2]. In Bali, the prevalence of diabetes mellitus reached 5.9%, where prevalence in males 6.1% and females 5.7%[3]. One of the complications of diabetes mellitus is hypertension. Based on data from the American Heart Association (AHA) in

May 2012, at least 65% of people with diabetes mellitus died of heart disease or stroke. Adults with diabetes mellitus have two to four times the risk of developing heart disease when compared with people without diabetes mellitus[4].

In the case of rational therapy is required regulation of drug selection (indication), dose, duration of therapy, duration of therapy and identification of the right side effects of the drug. Drug side effectsare a peripheral or secondary effect but most of all are the unexpected secondary effects of a drug and are usually a detrimental effect. Drug side effects can also be defined by the various unintentional effects of a pharmaceutical product that

occurs in normal dosage use and related to the pharmacological effects of a drug.

One of the side effects of drug use of insulin is hypoglycemia. Hypoglycemia occurs when blood glucose levels in patients reach less than 100 mg/dl. Clinical manifestations felt by the patient in the form of dizziness, nausea, chills, eyes dizzy, cold sweats, and decreased blood pressure. In many cases, hypoglycemia can lead to decreased consciousness and coma. Hypoglycemia is the leading cause of death in patients with diabetes mellitus who use insulin[5]. Meamwhile, patient also require antihypertensive therapy which has side effect such as hypokalemia and hyperkalemia. This study aims to determine the incidence of hypoglycemia, hypokalemia, and hyperkalemia side effects in patients with diabetes mellitus with hypertension, as well as the value of changes in blood glucose levels random and blood potassium levels before and after antidiabetic and antihypertensive therapy.

II. MATERIALS AND METHODS

This research used retrospective design with descriptive method and descriptive prevalence which was conducted at Diabetic Center and Installation of Medical Record of Sanglah General Hospital, Denpasar.

2.1 Research Tools
Research tools used include data collection sheets to record data on patient medical records that include clinical data, laboratory results and drugs used by patients.

2.2 Research Methods
A. Population and Sample

The population in this study were all patients with type 2 diabetes mellitus with hypertensive complications who underwent treatment at Sanglah General Hospital Denpasar which has met the criteria of inclusion and exclusion. Inclusion criteria included patients with a diagnosis of diabetes mellitus and hypertension who received antidiabetic and or antihypertensive drug therapy and performed routine blood tests of random blood glucose and blood potassium levels, both before and after therapy. The goal of controlling blood glucose levels with antidiabetic drugs is less than 200 mg/dl. The condition of hypoglycemia is a condition of random blood glucose levels of patients less than 80 mg/dl, and the condition of hypokalemia is potassium blood levels of patients less than 3.0 mEq/L, whereas hyperkalemia is a condition of potassium blood levels of patients more than 5.0 mEq/L.

B. Sampling

Sampling is done by recording the medical record number obtained from the registration book of Polyclinic Diabetic Center SanglahGeneral Hospital Denpasar. Furthermore,

the research subjects obtained 27 patients who meet the inclusion criteria.

C. Data Retrieval

The data were collected by recording patient data on medical record such as clinical data, laboratory data (random blood glucose level and potassium level) and data about the drugs used by patients (antidiabetesdrugs such as insulin and antihypertensives drugs such as diuretics or other agents).Evaluation was performed before drug administration (pretreatment) up to three months after drug administration (posttreatment). The evaluation was done by looking at the blood glucose level of random blood and potassium content of each 1 point of data retrieval on patient medical record data. After taking data within a period of three months, it will be seen whether the patient can achieve the target of successful therapy.

D. Data Analysis

The data of the research are analyzed into two types, namely descriptive data and descriptive prevalence data. Descriptive data include sex, age, and antidiabetic and antihypertensive drugs presented in tabular form describing the percentage of antidiabetic and antihypertensive drugs used by patients.

III. RESULTS

3.1 Result of Patient Characteristic Database
Data were collected and clasified into patient characteristic database and type of antidiabetes drugs and antihypertensive drugs. Table 3.1 describes patient characteristic database such as sex and age of patients.

Table 3.1 Patient Characteristic Database

Characteristic	Information (n=27 patients)	Patients
Sex	Male	20
	Female	7
Age	40- 50 years old	7
	51 - 60years old	11
	61 - 70years old	9
	>70years old	0

3.2 Type of Antidiabetic and Antihypertensive Drugs Usage in Patients
Data were collected and clasified into two tables, such as types of antidiabetics drug usage and types of antihypertensive drugs usage in patients. Table 3.2 describes type of antidiabetic drugs usage in patients. Table 3.3 describes type of antihypertensive drugs usage in patients.

Table 3.2 Type of Antidiabetic Drugs Usage

Type	Name of Drugs (n=27 patients)	Percentage
Insulin	Basal Insulin	22
	Rapid Insulin	
Oral Antidiabetic Agents	Glikuidon	10
	Glimepiride	
	Metformine	

Table 3.3 Type of Antihypertensive Drugs Usage

Type	Name of Drugs (n=27 patiens)	Percentage
Angiontensin Converting Enzyme Inhibitor (ACEI)	Captopril	11
	Lisinopril	
	Ramipril	
Angiotensin Receptor Blocker (ARB)	Valsartan	6
Diuretic	Furosemide	5

3.3 Measurement and Improvement of Patient Laboratory Result

Data were collected include blood glucose level and potassium level before treatment with antidiabetic and antihypertensive drugs and after treatment with antidiabetic and antihypertensive drugs. Table 3.4 shows the measurement and improvement of patients laboratory result.

Table3.4. Measurement and Improvement of Patient Laboratory Result

Patient Laboratory Data	Highest Value	Lowest Value	Mean of value (pre-treatment, n=27 patients)	Mean of value (post-treatment, n=27 patients)	Improvement along therapy period
Random blood glucose level (mg/dl)	530.0	67.0	280.89	189.15	91.74
Blood potassium level (mEq/L)	8.9	3.0	4.74	4.46	0.28

IV. DISCUSSION

4.1 Characteristics of Research Subjects

Characteristics of research subjects described the identity of 27 patients type 2 diabetes mellitus with hypertension at Sanglah General Hospital Denpasar. By characteristic database such as sex character, male patients experienced more cases than female patients (Table 3.1). When viewed from the age group obtained patients with age group 41-45 years and 56-60 years had the most cases (Table 3.1). This was in line with the results of research from Kekenusa et al. (2013) where patients aged over 45 years have an 8-fold greater risk of developing diabetes mellitus when compared with patients under 45 years of age[6]. This was also due to decreased function of renal excretion at age 30 or 40 years and the presence of comorbids that appear in adulthood[7].

4.2 Type of Drug Usage in Patients

Antidiabetic drugs and antihypertensive drug were used by patients with type 2 diabetes mellitus with hypertension complication at SanglahGeneral Hospital Denpasar using insulin, namely insulin basal and insulin rapid. The rest use oral antidiabetics were mostly biguanides such as metformin (Table 3.2). These results were in line with research from Ludirdja et al. (2010) and Saraswati (2009) that the most types of antidiabetics oral usage was biguanides[8,9]. According to the American Diabetes Association (2016), people with type 2 diabetes mellitus are considered to start therapy with insulin at the time of their first diagnosis. In addition the dose flexibility of insulin can be used to design both initiating and adjusting therapy in patients. Insulin is also encouraged to be used in patients with type 2 diabetes mellitus who have not been able to achieve the target of blood glucose therapy[1].

Meanwhile, the use of antihypertensive drugs of ACEI and ARB groups received the majority of captopril and valsartan therapy (Table 3.3). In addition to the use of ACEI and ARB, there is the use of a loop diuretic with strong potency for diuresis (furosemide). Use of antihypertensive drugs of the ACEI or ARB class is recommended as first-line therapy in patients with hypertension[10].

4.3 Improvement of Patient Condition

After administration of antihypertensive and antidiabetic therapy in patients type 2 diabetes mellitus with hypertensive, it was found that the target of random blood glucose reduction after antidiabetic use was achieved from 280.89 mg/dl to 189.15 mg/dl (less than 200 mg/dl). In patients receiving antihypertensive therapy, there were no patients with hypokalemia. From the average acquisition of potassium levels of patients before therapy 4.74 mEq/L to 4.46 mEq/L and still in normokalemia conditions. There are several diseases that can cause or aggravate the occurrence of kidney damage that eventually develops into Chronic Kidney Disease (CKD). In the study, it was shown some of the diseases that were the aetiology of CKD from patients[11]. From the data, it was found that Diabetes mellitus is the biggest cause of CKDexperienced by patients

that is as much as 8 events (42,1%), next is combination of hypertension and diabetes mellitus occured 5 incidence (26,3%), and hypertension counted 4 incidence(21%). According to the literature, about 50% of people with diabetes mellitus develop disease progression to kidney failure. Diabetes mellitus can cause protein glycosylation which can increase cross-linking proteins that can damage collagen in the glomerular basement membrane. Diabetes mellitus can also cause increased intraglomerular pressure[12].

From the results of the study, 1 patients had hypoglycemia and no patients had hypokalemia, but there were hyperkalemia conditions in the patients, where 3 patients had elevated potassium levels more than 5.0 mEq/L. Hyperkalemia occurs when potassium intake is greater than its excretion or transeluler potassium distribution is impaired[13]. The main causes of hyperkalemia are increased potassium intake, decreased potassium excretion, absence of tubular response to aldosterone and redistribution of potassium to extracellular[13]. The prevalence of hyperkalemia in patients undergoing hospitalization is about 1-10%[14]. In this study there were potential side effects of antihypertensive drug (ACEI) that potentially cause hyperkalemia[14].

Symptoms of hyperkalemia include muscle weakness or paralysis, dizziness and nausea. But sometimes these symptoms are not visible especially if the increase in hyperkalemia is very fast. Hyperkalemia is characterized by a change in Electrocardiograph profile including an increase in T waves followed by a decrease in the amplitude of R waves, a decrease in resting membrane potential in the heart muscle, this decrease can lead to weakening of heart contraction. Abnormality of potassium serum immediately will result in ventricular arrhythmia or cardiac arrest[14].

In asymptomatic patients or patients with mild to moderate hyperkalemia (serum potassium concentrations ranging from 5.5 to 6.9 mEq/L), aggressive therapy is not recommended. The choice of treatment is to use a cation exchange resin or sodium polystyrene sulphonate, which can be used orally or rectally with enemas.In patients with severe hyperkalemia symptoms (serum potassium level> 7 mEq/L), immediate treatment with intravenous administration of calcium may be 10% of chloride or gluconate to protect the heart from the onset of arrhythmias[15]. The calcium preparation is used as a first line drug with a rapid onset of action to stabilize the myocardial electrical activity. The important thing to consider in the use of calcium is the effect of hypercalcemia that may arise. Under these conditions calcium gluconate should be dissolved in 100 ml of D5W (5% of dextrose in water for injection) and administered with infusion for 30 minutes[16].

V. CONCLUSION

Based on the research that has been done, it can be concluded that in this studythere was 1 patient with condition of hypoglycemia (blood glucose level 67 mg/dl) and there is no patient with hypokalemia condition. However, from 27 patients, 3 patients with hyperkalemia (serum potassium level > 5 mEq/L) were suspected to occur due to side effects of ACEI class antihypertensive drugs. The decrease in random blood glucose levels averaged 280.89 mg/dl to 189.15 mg/dl (met the target of antidiabetic drug therapy, and decreased blood potassium levels by 4.74 mEq/L to 4.46 mEq/L.

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REFERENCES

[1] American Diabetes Association, 2016. Standards of Medical Care in Diabetes-2016. *Diabetes Care*. Volume 39. Supplement 1. S57.

[2] PERKENI. 2011. *Konsensus Pengelolaan dan Pencegahan Diabetes Melitus Tipe 2 di Indonesia 2011*. Jakarta: Perkumpulan Endokrinologi Indonesia.

[3] Suastika, Ketut, dkk. 2011. Prevalence of Obesity, Metabolic Syndrome, Impaired Fasting Glycemia, and Diabetes in Selected Villages of Bali, Indonesia. *Journal of the ASEAN Federation of Endocrine Societies.* Vol. 26, No.2. 159-162.

[4] American Diabetic Association. 2011. Living with Diabetes: Complications, Available at: http://www.diabetes.org/living-with-diabetes/complications/pregnant-women/after-delivery.html. cited on: 25 April 2015

[5] Soelistijo, Soebagijo Adi, dkk. 2015. *Konsensus Pengelolaan dan Pencegahan Diabetes Melitus Tipe 2 di Indonesia 2015*. Jakarta: PB PERKENI.

[6] Kekenusa, John S., Budi T. Ratag dan Gloria Wuwungan. 2013. *Analisis Hubungan Antara Umur dan Riwayat Keluarga Menderita DM dengan Kejadian Penyakit DM Tipe 2 Pada Pasien Rawat Jalan di Poliklinik Penyakit Dalam BLU RSUP Prof. Dr. R.D Kandou Manado*. Manado: Fakultas Kesehatan Masyarakat Universitas Sam Ratulangi.

[7] Jelantik, I G M Geria dan Erna Hayati. 2014. Hubungan Faktor Risiko Umur, Jenis Kelamin, Kegemukan dan Hipertensi dengan Kejadian Diabetes Melitus Tipe II di Wilayah Kerja Puskesmas Mataram. *Media Bina Ilmiah.* Volume 8, No.1. 39-44

[8] Ludirdja, Jovita Secunda, Leonard Kencana, Katrin Kurniawan, Michelle Prinka Adyana dan IGP Suka Aryana. 2010. Rerata Durasi Penderita Diabetes Melitus Terkena Nefropati Diabetik Sejak Terdiagnosis Diabetes Melitus Pada Pasien di Poliklinik Geriatri RSUP Sanglah. *IPTEKMA.* Volume 2 No.1. 15-19

[9] Saraswati, Ni Made Weda. 2009. *Studi Penggunaan Obat pada Pasien Diabetes Mellitus Tipe 2 dengan Komplikasi Hipertensi di Unit Rawat Inap RSUP Sanglah Denpasar Tahun 2008* (Skripsi). Bukit Jimbaran: Jurusan Farmasi Fakultas MIPA Universitas Udayana.

[10] Joint National Committee (JNC) VII. 2004. *The Seventh Report of the Joint National Committee on: Prevention, Detection, Evaluation, and Treatment of High Blood Pressure*. United States: National Institutes of Health.

[11] Haneda, Masakazu, dkk. 2015. A new Classification of Diabetic Nephropathy 2014: a report from Joint Committee on Diabetic Nephropathy. *Journal of Diabetes Investigation*. Vol. 6. No.2. 242-246.

[12] Gross, Jorge L., De Azevedo, Mirela J., Silviero, Sandra P., Canani, Luis Henrique, Caramori, Maria Luiza dan Zelmanovitz, Themis. 2005. Diabetic Nephropathy: Diagnosis, Prevention, and Treatment. *Diabetes Care.* Volume 28, Number 1. 164-176.

[13] Joy, M.S., Kshirsagar, A., Paparello, J., 2005. Chronic Kidney Disease: Progression-Modifying Therapies. *In*: DiPiro, J. T., Talbert, R. L., Yee, G. C., Matzke, G. R., Wells, B. G., Posey, L. M., ***Pharmacotheraphy A Pathophysiologic Approach***, Ed 6th, New York: McGraw Hill Medical Publishing Devision., p.799-820

[14] Rodriguez, Joyce C. Hollander., Calvert, James F., 2006. Hyperkalemia*. **American Family Physician** Volume 73, No 2.*www.aafp.org/afp*., p. 283-290

[15] Brophy, D. F., Gehr T. W. B., 2005. Disorder of Potassium and Magnesium Homeostasis. *In*: DiPiro, J. T., Talbert, R. L., Yee, G. C., Matzke, G. R., Wells, B. G., Posey, L. M., ***Pharmacotheraphy A Pathophysiologic Approach***, Ed 6th, New York: McGraw Hill Medical Publishing Devision., p. 967-979

[16] Andayani, Esthi. 2008, *Perubahan Kadar Gula Darah Pasien Penyakit Gagal Ginjal Kronik pada Terapi Hiperkalemia Dengan Insulin 2 Unit Dan Dextrose 40% 25 ml,*Tesis : Fakultas Farmasi Universitas Airlangga, p.69-79