ISSN 2808-4608

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

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Diabetic nephropathy (DN) is a major complication of diabetes, leading to proteinuria and declining kidney function. Candesartan, an angiotensin receptor blocker, may offer renal benefits beyond blood pressure control. Its specific effects on creatinine and proteinuria in geriatric DN patients remain underexplored. A cross-sectional study was conducted with 25 geriatric DN outpatients at Puri Raharja Hospital. Using consecutive sampling, subjects receiving 16 mg candesartan daily had their serum creatinine and proteinuria levels evaluated from medical records at baseline and after three months. The cohort (60-82 years) comprised 13 men and 12 women. Initial creatinine ranged from 0.80-2.60 mg/dL, with a final mean of 1.395 ± 0.50 mg/dL. Statistical analysis (paired T-test) showed no significant change in creatinine levels (p=0.892). However, proteinuria significantly decreased post-treatment (Wilcoxon test, p=0.005). Candesartan administration did not significantly reduce serum creatinine in geriatric DN patients over three months. However, the significant reduction in proteinuria indicates a beneficial effect on renal pathology, potentially slowing DN progression in this population.
Keywords: Candesartan, Creatinine, Proteinuria, Geriatrics, Diabetic Nephropathy

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1. Introduction

Diabetes mellitus (DM), a chronic disorder of carbohydrate metabolism characterized by persistent hyperglycemia, represents one of the most significant global health challenges of the 21st century. Its worldwide prevalence is immense, affecting over 2 million people, with a particularly alarming trajectory in Indonesia. Epidemiological projections highlight the scale of the problem: the World Health Organization (WHO) predicts an increase from 8.4 million cases in 2000 to approximately 21.3 million by 2030, a trend corroborated by International Diabetes Federation (IDF) estimates of a rise from 9.1 million in 2014 to 14.1 million by 2035 (Mezil and Abed, 2021).

The clinical burden of DM extends beyond hyperglycemia to devastating chronic complications, which are categorized into microvascular and macrovascular types, leading to substantially increased morbidity and mortality (Imanudin, Kurniawan and Rohmayanti, 2022). Among these, diabetic nephropathy (DN) is a predominant microvascular complication and a critical driver of end-stage renal disease. It is clinically defined by increased urinary albumin excretion (proteinuria) or a decreased glomerular filtration rate (Lim, 2014; Mezil and Abed, 2021).

The prevalence of proteinuria is notably high, found in 30% of patients with type 1 diabetes and 40% of those with type 2 diabetes, cementing DN's role as a leading cause of chronic kidney disease worldwide

(Pecová *et al*., 2023), The cornerstone of pharmacotherapy to retard DN progression is the use of renin-angiotensin system inhibitors, such as the angiotensin receptor blocker (ARB) candesartan. Previous research has robustly established that candesartan confers renoprotective benefits that extend beyond blood pressure control. By inhibiting the angiotensin II type 1 receptor, it decreases renal vascular resistance, leading to a significant reduction in proteinuria in diabetic patients, thereby slowing the progression of nephropathy (Mezil and Abed, 2021).

However, a critical and unresolved issue in translating this evidence into practice for all patient groups is the distinct physiological and clinical profile of the geriatric population. Diabetic nephropathy is a progressive condition, resulting in a high prevalence among elderly patients (Ganesan and Orgill, 2024). This demographic is particularly challenging to manage due to age-related pharmacokinetic changes, polypharmacy, and a higher burden of comorbidities, all of which may predispose them to a slower or attenuated response to standard therapies compared to younger adults. (Lim, 2014; John, 2016; Mezil and Abed, 2021).

Consequently, while the efficacy of ARBs like candesartan is well-documented in broad adult populations, there is a pronounced gap in targeted evidence regarding their effects on key renal parameters—specifically creatinine and proteinuria—in the geriatric subset with DN. This study is designed to address this specific evidence gap. Its novelty lies in its exclusive focus on evaluating the dual renal outcomes of serum creatinine and albuminuria following candesartan therapy specifically in elderly patients, a population that is both high-risk and underrepresented in existing clinical research. Therefore, the primary objective of this research is to determine the effect of candesartan administration on creatinine and albuminuria levels in geriatric patients diagnosed with diabetic nephropathy. Candesartan is an angiotensin receptor blocker (ARB) antihypertensive drug. It lowers blood pressure by inhibiting the angiotensin II type 1 receptor. Previous research has shown that in addition to lowering blood pressure, candesartan also decreases renal vascular resistance, resulting in reduced mineraloalbuminuria or proteinuria in patients with diabetes mellitus. This means candesartan can slow the progression of diabetic nephropathy (Mimran and Alfaro, 2003).

Diabetic nephropathy progresses over time. This results in a high prevalence of geriatric patients with diabetic nephropathy (Cahyani *et al*., 2024). Geriatric patients have numerous comorbidities and a likely slower response to therapy than adults. Research on the effects of candesartan on creatinine clearance and proteinuria, particularly in elderly patients with diabetic nephropathy, is still limited.

2. Methods

This study aimed to determine the effects of candesartan on creatinine clearance and albuminuria in geriatric patients with diabetic nephropathy. This was a cross-sectional study of 25 geriatric patients with diabetic nephropathy at the outpatient clinic of Puri Raharja Hospital, Denpasar. Subjects who met the inclusion and exclusion criteria were recruited using consecutive sampling. Inclusion criteria were subjects with diabetic nephropathy and aged ≥ 60 years. Exclusion criteria were patients with stage V chronic kidney disease undergoing hemodialysis.

Subjects with diabetic nephropathy who had been given 16 mg of candesartan were evaluated for creatinine clearance and proteinuria levels before and three months after administration. All data were obtained from medical records. Statistical analysis was performed to examine the effect of candesartan administration on renal parameters. The collected data were analyzed using statistical software. The Shapiro-Wilk test for normality of data distribution was first performed. Based on the results of the normality test, comparisons between pre- and post-therapy conditions were analyzed using two different methods: the paired sample t-test was used to compare normally distributed serum creatinine levels, while

the Wilcoxon signed-rank test (non-parametric test) was used to analyze differences in non-normally distributed albuminuria/proteinuria levels. The statistical significance value was set at $p < 0.05$, and the results are presented with 95% confidence intervals.

3. Results And Discussion

Results

The study involved 25 geriatric subjects with diabetic nephropathy, consisting of 13 men (52%) and 12 women (485%). The subjects were 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.

Table 1. Characteristics of Research Subjects

Characteristics	Frequency (%), mean ± SD, minimum-maximum
Gender	
- Male	13 people (52%)
- Female	12 people (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	+ 0-1

Based on the Shapiro-Wilk normality test, initial and final creatinine levels were not normally distributed. Data transformation was then performed, resulting in creatinine levels before and after transformation being normally distributed. A t-test showed no significant difference between initial and final creatinine levels, with a p-value of 0.892 (95% CI -0.045-0.051).

Based on the Shapiro-Wilk normality test, proteinuria levels before and after candesartan administration were not normally distributed before and after data transformation. Therefore, an alternative test, the Wilcoxon test, was performed. The Wilcoxon test revealed a decrease in proteinuria in 15 study subjects, an increase in proteinuria in 3 subjects, and persistent proteinuria in 7 patients. A Wilcoxon test revealed a significant difference between proteinuria levels before and after candesartan administration, with a p-value of 0.005 ($p<0.05$).

Discussion

In this study, there was a significant difference between proteinuria levels before and after candesartan administration with a p value of 0.005 ($p<0.05$), indicating that candesartan significantly reduced proteinuria in geriatric patients with diabetic nephropathy, thus improving the progression of diabetic nephropathy.

A previous study conducted by Carl Erik Mogensen in 2000 assessed and compared the effects of candesartan or lisinopril, or both, on blood pressure and urinary albumin excretion in patients with microalbuminuria, hypertension, and type 2 diabetes aged 30-75 years. The study was a prospective, randomized, parallel, double-blind study with four weeks of placebo and 12 weeks of monotherapy with candesartan or lisinopril followed by 12 weeks of monotherapy or combination treatment in hospitals and primary care centers in four countries. The results showed that candesartan 16 mg once daily was as effective as lisinopril 20 mg once daily in reducing blood pressure and microalbuminuria in hypertensive patients with type 2 diabetes ($p<0.001$) (Mogensen *et al.*, 2000).

ACE inhibitors or ARBs are recommended for all diabetic patients with blood pressure ≥ 130/80 mmHg regardless of kidney function, or albuminuria, i.e., persistent albumin-to-creatinine ratio (ACR) > 3 mg/mmol (Talari *et al.*, 2024), even if the patient has normal blood pressure. ACE inhibitors or ARBs are not recommended for primary prevention of DKD in normotensive diabetic patients with normal ACR and GFR (Horwitz and Schelling, 2014).

ACE inhibitors and ARBs preserve kidney function and slow the progression of DKD through two mechanisms (Sharma *et al.*, 2015): lowering blood pressure and inhibiting postglomerular arteriolar vasoconstriction to reduce intraglomerular pressure (No and Hartanto, 2023). ACE inhibitors and ARBs are equally effective in preventing the onset or progression of DKD. However, ACE inhibitors are more likely to have side effects, such as cough, than ARBs. ACE inhibitors and ARBs are generally started at low doses and titrated to the maximum tolerated dose in the management of patients with DKD (Horwitz and Schelling, 2014).

This study found no significant difference between initial and final creatinine levels after administration of 16 mg of candesartan (p=0.892) (95% CI -0.045-0.051), indicating no significant decrease in creatinine after candesartan administration (Iswanto and Silviani, 2024).

Serum creatinine is a commonly used routine test to measure kidney function. This test is quick and easy to perform (Kartono, Setiawan and Astuti, 2020). However, because creatinine is strongly influenced by muscle mass, in patients with relatively low muscle mass, such as women and the elderly, the results may not reflect true kidney function. Geriatric patients can have serum creatinine levels within the normal range despite severely impaired kidney function (Swedko *et al.*, 2003). In this study, the research subjects were geriatric patients, which means that the measured creatinine does not reflect actual kidney function.

4. Conclusion

This study concluded that candesartan significantly reduced proteinuria in geriatric patients with diabetic nephropathy, thus improving the progression of diabetic nephropathy. Furthermore, no significant reduction in creatinine was observed after candesartan administration in geriatric patients with diabetic nephropathy. This study has several limitations, and therefore, it is recommended that studies using better methods, such as clinical trials, be conducted to increase the validity of the study. Furthermore, more accurate kidney function tests, in addition to creatinine, are needed for geriatric patients, as muscle mass is not affected.

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