International Journal of Research in Pharmacy and Pharmaceutical Sciences
ISSN: 2455-698X; Impact Factor: RJIF 5.22
www.pharmacyjournal.in
Volume 2; Issue 2; March 2017; Page No. 01-03

A comparative study between losartan and cilnidipine on serum uric acid levels in chronic kidney disease patients with hypertension

[*1] Mathew George, [2] Lincy Joseph, [3] Mincy Mathew, [4] Alvi Varghese, [5] Beauny Ann Babu, [6] Ruby Varghese

[1] Department of Pharmacology, Pushpagiri College of Pharmacy, Thiruvalla, Kerala, India
[2-6] Department of Pharmaceutical Chemistry, Pushpagiri College of Pharmacy, Thiruvalla, Kerala, India

Abstract
Chronic Kidney Disease (CKD) is a worldwide epidemic and escalating problem. Approximately 20 million adults in the United States are in various stages of CKD, with >400,000 individuals with end stage kidney disease and >300,000 individuals requiring maintenance hemodialysis. Hypertension is the persistent elevation of arterial blood pressure in which DBP values > 90 mmHg and SBP values >140mmHg. Serum uric acid is commonly elevated in subjects with chronic kidney diseases. The present review is aimed on to study the effect of Losartan and Cilnidipine on uric acid levels in CKD patients with hypertension. Losartan enhances the renal excretion of uric acid by increasing the urinary pH and also inhibits the URAT1 expressed in the brush-border membrane of the renal proximal tubule and thus prevents the reabsorption of uric acid. Cilnidipine increases the uric acid clearance by enhancing the glomerular filteration of uric acid.

Keywords: chronic kidney disease, hypertension, serum uric acid, losartan, cilnidipine

Introduction

Chronic kidney disease (CKD) is defined by a reduction in the glomerular filtration rate (GFR) and/or urinary or structural abnormalities of the renal tract. The prevalence of CKD increases with age and is greater in females. CKD is classified according to severity from 1 to 5. CKD is an important risk factor for cardiovascular disease. Clinical signs and symptoms of severe CKD include oedema, anaemia, hypertension, bone-pain, nocturia, neurological changes and disordered muscle function. The cardiovascular risk increases with the severity of CKD. In addition, patients with CKD often have associated left ventricular hypertrophy which may be related to chronic volume overload and uremia.

Hypertension: can be defined as a condition in which blood pressure is elevated to an extend where benefit is obtained from blood pressure lowering. Hypertension is the persistent elevation of arterial blood pressure in which DBP values greater than 90mmHg and SBP values greater than 140mmHg.The complication of hypertension include stroke, myocardial infarction, heart failure, renal failure and dissecting aortic aneurysm. The mean blood pressure is the product of cardiac output and total peripheral resistance. In most hypertensive individuals cardiac output is not increased and high blood pressure arises as a result of increased total peripheral resistance caused by constriction of small arterioles. Hypertension results in atherosclerosis which can cause occlusive renovascular disease and small vessel damage. In patients with significant large vessel occlusive disease arteriolar nephrosclerosis, interstitial fibrosis, and glomerular collapse may be present. The effective management of hypertension is crucial to reduce renal damage.

Review of literature

1. Nidhi singh *et al.*, (2016); conducted a study on '***The Effects of Cilnidipine on heart rate and Uric acid metabolism in patients of essential hypertension'.***
The aim of this study is to compare the effectiveness of Amlodipine and Cilnidipine in patients of essential hypertension and their effects on heart rate and serum uric acid levels. Study enrolled 100 patients 92 completed the study. They are randomly assigned to amlodipine (47) and cilnidipine (45) and patients were followed up for a period of 6 months. Blood samples were taken at 12th week and 24th week and uric acid was measured. Patients were included in the study if they met the following criteria: ≥40 years of age of both sex, SBP/DBP of ≥140/90mmHg to ≤180/110mmHg. Patients with secondary hypertension of any causes angina pectoris or acute coronary artery disease, recent history of congestive heart failure, Valvular heart diseases, Cardiac arrhythmias, renal dysfunction and diabetes mellitus were excluded. The study concluded that both amlodipine and cilnidipine has similar hypotensive activity and cilnidipine alone reduces heart rate and improves serum uric acid metabolism.

2. Shunya Uchida *et al*., (2014); conducted a study **on '*The effects of the N/L type Calcium channel blocker Cilnidipine on nephropathy and uric acid metabolism in hypertensive patients with Chronic kidney disease'.***
This study assessed the urinary albumin/creatinine ratio and uric acid metabolism in 70 hypertensive patients with chronic kidney disease under the treatment of the L-type calcium channel blocker amlodipine then switched to cilnidipine and studied the changes in BP, Heart rate, Urinary Albumin creatinine ratio, serum uric acid level, urinary uric acid/creatinine ratio and fractional excretion of uric acid were

analysed at 3 months after switching and compared with the baseline values. Patients with chronic Glomerulonephritis were not included because hematuria was not evident. Patients with gout or urinary stones were not included. The values of BP were not controlled as inclusion/exclusion criteria, because the study design was a crossover method. The results of the study conclude that cilnidipine exerts hypotensive activity similar to amlodipine and it can also improve albuminuria and uric acid metabolism. Considering these features cilnidipine is a promising drug of choice for targeting CKD patients with hypertension and hyperuricemia

3. Yayoi Nishida *et al.*, (2013) [3]; conducted a study on the ***'Comparative effect of angiotensin 2 type 1 receptor blockers on serum uric acid in hypertensive patients with type 2 diabetes mellitus: a retrospective observational study***'.

Hypertensive patients with type 2 DM were enrolled in the study who had been treated with Losartan (214), Valsartan (266), Telmisartan (185), Candesartan (458), or Olmesartan (192). Excluded patients who had been treated with other antihypertensive drugs (ARB combination drugs, ACE inhibitors, CCB, Diuretic, alpha blocker, beta blocker, alpha and beta blocker, alpha agonist, reserpine, vasodilator or rennin inhibitor) during the study period. Also excluded patients who had been treated with drugs for hyperuricemia or Gout.

Study concluded that in losartan users mean SUA level was significantly decreased from baseline while it was conversely increased in users of other ARBs.

4. Toshihiro hamada *et al*., (2008) [4]; conducted a study on the '***Uricosuric action of losartan via the inhibition of urate transporter 1(URAT1) in hypertensive patients***'.

Thirty-two patients with hypertension were enrolled in the study and they were prescribed oral losartan (16) or candesartan (16).Before and after 1month of treatment serum concentration of urate (Sur) and creatinine (Scr) and clearance value of urate (Cur) and creatinine (Ccr) were determined. Blood pressure significantly decreased in the patients treated with either losartan or candesartan. Losartan significantly reduced Sur, which was associated with a concomitant increase in the Ccr/Cur ratio whereas candesartan did not alter these parameters. Results concluded that losartan significantly reduced Sur, which was associated with a concomitent increase in the Cur/Ccr ratio, whereas candesartan did not alter these parameters

5. Briyan L Ryner *et al*., (2006) [2]; conducted a study on ***'Effect of Losartan versus Candesartan on uric acid,renal function and fibrinogen in patients with hypertension and Hyperuricemia***'

A total of 59 patients were enrolled in the study (30 in the losartan and 29 in the candesartan group).Patients with hypertension and serum uric acid $\geq$ 0.42mmol/L were randomized to receive losartan 50 to 100 mg or Candesartan 8 to 16 mg for 24 weeks. At randomization and after 24 weeks, systolic and diastolic BP, serum uric acid, creatinine and fibrinogen were measured. Mean values of serum uric acid in the losartan and candesartan groups were similar at baseline (0.44 and 0.46 mmol/L), but they were lower in the losartan group (0.39 and 0.48mmol/L) after 24 weeks. Result concluded that candesartan and losartan reduced BP, but only losartan reduced uric acid. The lowering of fibrinogen in both groups may explain the reduction in stroke with ARBs.

6. Gerster JC *et al*., (2001) [1]; conducted a study on the ***'Comparative effects of Losartan and Irbesartan on serum uric acid in hypertensive patients with Hypeuricemia and gout'.***

The purpose of this study were: 1) to evaluate the effects of Losartan on serum uric acid in hypertensive patients with hyperuricemia and gout. 2) To compare the effects of losartan with those of Irbesartan. 3) To evaluate whether Losartan 50mg bid has a greater impact on SUA levels than Losartan 50mg once a day.

Thirteen hypertensive patients with hyperuricemia and gout completed this prospective, randomized, double blind, crossover study. Uric acid lowering drugs were stopped 3 weeks before the beginning of the study. Patients were randomized to receive either losartan 50mg or irbesartan 150mg once a day for 4 weeks. The study concluded that in contrast to irbesartan, losartan was uricosuric and decreased serum uric acid levels. Losartan 50mg bid did not produce a greater fall in serum uric acid than losartan.

Conclusion

Uric acid is a normal content of urine. In CKD patients, the serum uric acid level increases due to a reduction in the Glomerular Filtration Rate.In CKD patients half-life of renally excreted drugs increases due to a decline in the renal function and thereby increasing drug toxicity due to multiple therapeutic regimen. Losartan is an ARB and Cilnidipine is a CCB, both are beneficial in reducing the serum uric acid levels in chronic kidney disease patients with hypertension. So it offers a new therapeutic approach by reducing the number of drugs and better patient care.

References

1. Wurzner G, Gerster JC, Chiolero A, Maillard M, Brunner HR, Comparative effects of losaratan and irbesartan on serum uric acid level in hypertensive patients with hyperuricaemia and Gout, 2001; 19(10):1855-60.
2. Brian L. Rayner, Ybonne a Trinder, Donette Baines Sedick Isaacs, Effect of losartan versus Candesartan on uric acid, renal function and fibrinogen in patients with hypertension and hyperuricemia associated with diuretics, Am J Hypertens 2006; 19(2):208-213.doi:10.1016/j.amjhyper. 2005.08.005
3. Yayoi Nishida, Yasuo Takahashi, Norio Susa, Nobukazu Kanou, Comparitve effect of angiotensin II type I receptor blockers on serum uric acid in hypertensive patients with type 2 diabetes mellitus: a retrospective observational study Cardiobasc Diabetol. 2013; 12:159.
4. Hamada T, Ichida K, Hosoyamada M, Mizuta E, Yanagihara K, Uricosuric action of losartan via the inhibition of urate transporter I (URATI) in hypertensive patients Am J Hypertens.2008; 21(10):1157-62.Epub.
5. Marissa L Wolff, Jennifer L Cruz, Adam J Vanderman, Jaimie N Brown. The effect of angiotensin II receptor blockers on hyperuricemia. Ther Adv Chronic Dis. 2015; 6(6):339-346.

6. A Dang, Y Zhang, G Liu, G Chen, W Song, B Vang. *Et al.* Effects of losartan and irbesartan on serum uric acid in hypertensive patients with hyperuricemia in Chinese population.Journal of human hypertension. 2006; 20(10). Nov 2005.
7. Toshihiro Hamda, Aensaku Yamada, Einosuke Mizuta, Arisa Watanabe, Tomohiro Osaki. Effects of cilnidipine on serum uric acid level and urinary nitrogen monoxide excretion in patients with hypertension. Clinical and experimental hypertension, 2012; 34(7).
8. Johnson RJ, uric acid and chronic kidney disease which is chasing which? Nephrol Dial transplant. 2013; 28(9):2221-8. doi:10.1093/ndt/gft029.EPUB 2013March 29.
9. Roger walker, Cate Whittlesea, Clinical pharmacy and Therapeutica, 5th edition,page no 272,295.