Jurnal Eduhealth
Volume 16, Number 04 2025 DOI 10.54209/eduhealth.v16i04
ESSN 2808-4608 (Online)
https://ejournal.seaninstitute.or.id/index.php/healt

Effect of Candesartan on Creatinine and Albuminuria in Geriatric Patients with Diabetic Nephropathy

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Article Info
Keywords:
candesartan, creatinine, proteinuria, diabetic, nephropathy

ABSTRACT
Diabetes can cause various chronic complications, one of the most feared being diabetic nephropathy. Diabetic nephropathy is characterized by proteinuria and/or decreased glomerular filtration rate. Diabetic nephropathy is a major cause of chronic kidney disease, which can lead to end-stage renal disease requiring hemodialysis. Candesartan is an angiotensin receptor blocker antihypertensive drug. In addition to lowering blood pressure, candesartan is also thought to decrease renal vascular resistance, resulting in a decrease in microalbuminuria or proteinuria in patients with diabetes mellitus. Diabetic nephropathy increases with age, and geriatric patients have a lower response to therapy than adults. To determine the effect of candesartan on creatinine and albuminuria in geriatric patients with diabetic nephropathy. This was a cross-sectional study of 25 geriatric patients diagnosed with diabetic nephropathy who had been given 16 mg of candesartan as an antihypertensive at the Puri Raharja Hospital Denpasar outpatient clinic. Subjects who met the inclusion and exclusion criteria were recruited using consecutive sampling. The diabetic nephropathy subjects were evaluated for creatinine and proteinuria levels at the time of diagnosis and 3 months after receiving 16 mg of candesartan. All data were obtained from medical records. The study involved 25 patients consisting of 13 men (52%) and 12 women (485%). Subjects aged between 60-82 years with initial creatinine levels of 0.80-2.60 mg/dL, final creatinine levels of 1.395 ± 0.50 SD, initial positive proteinuria levels of 0-2, and final positive creatinine levels of 0-1. Based on the T-test, there was no significant difference between initial and final creatinine levels with a p value = 0.892 (95% CI -0.045-0.051). Based on the Wilcoxon test, there was a significant difference between proteinuria levels before and after candesartan administration with a p value p <0.05. This study did not find a significant decrease in creatinine after candesartan administration. However, candesartan significantly reduced proteinuria in geriatric patients with diabetic nephropathy.

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INTRODUCTION

Diabetes mellitus (DM) is a chronic carbohydrate metabolism disorder characterized by hyperglycemia caused by defects in insulin secretion, defects in insulin action, or both.[1]

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Diabetes mellitus (DM) currently affects more than 2 million people worldwide. The World Health Organization (WHO) predicts an increase in the number of people with diabetes in Indonesia from 8.4 million in 2000 to around 21.3 million in 2030. The International Diabetes Federation (IDF) predicts an increase in the number of people with diabetes in Indonesia from 9.1 million in 2014 to 14.1 million in 2035. [1,2]

Without good blood sugar control, this disease can lead to various chronic complications, including microvascular and macrovascular complications. These complications lead to increased mortality and morbidity. Microvascular complications include nephropathy, retinopathy, and neuropathy. Macrovascular complications include peripheral artery disease, cerebrovascular disease, and cardiovascular disease. [1]

Diabetic nephropathy is a chronic microvascular complication characterized by increased urinary albumin excretion (proteinuria) or a decreased glomerular filtration rate. Proteinuria is found in 30% of patients with type I diabetes and 40% of patients with type II diabetes. Diabetic nephropathy is a leading cause of chronic kidney disease requiring hemodialysis or kidney transplantation.[1,2,3]

Candesartan is an angiotensin receptor blocker (ARB) antihypertensive drug. It lowers blood pressure by inhibiting the angiotensin II type I receptor. Previous research has shown that in addition to lowering blood pressure, candesartan also decreases renal vascular resistance, resulting in a reduction in microalbuminuria or proteinuria in patients with diabetes mellitus. This suggests that candesartan may slow the progression of diabetic nephropathy.[4]

With increasing age, the course of diabetic nephropathy becomes more progressive. This results in an increased incidence of diabetic nephropathy in geriatric patients. Geriatric patients also have numerous comorbidities and may respond to therapy more slowly than adults. Research on the effects of candesartan on creatinine clearance and proteinuria, particularly in elderly patients with diabetic nephropathy, is still limited.

RESEARCH METHODS

This study aimed to determine the effect of candesartan on creatinine and albuminuria in geriatric patients with diabetic nephropathy. This was a cross-sectional study involving 25 geriatric patients with diabetic nephropathy who also suffered from hypertension at the outpatient clinic of Puri Raharja Hospital, Denpasar. Subjects who met the inclusion and exclusion criteria were recruited using consecutive sampling. The inclusion criteria were subjects who had been diagnosed with diabetic nephropathy and were ≥ 60 years old. The exclusion criteria were patients with stage V chronic kidney disease undergoing hemodialysis therapy. The subjects with diabetic nephropathy were evaluated for creatinine and proteinuria levels at the time of initial diagnosis and 3 months after administration of 16 mg candesartan. All data were taken from medical records. To determine the difference in creatinine and proteinuria levels before and after treatment in the same group, a paired comparative test was used, namely the Paired Sample t-Test and the alternative Wilcoxon Signed-Rank Test. Data analysis used SPSS software.

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RESULTS AND DISCUSSION

The study involved 25 geriatric subjects with diabetic nephropathy, consisting of 13 men (52%) and 12 women (48%). Subjects were aged 60-82 years, with initial creatinine levels of 0.80-2.60 mg/dL, final creatinine levels of 1.395 ± 0.50 SD, initial positive proteinuria levels of 0-2, and final positive creatinine levels of 0-1.

Table 1. Characteristics of Research Subjects

Characteristics	Frequency (%), mean±SD, minimum-maximum
Gender	
- male	13 (52%)
- female	12 (48%)
Age	60-83 years old
Initial creatinine level	0,80-2,60 mg/dL
Final creatinine level	1,395±0,50 mg/dL
Initial proteinuria	(0)- (+2)
Late proteinuria (Dipstick score)	(0)-(+1)

Table 2. Comparison of Creatinine Levels Before and After Intervention

Variable	Pre-test	Post-test	p	95% Confidence Interval (CI)
Creatinine level (mg/dL)	0,80-2,60	1,395±0,50	0,892	-0,045-0,051

Based on the T Test, there was no significant difference between initial and final creatinine levels with a p value of 0.892 (95% CI -0.045-0.051).

Table 3. Changes in Proteinuria Score Before and After Candesartan Administration

Variable	Pre-test	Post-test	P Wilcoxon
Proteinuria Level (Dipstick score)	(0) – (+2)	(0) – (+1)	0.005

Based on the Wilcoxon test, proteinuria decreased in 15 study subjects, proteinuria increased in 3 subjects, and proteinuria persisted in 7 patients. The Wilcoxon test showed a significant difference between proteinuria levels before and after candesartan administration with a p value of 0.005 ($p<0.05$).

In this study, there was a significant difference between proteinuria levels before and after administration of candesartan with a p value <0.05, which means that candesartan significantly reduced proteinuria in geriatric patients with diabetic nephropathy, which means it improved the progression of diabetic nephropathy.

Candesartan is an ARB that works by inhibiting the AT1 receptor. In patients with diabetic nephropathy, this drug helps lower intraglomerular pressure, which directly reduces protein leakage (proteinuria) and slows the progression of kidney damage. Candesartan not only lowers blood pressure but also reduces oxidative stress in kidney podocytes.[8]

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ACE inhibitors or ARBs are recommended for all diabetic patients with blood pressure ≥ 130/80 mmHg regardless of kidney function. ACE inhibitors or ARBs are also recommended for persistent albuminuria (albumin-to-creatinine ratio (ACR) > 3 mg/mmol) even if the patient has normal blood pressure.[8,9,10]

ACE inhibitors and ARBs are equally effective in preventing or slowing the progression of DKD. However, ACE inhibitors have more side effects, such as coughing, making ARBs superior to ACE inhibitors. ACE inhibitors and ARBs are generally started at low doses and titrated to the maximum tolerated dose in the management of patients with DKD.[9]

In this study, there was no significant difference between the initial and final creatinine levels after administration of 16 mg of candesartan with p = 0.892 (95% CI -0.045-0.051), which means that there was no significant decrease in creatinine after administration of candesartan.

Serum creatinine is a commonly used routine test to assess kidney function. It's quick and easy to perform. However, because creatinine is strongly influenced by muscle mass, in patients with relatively low muscle mass, such as women and the elderly, the results sometimes don't reflect true kidney function. Geriatric patients can have serum creatinine levels within the normal range even though their kidney function is severely impaired. In this study, the subjects were geriatric patients, which means the measured creatinine may not reflect true kidney function.

CONCLUSION

Candesartan significantly reduced proteinuria in geriatric patients with diabetic nephropathy, which means it improved the progression of diabetic nephropathy. No significant reduction in creatinine was observed after candesartan administration in geriatric patients with diabetic nephropathy. This study has limitations due to its cross-sectional nature. Further research using better methods, such as case-control studies or longer-term clinical trials, is recommended to increase the validity of the study.

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