Therapeutics Effect Of Losartan Potassium And Ramipril As Combination Drugs On Kidney Function Tests In Hypertensive Patient In Al-Bayda, Libya

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Abstract

To investigate the results of Losartan and Ramipril as combination medication on some kidney function tests (KFTs) in patients with hypertension. a complete of 50 patients with stage I essential hypertension were recruited and investigated for KFTs that include, serum creatinine, creatinine clearance, blood urea ,serum sodium and serum potassium. The patients were divided into two groups, namely the losartan group, which consisted of 25 patients, and the Ramipril group which consisted of 25 patients. The patient groups were followed- up for six weeks throughout which KFTs were measured before beginning therapies and at the end of the follow-up period using commercially obtainable kits. The patient groups were compared with an impact group consisted of twenty apparently healthy subjects. The KFTs at baseline in each patient groups were found elevated as compared to the control group ($p < 0.001$), apart from serum potassium concentration that was comparable. The KFTs in patient groups were comparable before and once therapies. The utilization of losartan and Ramipril for six weeks in hypertensive patients has no adverse effects on KFTs.

Keywords: Hypertensive patient, losartan potassium, Ramipril , Kidney function tests.

1. Introduction

The exact prevalence of chronic kidney disease is unknown; however, current estimates supported a community-based survey that was conducted on a nationally representative sample with the help of WHO showed that the prevalence of high blood pressure was 40. 4% whereas that for diabetes was 6.5% among permanent home of 35-65 years[1]. Each hypertension and diabetes represent important risk factors for the event of chronic kidney diseases [1]. One among the most important health consequences of chronic kidney disease is end-stage renal disease (ESRD), of which 23% of cases in 2000 were judged by nephrologists to be caused by hypertension [2]. Despite the provision and widespread use of antihypertensive medication, elevated BP continues to be a significant contributor to chronic kidney disease and therefore the leading cause of

ESRD in African- Americans [3]. A high-normal blood serum creatinine level in an untreated patient with cardiovascular disease ought to be regarded not only as a risk factor for renal disorder however as a vital sign of target organ damage [4]. there's unequivocal proof that lowering elevated BP slows the progression of renal disease, particularly in patients with albuminuria [5]. The national kidney foundation-kidney disease outcomes quality initiative working group guidelines indicate that the goals of antihypertensive medical aid in patients with chronic renal disorder are to decrease blood pressure, further as slow the progression of urinary organ disease and cut back the risk of cardiovascular disease [6]. The renin angiotensin aldosterone system has numerous direct and indirect actions on the kidney that modify general BP homeostasis and regulate intravascular volume status. Activation by angiotonin of the AT1 receptors present within the kidney stimulates a variety of effects in humans, including modulation of renal vasomotor tone, management of endocrine functions and regulation of cellular growth and proliferation [7]. However, unregulated and excessive production of angiotensin is associated with renal injury, which will become progressive and irreversible. Examples of this phenomenon include each diabetic and non-diabetic nephropathies [8,9].Angiotensin changing accelerator inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) have favorable effects on the progression of diabetic and nondiabetic renal disease [10]. Ramipril is an ACEIs[11] act by suppressing renin angiotensin system by inhibiting ACE that is widely distributed within the circulation and tissues. This action decreases the formation of a potent vasoconstrictor, angiotensin II, and slows the degradation of the potent vasodilator, bradykinin [12]. Losartan is associate ARBs [13] act by inhibiting the binding of formed angiotensin ii to its receptors [14]. Each these two medication cut back the activity of the RAAS and so increasing renal blood flow and glomerular filtration rate through dilating the efferent arterioles and reducing the intra glomerular pressure. several basic studies and clinical studies in humans have currently shown that inhibition of the RAAS reduces the injurious effects of Hypertension (constricts both afferent and efferent arterioles, stimulate mesangial cell contraction, stimulate the discharge of aldosterone and mediate proliferative effects concerned in atherosclerosis) in diabetic and non-diabetic nephropathies[15]. So this study was undertaken to analyze the effects of Ramipril and Losartan as combination on some kidney function parameters in a number of hypertensive patients.

2. Materials And Methods

Fifty recently diagnosed essential hypertensive patients were participated during this study. The patients were divided into a pair of groups. Group one consisted of 25 patients, whose ages mean is 45.2 ± 8.6 years and involved 10 males and 15 females. They were kept on ramipril therapy (Tritace tablets, Germany) in a dose of 5 to 10 mg two daily. Group two consisted of 25 patients whose age mean is 44 ± 8.6They were kept on losartan potassium therapy (losartan potassium tablets, Bristol, UK) in a dose of 50 to 100 mg once daily. Inclusion criteria including recently diagnosed, hypertensive patients having stage I highly blood pressure according to JNS-7 categories[10].Exclusion criteria as well as patients with a history of cardiac diseases or diabetes mellitus. Patients on antihypertensive drug or any drug that affects blood pressure. Patients having hypersensitivity to ACE inhibitors. Patients with a history of severe hypertension (Stage Π), according to NJC-7 categories[10]. Twenty apparently healthy normotensive individuals, whose mean of ages was 43.8±7.4 years, were used as a control group. Before and at the end of treatment, 5 millilitre blood samples were withdrawn from every patient and control subject [6]. The blood serum samples were used to estimate kidney operate parameters immediately when the withdraw of blood. blood pressure was measured for each subject by standard mercury sphygmomanometer from the arm at the lying position. Mensuration was performed after at least five minutes of rest at the morning between 8.00 to 10.00 A.M. blood pressure was measured at baseline and every one weeks for six weeks duration during treatment with Ramipril or losartan potassium. Blood serum urea concentration, serum creatinine concentrations is determined by I-Flash® 1200-Fully automated bioassay analyzer. Determination of sodium and potassium concentrations were done by using COBAS INTEGRA® 400 fully automated biochemical analyzer [24]. Unpaired t-test was used to compare between age, 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 when therapy with ramipril or losartan potassium. Results were considered significant at p value equal or less than 0.05 [17].

3. Results

Age and gender distribution of the patients with hypertension and the control group were appeared in Table 1. The patients and the control group are matched regarding age and gender distribution with non-significant values (p =0.91and 0.53 regarding).Serum

sodium concentration , creatinine clearance, serum creatinine concentration, and blood urea of the patients at baseline (before drug administration of the two groups) were significantly elevated at $p \leq 0.001$ as compared with control group while there was no significant differences between potassium concentration of the patient' and control' groups as shown in Tables 2 Comparison of the studied parameters before and after therapy with Ramipril or losartan potassium showed non-significant differences at $p \leq 0.001$ for all studied parameters as shown in Tables 3

Table 1. Characteristics of control group and patients on hypertension

Groups	Variables		Mean ± SD		*P*- Value	
Control	**Age**		43.8 ± 7.4			
Patient on Ramipril / losartan potassium thereby	**Age**		45.2 ± 8.6 / 44 ± 8.6		*0.91/ *0.54	
	Control N 20 (%)		**Ramipril N 25 (%)**		**Losartan N 25 (%)**	
Gender (M\F)	**M**	**F**	**M**	**F**	**M**	**F**
	10 (50)	10 (50)	10 (20)	15 (80)	10 (20)	15 (80)

*Non-Significant difference from control at p<0.001

Table 2. Comparison of kidney function tests between control group and before administered of Ramipril and Losartan potassium therapy.

Kidney function test	Mean ± SD		
	Control (n = 20)	**Before Ramipril therapy (n =25)**	**Before Losartan potassium therapy (n =25)**
Serum potassium	4.00 ± 0 .6	4.16 ± 0.7*	4.01 ± 0.56**
Serum Sodium	127.40 ± 4.97	133.6 ± 3.00**	133.3 ± 3.04**
Cr. Clearance	92.12 ± 7.3	85.45 ± 13.48**	96.97 ± 9.68**
Serum Creatinine	62.97 ± 9.4	80.2 ± 13.4**	83.75 ± 4.00**
Blood Urea	3.40 ± 0.90	3.67 ± 0.1**	4.45 ± 0.61*

* Non- significant difference from control at p<0.001

**Significant difference from control at p<0.001

Table 3. Comparison of kidney function tests in Ramipril and Losartan groups therapy

Kidney function test	Group on Ramipril therapy (n =25)	Mean ± SD	Group on Losartan therapy (n =25)	Mean ± SD	*p*-value
Serum potassium	**Before**	4.16 ± 0.7	**Before**	4.01 ± 0.56	Non-significant
	After	4.13±0.57	**After**	3.87 ± 0.54	
Serum Sodium	**Before**	133.6±3.00	**Before**	133.3±3.04	Non-significant
	After	92.1±13.45	**After**	132.15±2.93	
Cr. Clearance	**Before**	85.45±13.84	**Before**	96.97±9.68	Non-significant
	After	83.1±13.40	**After**	96.65±9.3	
Serum Creatinine	**Before**	80.2±13.4	**Before**	83.75±4.00	Non-significant
	After	79.5±12.10	**After**	81.10±15.50	
Blood Urea	**Before**	3.67±0.1	**Before**	4.45±0.61	Non-significant
	After	4.71±0.70	**After**	4.44±0.52	

4. Discussion

The present study showed that the measured renal parameters are higher in hypertensive patients as compared with control group. This is may be attributed to alterations in the renal auto regulation due to endothelial dysfunction which lead to reduced vasodilatation of the afferent arteriole in response to change in arterial blood pressure. These outcomes are in agreement with the results of Lacourcière et al. [18] and Brenner et al.[19] who demonstrated that high serum creatinine level, an indicator of chronic renal disease, is common and strongly related to inadequate treatment of high blood pressure. He and Whelton et al [20] showed that many observational epidemiologic studies and randomized controlled trials have demonstrated that systolic blood pressure is an independent and strong predictor of risk of renal and cardiovascular disease. The present study showed that administration of Ramipril or Losartan potassium for six weeks to hypertensive patients has resulted in good control of the blood pressure in all patients based on the records of blood pressure during the follow-up period and both these two drugs produced no adverse effects on the measured renal 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 kidney function. Our results are in agreement with Hayder S et al [16], Carides et al [21]. Those authors found that the administration of certain category of antihypertensive drug for hypertensive patients for six weeks did not show significant effects on blood serum urea, serum creatinine and creatinine clearance. Ramipril in the current study produced no effects on serum sodium and potassium, which goes in agreement with the results of Yasuda et al [22] who reported that significant sodium and potassium disturbances rarely occurred in hypertensive patient kept on Ramipril while not renal or heart failure. relating to the consequences of Losartan potassium on the studied parameters, the obtained results are in accordance with those of Kurokawa et al. [23] and Rabbat C et al. [24] who showed that the angiotensin receptor blocker, Losartan potassium is ready to boost renal operate by reducing renal tube resistance in hypertensive patients, particularly in patients with microalbuminuria, and may stop future renal disorder in patients with essential hypertension. Our results are in accordance with those of Brewster et al.[5] who reported that angiotensin II receptor antagonists have no effects on renal function as shown by the neither rise in blood serum creatinine nor decrease in creatinine clearance during the administration of the drug. Compared between two medication and in agreement with our results Hayder S. et al [6]. Showed the beneficial effects of losartan and ACE inhibitor on conserving renal function by decreasing urea, creatinine and increasing creatinine clearance.

5. Conclusion

The use of Ramipril and Losartan potassium in patients with hypertension for six weeks produces no adverse effects on renal function tests and both drugs can be used safely because of their reno-protective effects and smooth control of the blood pressure.

6. Financial Support And Sponsorship

Nil.

7. Conflicts of Interest

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

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9. Ethics

All participants provided written informed consent before collecting data to conduct this research study.

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