# Influence of Candesartan Cilexetil on Kidney Function Tests in Stage I Hypertensive Patients in Albayda Medical Center, Libya

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**Abstract**

Candesartan cilexetil is a potent, AT1 selective, and long-acting angiotensin II receptor blocker (ARB) commonly used for the treatment of hypertension, heart failure, and diabetic nephropathy. The current study was designed to evaluate the influence of candesartan cilexetil on kidney function tests in stage I hypertensive patients. The study was conducted on 200 hypertensive patients in Albayda Medical Center's Department of Internal Medicine in Albayda, Libya. Upon recruiting, the following kidney function tests were performed on all patients: blood urea nitrogen (BUN), creatinine (CRE), uric acid (UA), creatinine clearance (CC), sodium ($Na^+$), chloride ($Cl^-$), and potassium ($K^+$). The patient group was followed up after 12 weeks, and the kidney function tests were measured at baseline and at the 12-week follow-up. Comparison was made with the control group, which consisted of 100 healthy individuals. The results show that the kidney function tests results of the patient group at baseline were significantly ($p < 0.05$) higher than the control group, except serum $K^+$, which was comparable. However, there were no statistically significant changes in the kidney function tests results of the patient group at baseline and at the 12-week follow-up. The obtained results suggest that the influence of candesartan cilexetil on kidney function tests is small and it can be safely administered in this subset of hypertensive patients.

**Keywords:** Candesartan cilexetil, Hypertension, Kidney function tests, Albayda, Libya.

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## Introduction

Chronic kidney disease (CKD) is a major health issue in many countries. For example, around 20 million American adults in the United States have CKD [1]. CKD may progress to end stage renal disease (ESRD) and chronic renal failure [2]. The exact prevalence of CKD is unknown, however; current estimates based on a community-based survey conducted in Libya in 2007, with the help of the WHO STEPwise approach to surveillance, showed that among permanent households of 25–65 years, the prevalence of hypertension was 35.2% while diabetes was 10.4% [3].

Both hypertension and diabetes represent essential risk factors for the development of chronic kidney diseases [3]. Despite the availability and widespread use of antihypertensive medications, elevated blood pressure continues to be a significant contributor to CKD and the leading cause of ESRD in African Americans [4]. A high serum creatinine level in an untreated patient with hypertension should be regarded not only as a risk factor for renal failure, but as an essential sign of target organ damage [5].

There is unequivocal evidence that lowering elevated blood pressure slows the progression of renal disease, especially in patients with proteinuria [6,7]. The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) guidelines indicate that the goals of antihypertensive therapy for patients with chronic kidney disease are to decrease blood pressure, slow the progression of renal disease, and reduce the risk of cardiovascular disease [8]. The renin angiotensin aldosterone system (RAAS) performs various direct and indirect actions on the kidney that modify systemic blood pressure homeostasis and regulate intravascular volume status [9]. Activation by angiotensin II of the AT1 receptors present in the kidney stimulates a variety of effects in humans, including modulation of renal vasomotor tone, control of endocrine functions, and regulation of cellular growth and proliferation [10]. However, unregulated and excessive production of angiotensin II is associated with renal injury that can become progressive and irreversible.

Candesartan cilexetil, or Atacand, is the most potent available ARB that acts by inhibiting the binding of formed angiotensin II to its receptors [11, 12]. Candesartan cilexetil is chemically

known as 2-ethoxy-3-[21-(1H-tetrazol-5-yl) biphenyl-4ylmethyl]-3H-benzoimiadazole-4-carboxylic acid 1-cyclohexyloxycarbonyloxy ethyl ester, with the chemical formula C33H34N6O6, and a molecular weight of 610.67 [13]. It is a prodrug which is rapidly converted into the active drug, candesartan, during absorption in the gastrointestinal tract [14]. Candesartan cilexetil reduces RAAS activity by increasing the renal blood flow and glomerular filtration rate, and reducing the intraglomerular pressure [15]. Therefore, the present study was designed to evaluate the influence of candesartan cilexetil on kidney function tests in stage I hypertensive patients.

**Materials and Methods**

This study was done in Albayda Medical Center's Department of Internal Medicine in Albayda, Libya from December 2020 to March 2021 on 200 newly diagnosed hypertensive patients (120 males and 80 females) with stage I hypertension (SBP 140–159 mmHg and/or DBP 90–99 mmHg, according to JNC-8 hypertension guidelines [16]) and a mean age of 44.60 ± 8.90 years. They were kept on candesartan cilexetil (Atacand by AstraZeneca, from Turkey), with a daily dose of 4 to 16 mg.

Patients with severe stage II hypertension, cardiac, hepatic, or renal disease, diabetes mellitus, or other serious illnesses were excluded from this study. We also excluded patients who had been treated with other antihypertensive drugs and who were allergic to candesartan cilexetil. 100 healthy subjects (58 males and 42 females) with a mean age of 43.37 ± 8.47 years were used as a controlgroup. The study protocol was approved by the medical ethics board of Albayda Medical Center. The study included only adults and written informed consent was provided by all participants.

The systolic and diastolic blood pressures of each participant were measured by a standard cuff sphygmomanometer after at least 10 minutes in the sitting position. Blood pressure was measured at baseline and every 2-week interval for 12 weeks during the treatment period. Before and at the end of treatment, 10 ml blood samples were withdrawn from each patient and control subject for the following kidney function tests: blood urea nitrogen (BUN), creatinine (CRE), uric acid (UA), creatinine clearance (CC), sodium ($Na^+$), chloride ($Cl^-$), and potassium ($K^+$) by using the Mindray BA-88A Semi-Auto Chemistry Analyzer. Data was reported as mean ± SD

and analyzed using SPSS 23 with one-way ANOVA then LSD test. *P*-values less than 0.05 were considered statistically significant.

**Results**

As can be seen in **Table 1** below, the blood urea nitrogen (BUN), creatinine (CRE), uric acid (UA), creatinine clearance (CC), sodium ($Na^+$), and chloride ($Cl^-$) of the patient group at baseline were significantly ($p < 0.05$) higher than the control group, except serum $K^+$, which was comparable.

**Table 1:** Kidney function tests results of patient group (at baseline) and control group.

| Kidney Function Tests | Mean ± SD | |
|---|---|---|
| | **Control group (n=100)** | **Patient group at baseline (n=200)** |
| **BUN** (mmol/L) | 4.50 ± 1.00 | 9.42 ± 0.95**** |
| **CRE** (mg/dL) | 0.81 ± 0.16 | 3.31 ± 0.35**** |
| **UA** (mg/dL) | 4.90 ± 0.80 | 9.43 ± 0.54**** |
| **CC** (mL/min) | 95.12 ± 6.30 | 115.45 ± 7.10**** |
| **$Na^+$** (mmol/L) | 138.60 ± 2.67 | 150.60 ± 2.08**** |
| **$Cl^-$** (mmol/L) | 97.45 ± 1.23 | 109.44 ± 2.30** |
| **$K^+$** (mmol/L) | 4.11 ± 0.62 | 4.36 ± 0.65* |

****Significant difference from control group at $p < 0.05$**
***Non-significant difference from control group at $p < 0.05$**

**Table 2** below shows that the mean systolic and diastolic blood pressures of the patient group were significantly ($p < 0.05$) reduced from 150.13 ± 2.47 mmHg at baseline to 130.24 ± 2.70 mmHg at the 12-week follow-up, and from 92.03 ± 1.67 mmHg to 82.29 ± 2.05 mmHg, respectively. It also shows that there were no statistically significant differences in the mean values for all laboratory tests at baseline and at the 12-week follow-up.

**Table 2:** Mean systolic/diastolic blood pressures and kidney function tests results of patient group at baseline and at the 12-week follow-up.

| Variables | Patient group | Mean ± SD | *P*-Value |
|---|---|---|---|
| **SBP (**mmHg) | **Baseline** | 150.13 ± 2.47 | < 0.05 |
| | **12-week** | 130.24 ± 2.70** | |
| **DBP (**mmHg) | **Baseline** | 92.03 ± 1.67 | < 0.05 |
| | **12-week** | 82.29 ± 2.05** | |
| **BUN** (mmol/L) | **Baseline** | 9.42 ± 0.95 | 0.3956 |
| | **12-week** | 9.71 ± 0.89 | |
| **CRE** (mg/dL) | **Baseline** | 3.31 ± 0.35 | 0.2373 |
| | **12-week** | 3.65 ± 0.31 | |
| **UA** (mg/dL) | **Baseline** | 9.43 ± 0.54 | 0.3645 |
| | **12-week** | 9.76 ± 0.46 | |
| **CC** (mL/min) | **Baseline** | 115.45 ± 7.10 | 0.4586 |
| | **12-week** | 116.02 ± 8.24 | |
| **$Na^+$** (mmol/L) | **Baseline** | 150.60 ± 2.08 | 0.5130 |
| | **12-week** | 150.81 ± 3.28 | |
| **$Cl^-$** (mmol/L) | **Baseline** | 109.44 ± 2.30 | 0.4178 |
| | **12-week** | 109.76 ± 3.09 | |
| **$K^+$** (mmol/L) | **Baseline** | 4.36 ± 0.65 | 0.2837 |
| | **12-week** | 4.41 ± 0.55 | |

**Discussion**

In this study, we evaluated the effect of candesartan cilexetil on kidney function tests in stage I hypertensive patients. We found that the kidney function tests results of the patient group at

baseline were significantly ($p < 0.05$) higher than the control group, except serum $K^+$, which was comparable. These findings are in accordance with the results of Perticone et al. [17] and Coresh et al. [18] who demonstrated that the elevated serum creatinine level is common and strongly related to poor treatment of high blood pressure.

The present study showed that the administration of candesartan cilexetil to stage I hypertensive patients for 12 weeks resulted in good control of all patients' blood pressure, based on the blood pressures recorded during the follow-up period. There were also no significant differences in the mean values of all tests results at baseline and at the 12-week follow-up. These results suggest that candesartan cilexetil has a minimal effect on kidney function tests and may be safely used for patients with hypertension.

Additionally, the obtained results are in accordance with Philipp et al. [19] who showed that the angiotensin II receptor blocker, candesartan cilexetil, improved blood pressure control and decreased proteinuria in patient with microalbuminuria, and may prevent future renal failure in patients with essential hypertension.

Our study's findings are also in agreement with Nishida et al. [20], Liu et al. [21], and Granger et al. [22] who found that the administration of candesartan cilexetil to hypertensive patients for 6 months did not show significant effects on blood urea nitrogen, creatinine, and creatinine clearance.

Our obtained results are also in accordance with the results of Othman [23] who reported that the administration of angiotensin II receptor blocker, valsartan for 8 weeks in hypertensive patients had no adverse effects on some renal function tests.

Candesartan cilexetil in the current study produced no effects on potassium level, which is in agreement with the results of Giasuddin et al. [24] who reported that significant potassium disturbance rarely occurred in hypertensive patients without renal or cardiac failure who were kept on candesartan cilexetil.

**Conclusion**

In this study, we observed that there were no clinically significant changes in the BUN, CRE, UA, CC, $Na^+$, $Cl^-$, and $K^+$ levels of the patient group at baseline and at the 12-week follow-up. Our results suggest that the influence of candesartan cilexetil on kidney function tests is small

and it can be safely used for hypertensive patients because of its reno-protective effect and smooth control of blood pressure.

**Conflicts of Interest**

We hereby declare that there are no conflicts of interest regarding the publication of this research study.

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**Authors' Contributions**

This work was carried out in collaboration between all authors. Authors NAMI and YSEM designed the study, wrote the protocol, and collected the data. Authors AA and AAAR wrote the manuscript and managed the literature reviews. Authors FHA and HSAH performed all of the statistical analyses. All authors reviewed and approved the final manuscript.

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