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Impact of valsartan on some renal function parameters in hypertensive patients

Hayder S Hussein[1*], Nusieba A Mohammed Ibrahim[2]
[1] Department of Pharmacology, Faculty of Pharmacy, University of Mosul, Mosul, Iraq
[2] Department of Pharmacology and Toxicology, Faculty of Pharmacy, Omar Al-Mukhtar University, El-beida, Libya

Abstract
Objective: The main aim of this current research study was to test the effect of valsartan on some renal function parameters (RFPs) in some hypertensive patients.
Materials and Methods: This study was conducted in Nablus Hospital, Department of Internal Medicine, Mosul, Iraq, on 20 hypertensive patients. They were recruited and investigated for RFPs, which include: blood urea, serum creatinine, creatinine clearance, serum Na^+, and serum K^+. The patient (valsartan) group was followed-up for 8 weeks, during which RFPs were measured before starting therapy and at the end of the follow-up period using commercially available kits. The patient group was compared with a control group consisted of 30 healthy subjects.
Results: The RFPs at baseline (before valsartan administration) in the patient group were found elevated as compared to the control group ($p<0.001$), except for serum K^+ concentration, which was comparable. The RFPs in the patient group were similar before and after therapy.
Conclusion: The use of valsartan for 8 weeks in some hypertensive patients had no adverse effects on RFPs.

Keywords: hypertension, valsartan, angiotensin II receptor blocker (ARB), renal function parameters (RFPs)

1. Introduction
The exact prevalence of chronic kidney disease is unknown, however; current estimates based on a community-based survey which was conducted on a nationally representative sample with the aid of WHO stepwise approach done in Iraq in 2006, showed that the prevalence of hypertension was 40.4% while that for diabetes was 6.5% among permanent household of 25-65 years [1]. Both hypertension and diabetes represent essential risk factors for the development of chronic kidney diseases [1]. One of the most significant health consequences of chronic kidney diseases is end-stage renal disease (ESRD), of which 23% of cases in 1999 were judged by nephrologists to be caused by hypertension [2]. Despite the availability and widespread use of antihypertensive medications, elevated blood pressure (BP) continues to be a significant contributor to chronic kidney disease and the leading cause of ESRD in African-Americans [3]. A high-normal 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 [4]. There is unequivocal evidence that lowering elevated BP slows the progression of renal disease, especially in patients with proteinuria [5]. The national kidney foundation (NKF)-kidney disease outcomes quality initiative (K/DOQI) working group guidelines indicate that the goals of antihypertensive therapy in patients with chronic kidney disease are to decrease BP, as well as slow the progression of kidney disease and reduce the risk of cardiovascular disease [6]. The renin-angiotensin-aldosterone system (RAAS) has various direct and indirect actions on the kidney that modify systemic BP homeostasis and regulate intravascular volume status. Activation by angiotensin II of the AT_1 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 [7]. However, unregulated and excessive production of angiotensin II is associated with a renal injury that can become progressive and irreversible. Examples of this phenomenon include both diabetic and nondiabetic nephropathies [8, 9]. Valsartan is an angiotensin II receptor blocker (ARB) [10] acts by inhibiting the binding of formed angiotensin II to its receptors [11]. Valsartan reduces the activity of the RAAS and thus increasing renal blood flow and glomerular filtration rate through dilating the efferent arterioles and reducing the intraglomerular pressure [11]. Many basic and clinical studies in humans have now shown that inhibition of the RAAS reduces the harmful effects of angiotensin II in diabetic and nondiabetic nephropathies [7]. Thus, the present study was undertaken to investigate the effect of valsartan on some kidney function parameters in some hypertensive patients.

2. Materials and Methods
This study was done in the Department of Internal Medicine in Nablus Hospital in Mosul, Iraq from November 2018 to January 2019 on 20 newly diagnosed hypertensive patients (10 males and 10 females) with a mean age 45.2±8.6 years. They were kept on valsartan therapy (Valent Tablets, India) in a dose of 80 to 160 mg once daily.

Inclusion Criteria
Including newly diagnosed and hypertensive patients having stage I hypertension according to JNC-7 categories [12].

Exclusion Criteria

Including patients with a history of hepatic diseases, cardiac diseases or diabetes mellitus, patients on antihypertensive therapy or any drug that affects blood pressure, patients having hypersensitivity to ARBs, and patients with a history of severe hypertension (stage II) according to JNC-7 categories [12].

30 apparently healthy individuals (15 males and 15 females) with a mean age 43.8±7.4 years were used as a control group. Before and at the end of treatment, 5 ml blood samples were withdrawn from each patient and control subject. The blood serum samples were used to estimate kidney function parameters immediately after the withdraw of blood. Blood pressure was measured for each subject by standard mercury sphygmomanometer from the arm at the sitting position. Measurement was performed after at least 5 minutes of rest in the morning between 9.00 to 11.00 A.M. Blood pressure was measured at baseline and every 2 weeks for 2 months duration during treatment with valsartan. Serum urea concentrations were determined by the enzymatic method by using a kit provided by Biomerieux company (France). Estimation of serum creatinine concentrations was based upon Jaffe reaction by using a kit provided by Syrbio company (France). Evaluation of creatinine clearance was made by using the equation of Cockroft and Gault [13]. Determination of serum Na^+ and K^+ concentrations were done by using flame photometer [14]. Unpaired t-test was used to compare between age and sex and kidney parameters of the control and the patient groups. Paired t-test was used to compare between the studied kidney parameters before and after therapy with valsartan. Results were considered significant at *p* value equal or less than 0.05 [15].

3. Results

Age and sex distribution of the patients and the controls have appeared in Table 1. The patients and the controls are matched regarding age and sex distribution with non-significant values (p=0.93 regarding age and p=0.37 regarding sex for valsartan).

Blood urea, serum creatinine concentration, creatinine clearance and serum Na^+ concentration of the patients at baseline (before valsartan administration) were significantly elevated at $p \leq 0.001$ as compared with control group while there were no significant differences between serum K^+ concentration of the patient' and control' groups as shown in Table 2. Comparison of the studied parameters before and after therapy with valsartan showed non-significant differences at $p \leq 0.001$ for all studied parameters as shown in Table 3.

Table 1: Characteristics of control group and valsartan group.

Groups	Parameters	Mean ± SD		*P*-Value	
Control	Age (Year)	43.8 ± 7.4			
Valsartan	Age (Year)	45.2 ± 8.6		0.93***	
		Control		Valsartan	
		No.	%	No.	%
Sex	Male	15	50.0	10	50.0
	Female	15	50.0	10	50.0
	Total	30	100	20	100
	P-Value			0.37***	

***Non-significant difference from control at $p \leq 0.001$

Table 2: Comparison of renal function parameters between control group and valsartan group (before therapy).

Parameters	Mean ± SD	
	Control (n=30)	Before (n=20)
Blood Urea	3.40 ± 0.90	4.67 ± 0.99***
Serum Creatinine	62.97 ± 9.40	82.20 ± 15.40***
Cr. Clearance	92.12 ± 7.30	94.45 ± 13.84***
S. Na^+	127.40 ± 4.97	136.60 ± 4.00***
S. K^+	4.00 ± 0.60	4.17 ± 0.60*

***Significant difference from control at $p \leq 0.001$
*Non-significant difference from control at $p \leq 0.001$

Table 3: Comparison of renal function parameters in valsartan group (before & after therapy).

Parameters	Groups	Mean ± SD	*P*-Value
Blood Urea	Before	4.67±0.99	NS
	After	4.81±0.87	
Serum Creatinine	Before	82.20±15.40	NS
	After	82.50±14.10	
Cr. Clearance	Before	94.45±13.84	NS
	After	94.10±13.40	
S. Na^+	Before	136.60±4.00	NS
	After	136.40±3.34	
S. K^+	Before	4.17± 0.60	NS
	After	4.10±0.58	

NS= Non-significant

4. Discussion

The present study revealed that the measured renal function parameters are higher in hypertensive patients as compared with the control group. This may be attributed to alterations in the renal auto-regulation due to endothelial dysfunction, which leads to impaired vasodilatation of the afferent arteriole in response to change in arterial BP. These findings are in accordance with the results of Perticone *et al*. [16] and Coresh *et al*. [17] who demonstrated that elevated serum creatinine level, an indicator of chronic renal disease, is common and strongly related to poor treatment of high blood pressure. He and Whelton [18] showed that many observational epidemiologic studies and randomized controlled trials have demonstrated that systolic blood pressure is an independent and robust predictor of the risk of cardiovascular and renal diseases. The present study showed that administration of valsartan for 8 weeks to hypertensive patients has resulted in good control of the BP in all patients based on the records of BP during the follow-up period and it produced no adverse effects on the measured renal function parameters as shown by the insignificant changes in these parameters. Many previous studies demonstrated that the administration of antihypertensive drugs in patients with hypertension have different effects on the kidneys. Regarding the effect of valsartan on the studied parameters, the obtained results are in accordance with those of Watanabe *et al*. [19] and Plum *et al*. [20] who showed that the angiotensin II receptor blocker, valsartan, is able to improve renal function by reducing renal vascular resistance in hypertensive patients, especially in patients with microalbuminuria, and may prevent future renal failure in

patients with essential hypertension. Our results are in accordance with those of Shahanz *et al*. [21] and Priscilla *et al*. [22] who demonstrated that angiotensin II receptor antagonists (such as losartan) have no effects on renal function as shown by neither rising in serum creatinine nor decreasing in creatinine clearance during the administration of the drug.

5. Conclusion
The use of valsartan for 2 months in some hypertensive patients produced no side effects on RFPs, and it can be used safely because of its reno-protective effect and smooth control of the blood pressure.

6. Conflicts of Interest
We hereby declare that there are no conflicts of interest regarding the publication of this research paper.

7. Acknowledgment
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8. Ethics
All patients provided written permission and consent before collecting data to conduct this research study.

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