

Drug Related Problems of Diabetic Nephropathy Patients in a Tertiary Hospital in Malaysia

Dika P. Destiani, Athirah Ghazali

Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Universitas Padjadjaran, Jatinangor, West Java, Indonesia

Abstract

Patients with diabetic nephropathy (DN) are particularly vulnerable to drug related problems (DRPs) due to complex medication regimen and renal dysfunction. However, there was limited information regarding prevalence of DRPs among patients with DN in Malaysia. This research was conducted to determine the prevalence of DRPs among hospitalized patients with DN at tertiary hospital in Malaysia during June 2014-May 2015. This was a retrospective observational descriptive study that used patients medical records as data source. There were 104 subjects included in this study. The prevalence of DRPs among the included subjects was 74%. Most DRPs observed were from two categories, namely non-compliance to medication and adverse drug reactions (20.93% for both categories). These categories were followed by the category of unnecessary drugs (16.28%), too low dose (15.81%), inappropriate drugs (11.16%), untreated indication (10.23%) and too high dose (4.65%). The prevalence of DRP was high among DN patients, thus pharmacists are encouraged to perform comprehensive medication review to improve health outcomes and enhance patients safety.

Keywords: drug related problems, diabetic nephropathy, T2DM

Introduction

Type 2 diabetes mellitus (T2DM) is a metabolic disorder characterized by hyperglycemia caused by either a lack of insulin or the body's inability to use insulin efficiently. The chronic hyperglycemia is associated with long-term damage and dysfunction of various organs.^{1,2} T2DM increases the risk of microvascular complication, such as diabetic nephropathy (DN).³

Diabetic nephropathy (DN) is a major cause

of chronic kidney disease and end-stage renal failure worldwide. Its clinical syndromes include the presence of pathological quantities of urine albumin excretion, diabetic glomerular lesions, and loss of glomerular filtration rate (GFR) in diabetics. Poor control of blood glucose is one of the risk factors of DN.^{4,5}

Patients with DN often receive complex medication regimen. This condition may increase the risk of drug related problems (DRPs) among DN patients. DRPs represent

Corresponding author: Dika P. Destiani. Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Universitas Padjadjaran, Jatinangor, West Java, Indonesia. Email: dika.pramita@unpad.ac.id

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the categorization of clinical problems related to the use of medications, including inappropriate drugs, non-compliance, adverse drug reaction (ADR), *etc.*⁶⁻¹⁰

However, there was limited information regarding the prevalence of DRPs among DN patients in Malaysia. This study was conducted to investigate the prevalence of DRPs and the most common DRPs categories in hospitalized DN patients in a tertiary hospital in Malaysia.

Methods

This retrospective study involved hospitalized DN patients at a tertiary hospital in Malaysia from June 2014 to May 2015. The data source was the medical records of the patients. We included DN patients whose age ≥ 18 years old and those who received at least two drugs for the treatment of DN. The exclusion criteria was incomplete patient data

From each record, the following data were extracted; medical prescriptions and patient data, *i.e.*, name, age, sex, duration of illness, duration of treatment, the results of treatment, diagnosis, number of drug doses, type of drug administered, concomitant drugs, and laboratory tests data. The data obtained were transferred and summarized in data collection sheet.

DRPs were further analyzed using standard

literature of appropriate drug use such as the British National Formulary, Monthly Index of Medical Specialities, Drug Information Handbook and Drug Interaction Facts.

Results and Discussion

104 participants were included in this study. Data regarding patient profile and DRPs were obtained.

Patient profile

The number of female patients was dominant compared to the male patients (61%). Previous study showed that both men and women had the same prevalence and risk of DN.¹¹ Most patients were in the age of 45 to 64 years (61%). American Diabetes Association (ADA) stated that one of the risk factor in developing complication among T2DM patients is ≥ 45 years old.² The average duration of hospitalization was 1-3 days which was related to the effectiveness of treatment and comorbidities. About 54% of the patients had improved condition when discharged from the hospital. 45% of the patients have been diagnosed with T2DM for 11-15 years. Duration of disease was related to the development of complication.⁵

The most widely use antidiabetic drugs was insulin group. Insulin is the most appropriate drug therapy for DN patients.¹² The use of metformin should be given in a controlled

Table 1. Total of DRPs among patients with DN

No	Classification of DRPs	Frequency	Percentage (%)
1	Untreated indication	22	10.23
2	Unnecessary drug	35	16.28
3	Inappropriate drug	24	11.16
4	Too high dose	10	4.65
5	Tow low dose	34	15.81
6	Non-compliance to medication	45	20.93
7	ADR	45	20.93
Total		215	100

Table 2. Causes of DRPs in the category of inappropriate drugs

No	Causes of DRPs	Frequency
1	Drugs given were not the most effective drugs	13
2	Drugs given were effective, but not safe	9
3	Drugs given were right, but inappropriate for patient's condition	4
	Total	26

dosage.¹³ The most commonly used drugs to control DN was Angiotensin II Receptor Blocker (ARB) and angiotensin-converting enzyme inhibitor (ACEI). Previous studies showed that ARB triggers favorable changes in systemic blood pressure, renal hemodynamics, and proteinuria similar to those induced by ACEI. The combination of ARB and ACE inhibition is safe and more effective than monotherapy to reduce systemic blood pressure and albuminuria in DN.¹⁴

DRPs

The prevalence of DRPs was 77%. The most common DRPs experienced by patients were non-compliance to medication and adverse drug reaction (ADR), in which 45 cases (20.93%) were observed in both categories respectively. The other DRPs observed included untreated indication (10.23%),

unneeded drug (16.28%), inappropriate drug (11.16%), too high dose (4.65%), and too low dose (15.81%). (Table 1)

Untreated indication

17 patients had symptoms of health problem with no drugs were given to address such issue. For example, the patient had a fever but an antipyretic was not prescribed. In other 15 cases, patients were not given additional medication for the prevention of side effects that arise when taking medication.

Unnecessary drugs

The main cause of such cases were due to redundant effects from duplication of treatment whose mechanism of actions were similar (22 cases). Another cause was the administration of drugs without indication (13 cases).

Table 3. Group of drugs that caused DRPs in the category of too low dose

No	Group of Drugs	Frequency
1	Antidiabetic drugs:	
	Biguanide	11
	Sulphonylurea	2
	Subtotal	13
2	DN drugs:	
	ACEI	10
	ARB	7
	Calcium channel blocker	3
	Diuretic	1
	Subtotal	21
	Total	34

Table 4. Class of drugs that caused ADR

Class of Drugs	Frequency	%
ACEI	10	43.48
Antidiabetic	6	26.10
Calcium channel blocker	4	17.39
Diuretic	3	13.03
Total	23	100

Inappropriate drugs

There were three main causes of inappropriate drugs given in this study. First, patients received the drug but not the most effective. For example, metoprolol, a beta blocker, was given to patients. However, the more appropriate drug for DN patients was ACEI, such as perindopril. Previous study showed that ACEI could reduce the symptoms of albuminuria with a higher percentage from beta blocker.¹⁵ Second, the patients received the drugs that were effective, but not safe. Gliclazide was not appropriate for patients who had renal impairment.¹⁶ Third, the patients received the right type of drug, but it was inappropriate for patients condition. Irbesartan 300mg can only be used in T2DM patients who had a serum creatinine > 300 mg/ml.¹⁷ (Table 3)

Too low dose

The most frequent DRPs in this category came from biguanide group. Metformin should be given in a dose of 500 mg, but it was given in a dose of 250 mg twice daily. Irbesartan, an ACEI, was prescribed with a dose of 150 mg 1x/day which is not sufficient because the required dose for nephropatic complication is 300 mg 1x/day.¹⁷ (Table 4)

Too high dose

Gliclazide was often given in the dose of 160 mg 1x/day, while the appropriate dose for DN patients was 80 mg 1x/day.¹⁸ (Table 5)

Non-compliance

Patient compliance to medication is necessary to achieve the optimum therapeutic effect. Non-compliance could be resulted from the administration of too many combinations of drugs and inconvenience frequency and dosing. Besides, error in taking medication was also one of the causes of the non-compliance. It was found that most patients stored drugs in wrong and incompatible container for example Telmisartan 80 mg medication stored in the Ranitidine 150 mg container. Poor adherence was associated with development of complications.^{19,20}

ADR

We found that most frequent ADR observed were associated with the use of ACEI, such as dry cough and hyperkalemia. Hypoglycemia was also one of the side effects of antidiabetic drugs that was frequently reported by patients (Table 4). Drug interactions occur when one drug alters the pharmacological effect of another drug. The pharmacological effect of one or both drugs may be increased or decreased, or a new and unanticipated toxicity may be produced. Increased toxicity can be resulted from pharmacodynamic or pharmacokinetics interaction.²¹⁻²⁴

Conclusion

The prevalence of DRP was high among DN patients, thus pharmacists are encouraged to perform comprehensive medication review to improve health outcomes and enhance patients safety.

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Conflict of Interest

None declared.

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Antioxidant Activity of Ethanol Extract of *Polygonum pulchrum* Blume

Asman Sadino¹, Idin Sahidin¹, Wahyuni Wahyuni²

¹ Department of Natural Products Chemistry, Faculty of Pharmacy, Halu Oleo University, Kendari, South East Sulawesi, Indonesia

² Department of Pharmacology and Toxicology, Faculty of Pharmacy, Halu Oleo University, Kendari, South East Sulawesi, Indonesia

Abstract

The use of antioxidants from natural resources has attracted increasing interest. One of the plant that was empirically used as an antioxidant dietary supplement was *Polygonum pulchrum* Blume (*P. pulchrum* Blume). This study aimed to investigate antioxidant activity of roots, stems, leaves and flowers ethanol extract of *P. pulchrum* Blume. The extract was obtained by maceration method using ethanol solvent. Antioxidant activity was determined with 1,1-diphenyl-picrylhydrazyl (DPPH) method. We found that ethanol extracts of *P. pulchrum* Blume roots and stems had strong antioxidant activity with IC₅₀ values of 25.2 mg/l and 43.26 mg/l, respectively. Ethanol extract of flowers had the weakest antioxidant activity with IC₅₀ value of 202.96 mg/l. Vitamin C had very strong antioxidant activity with IC₅₀ value of 3.97 mg/l. In conclusion, this study revealed that ethanol extract of *P. pulchrum* Blume roots and stems had strong antioxidant activity, therefore, this plant might be potential as an excellent source for natural antioxidant agents for medical application.

Keywords: *Polygonum pulchrum* Blume, DPPH, antioxidant, maceration, ethanol

Introduction

The use of antioxidants derived from plants have widely improved around the world. Many plants contain various phytochemicals which possess antioxidant activity to protect cells from damaging effects of reactive oxygen species (ROS), such as superoxides, peroxy radicals, hydroxyl radicals and peroxynitrites.^{1,2}

In human, production of ROS as the result of biochemical process might increase with several factors, including toxins and chemicals in food, pollutants, radiations, etc. Antioxidants compounds are needed to tackle this problem. However, synthetic antioxidant compounds such as butylated hydroxytoluene and hydroxyanisole might cause various side effects.³ This encourage researchers to find

Corresponding author: Asman Sadino, Department of Natural Products Chemistry, Faculty of Pharmacy, Halu Oleo University, Kendari, South East Sulawesi, Indonesia. Email: asmansadino51@gmail.com

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