The quality of life of chronic kidney disease patients with hypertension treated with angiotensin system-related agents

Mohammed Salim KT1*, Saravanakumar RT1, Dilip C2, Amrutha KP2

1Department of Pharmacy, Annamalai University, Annamalai Nagar, Chidambaram, Tamil Nadu – 608002 India
2Department of Pharmacy Practice, Al Shifa College of Pharmacy, Kizhattur, Malappuram, Kerala – 679325 India

ABSTRACT

The chronic kidney disease (CKD) co-exist with hypertension in approximately 80 to 85 per cent of patients. The CKD stages can be defined by glomerular filtration rate (GFR), and the deterioration of kidney function or reduction in GFR has observed in those with uncontrolled blood pressure (BP). We had conducted a prospective study to analyse the impact of the angiotensin system-related agents on the quality of life of CKD patients with hypertension. The SF-36 questionnaire, direct patients interview and medical records were the sources for retrieval of information. We observed that male patients were more prone to CKD than female. Hypertension was the primary (77.8%) aetiology behind the incidence of CKD. The angiotensin-converting enzyme inhibitors (ACEI) was responsible for very low (58%) and low (44%) health disabilities to the patients. In contrast, the angiotensin receptor blockers (ARB) even though it has a limited adverse effect, the patients complained of medium (9%) and high disabilities than the ACEIs. The discontinuation of the antihypertensive drugs by the CKD patients was almost negligible (3.4%). The study concludes that a balanced diet and reasonable blood pressure control is essential to prevent the progression of CKD and to improve the quality of life.

INTRODUCTION

The Kidney Disease Improving Global Outcomes (KDIGO) has defined chronic kidney disease (CKD) as abnormalities of kidney structure or function presented for greater than three months with implications for health (Kidney International Supplements, 2013). Hypertension and CKD are inter-related and represent global public health challenges. The progression of kidney impairment may be due to changes in the demographics of the population, differences in disease burden among age groups and under-recognition of earlier stages of CKD and risk factors for CKD may partially explain this growth (National Kidney Foundation, 2002). We had conducted an epidemiological study on hypertension with CKD in our locality.

Methodology

The prospective observational study was conducted at the nephrology department of KIMS Al Shifa hospital, tertiary care referral hospital from October 2018 to August 2019. The ethical committee approval and informed consent were obtained. The chronic kidney disease outpatients with hypertension were enrolled, and they were followed up for three consecutive consultations. The study
Mohammed Salim KT et al., Int. J. Res. Pharm. Sci., 2020, 11(4), 6633-6639

focused on angiotensin system-related agents; those are the angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB). Patients with acute kidney injury, unconscious or those with serum creatinine greater than 3.5mg/dl are excluded from the study. The SF — 36 questionnaire assessed the patients’ quality of life. Direct patient interview, discussion with a physician, medical record database and prescription were the source for retrieval of patient demographics details, aetiology, stage and duration of CKD as well as blood pressure, glomerular filtration rate.

The data collected was spread into an excel sheet which was then imported into Statistical Package Of Social Science (SPSS) software version 23. The Chi-square was applied to relationships among the different variables and the repeatability among clinical parameters, respectively.

RESULTS AND DISCUSSION

Total of 495 patients was enrolled in the study as per the study specification. CKD was prominent among the age group above 60 years (Park et al., 2011). In our study, we observed a similar observation and the least below to the age of 50 years, as per Table 1. However, the pattern had extended down to adults, and this could be due to several factors such as over usage of medicines especially NSAIDs (Baker and Perazella, 2020), inherited disease (Hildebrandt, 2010) and lifestyle changes (Shankar et al., 2006).

Figure 1: The graph showing the blood pressure of the patients at three consecutive consultations

The people in the United States and Norway had a large density of CKD patients below the age of 65 years (Hallan et al., 2006). The early detection of kidney deterioration may be due to fetal nephrotoxicity of drugs administered by pregnant ladies. The practice of polypharmacy might be a reason for the early age diagnosis of CKD among their offspring (Bernstein et al., 1998).

Man (60.4%) had more prevalence of CKD with hypertension than female (Ojji et al., 2009). When we analysed the chronic kidney disease patient’s stage, 46.9% had stage 3 CKD followed by stage 4 (36.8%) and only one person in stage 5 (End-Stage Renal Disease). The study conducted in Karnataka also had a high prevalence of CKD stage 3 patients, then followed by stage 4 (Duan et al., 2019). Only a few patients (16.1%) were identified to be in stage 1 (4.8%) and stage 2 (11.3%), as shown in Table 2. From our study, 66 and 69 patients belong to the age group between 60 to 70 had stage 3 and stage 4 CKD, respectively.

Figure 2: The association between stages of CKD concerning the age of the patient

Even though the total patients in stage 2 were small, most patients belonged to 60 to 70 years age group, which was followed by those with age between 50–60 years. Only in stage 1 and stage 5, we observed the patients with age less than 50 years. From Figure 2, the relationship between age and stages of chronic kidney disease was analysed with the chi-square test. There was a statistical difference in the occurrence of various stages of the disease according to age (P<0.05). Hence, we reject the null hypothesis; there is significance between the age and the stages of chronic kidney disease.

Only 13 female CKD patients were observed to be more in stage 1 than the male. However, while the stage progressed, the contribution of the male was superior. This association was evaluated with the chi-square test, and the inference showed to have no significant difference among male and female for dif-

Figure 3: The association between the CKD stage with the gender of the patient
Table 1: Demographic details distributed per age, gender, a lean Body weight of the CKD Patients

| Particular                | Obtained Number | Percentage |
|---------------------------|-----------------|------------|
| Below 50 Years of Age     | 101             | 20.4%      |
| 50 to 60 Years of Age     | 111             | 22.4%      |
| 60 to 70 Years of Age     | 154             | 31.1%      |
| Above 70 Years of Age     | 129             | 26.1%      |

**Gender**

| Particular | Obtained Number | Percentage |
|------------|-----------------|------------|
| Female     | 196             | 39.6%      |
| Male       | 299             | 60.40%     |

**Lean Body Weight**

| Particular          | Obtained Number | Percentage |
|---------------------|-----------------|------------|
| Below 55 Kg         | 80              | 16.16%     |
| Between 55 to 65 Kg | 179             | 36.16%     |
| Between 65 to 75 Kg | 136             | 27.47%     |
| Above 75 Kg         | 100             | 20.20%     |

Table 2: Number and percentage of patients based on cause, CKD stages and duration of disease

| Particulars          | Chronic Kidney Disease Stage | Obtained Number | Percentage |
|----------------------|------------------------------|-----------------|------------|
| CKD Stage 1          |                              | 24              | 4.8%       |
| CKD Stage 2          |                              | 56              | 11.3%      |
| CKD Stage 3          |                              | 232             | 46.9%      |
| CKD Stage 4          |                              | 182             | 36.8%      |
| CKD Stage 5          |                              | 1               | 0.2%       |

**Chronic Kidney Disease Duration**

| Particulars          | Obtained Number | Percentage |
|----------------------|-----------------|------------|
| 1 to 6 months        | 29              | 5.9%       |
| 6 to 12 months       | 74              | 14.9%      |
| 1 to 2 years         | 90              | 18.2%      |
| 2 to 3 years         | 76              | 15.4%      |
| 3 to 4 years         | 53              | 10.7%      |
| 4-5 years            | 58              | 11.7%      |
| Above 5 years        | 115             | 23.2%      |

**Cause of Chronic Kidney Disease**

| Particulars | Obtained Number | Percentage |
|-------------|-----------------|------------|
| Hypertension| 385             | 77.8%      |
| Other       | 110             | 22.2%      |

ferent stages of chronic kidney disease (P>0.05), as observed from Figure 3.

52.32% of patients had lean body weight between 55 to 65kg, and those below 55 kg were the least. The Cockcroft-Gault equation, the tool widely used to calculate the creatinine clearance (one of a parameter to analyze the kidney function). Accordingly states that, an increase in lean body weight without a proportional increase in serum creatinine will tend to have a favourable impact on the patient (Walker and Whittlesea, 2015). Hence, a healthy diet would improve the patients well being as well as prevent the progress of CKD (Rysz et al., 2017).

The quality of life (QOL) of 93.9% patient under treatment had low or very low disabilities, as shown in Table 3. The age, gender, stage of CKD and presence of other co-morbidities can affect the quality of
Table 3: The number and percentage of patients based on the treatment provided, discontinued and also the quality of life

| Particulars                        | Obtained Number | Percentage |
|------------------------------------|-----------------|------------|
| ACE Inhibitors                     | 196             | 39.6%      |
| Ramipril                           | 194             | 39.2%      |
| Enalapril                          | 2               | 0.4%       |
| Angiotensin Receptor Blockers      |                 |            |
| Losartan                           | 186             | 37.6%      |
| Telmisartan                        | 90              | 18.2%      |
| Olmesartan                         | 23              | 4.6%       |

Incidence of Medicine Discontinuation

| Particulars | Obtained Number | Percentage |
|-------------|-----------------|------------|
| Yes         | 17              | 3.4%       |
| No          | 478             | 96.6%      |

Distribution of Discontinued Drug

| Particulars | Obtained Number | Percentage |
|-------------|-----------------|------------|
| Losartan    | 4               | 0.8%       |
| Ramipril    | 9               | 1.8%       |
| Telmisartan | 4               | 0.8%       |
| None        | 478             | 96.7%      |

Quality Of Life (score)

| Particulars               | Obtained Number | Percentage |
|---------------------------|-----------------|------------|
| High Disability (0-25)    | 1               | 0.2%       |
| Medium Disability (25-50) | 29              | 5.9%       |
| Low Disability (50-75)    | 202             | 40.8%      |
| Very Low Disability (75-100) | 263        | 53.1%      |

life of patients. Anaemia and low-income status were significantly associated with poor QOL (Tannor et al., 2019). A reduction in physical functioning, physical role functioning and in the physical component summary was observed progressively in the different stages of kidney disease. Individuals with higher educational level who were professionally active displayed higher physical component summary values, whereas men and those with a higher income presented better mental component summary values. Older patients performed worse on the physical component summary and better on the mental component summary (Lekpa et al., 2017).

Majority of CKD patients of stage 1,2,3,5 had very low disabilities as observed from Figure 4. However, stage 4 had less health satisfaction compared to other stages. Chi-square test analysis rejected the null hypothesis, and it was found that there was a significant difference in Quality of Life (QOL) among various stages of CKD (P > 0.05).

Hypertension is a risk factor for the onset and progression of CKD, a reduction in the glomerular filtration rate (GFR), occurs at a variable rate, ranging from less than 1 to more than 12 mL/min per 1.73 m$^2$ per year (Levey et al., 2011). The primary cause of progressive kidney damage is found to be due to hypertension which accounts to have a 77.8% distribution among the total chronic kidney disease patient on angiotensin related drugs, as shown in Table 2. This put light that elevated BP is one among the predominant cause of kidney damage than diabetes mellitus (Walker and Whittlesea, 2015).

Figure 4: The association between the CKD stage with the patient’s Quality of Life

Increased awareness and treatment of hyperten-
sion among CKD patients had improved blood pressure control. Each of the antihypertensive agents is roughly equally effective in lowering the blood pressure, producing an excellent antihypertensive response in 30 to 50 per cent of patients. Joint National Committee (JNC) 8 recommends initiating a renin-angiotensin-aldosterone system (RAAS) inhibitor, thiazide diuretic or a calcium channel blocker for normalising the blood pressure in CKD patients. Among them, ACE inhibitors or ARBs was most frequently administered drug (39%) as monotherapy followed by calcium channel blockers, diuretics and beta-blocker (Ridao et al., 2001).

The angiotensin receptor blockers opted by the nephrologist in our study was losartan (37.6%), telmisartan (18.2%) and olmesartan (0.4%). The prescription pattern of the physician also had more ramipril (39.2%) than enalapril (0.4%), as observed in Table 3. In a meta-analysis on 22 studies, Wang et al. indicated that olmesartan provided greater reduction in both diastolic and systolic blood pressure than losartan and systolic blood pressure compared to valsartan (Wang et al., 2012). In the HOPE and EUROPA trails, ramipril had a better outcome than placebo.

![Figure 5](image1.png)

Figure 5: The association between the Quality of Life of the patient with the ACE Inhibitors and Angiotensin Receptor Blockers

We obtained a greater strength (23.2%) among the group who had been diagnosed with the disease more than five years, followed by those with a duration between 1 and 2 years and least was observed in the group with a duration between 1 to 6 months, shown in Table 2. Majority of the CKD population had the long-standing disease (greater than five years), this can be attributed to the suppression of known “causes” of progression by targeting high blood pressure (BP) as well as the impact of renin-angiotensin system (RAS) related drugs (Brenner et al., 2001).

In particular, an elevation of 20 mm Hg accounts for many increased mortality (Forouzanfar et al., 2013). There are two major components to slow the rate of progression of CKD: treatment of the underlying disease, if possible; and treatment of secondary factors that are predictive of progression, such as elevated blood pressure (Coresh et al., 2001).

Among the 495 patients, 348 patients had blood pressure controlled on the last visit. Only 195 patients were stable with the best control on all the three visits. A majority had fluctuated BP during their three consecutive visits, shown in Figure 1. Tozawa et al. also argued that controlling blood pressure within normal levels can prevent the development of ESRD in both male and female patients (Tozawa et al., 2003). We had patients with poor blood pressure control which could be attributed to the advancement of CKD irrespective of gender.

The discontinuation rate was found to low (3.4%), and among them, ramipril (1.8%) was the main culprit, shown in Table 3. ARBs have demonstrated excellent safety profiles alone and in combination with other antihypertensive therapies during the past 20 years. The tolerability profiles of ARBs are similar to placebo and superior to ACE inhibitors.

The risk of discontinuation for an adverse event was reduced by 29% with ARB treatment, by 10% with diuretics, and by 2% with calcium-channel blockers. In contrast, it was increased by 18% with ACE-inhibitors and by 13% with beta-blockers (Barrreras and Gurk-Turner, 2003). The health status of patients on ACEIs was better than ARBs, observed in Figure 5. The null hypothesis was accepted using chi-square analysis, and it was observed that there is no significant statistical difference (P>0.05) among the administration of angiotensin related drugs on patients Quality of Life (QOL).

CONCLUSIONS

Proper diet and blood pressure control had more significant impact on the progression of CKD. Hence the administration of a safer drug, ACEI was found to influence the quality of life of the patients. Even though ARBs claim to have a lesser side effect, patients had much better health outcomes with ACEI.

Conflict of Interest

The authors declare that they have no conflict of interest for this study.

Funding Support

The authors declare that they have no funding support for this study.
REFERENCES

Baker, M., Perazella, M. A. 2020. NSAIDs in CKD: Are They Safe? American Journal of Kidney Diseases, 76(4):546-557.

Barreras, A., Gurk-Turner, C. 2003. Angiotensin ii Receptor Blockers. Baylor University Medical Center Proceedings, 16(1):123–126.

Bernstein, J., Werner, A. L., Verani, R. 1998. Non-steroidal Anti-Inflammatory Drug Fetal Nephrotoxicity. Pediatric and Developmental Pathology, 1(2):153–156.

Brenner, B. M., Cooper, M. E., de Zeeuw, D., Keane, W. F., Mitch, W. E., Parving, H.-H., Remuzzi, G., Snapinn, S. M., Zhang, Z., Shahinfar, S. 2001. Effects of Losartan on Renal and Cardiovascular Outcomes in Patients with Type 2 Diabetes and Nephropathy. New England Journal of Medicine, 345(12):861–869.

Coresh, J., Wei, G. L., Mcquillan, G., Brancati, F. L., Levey, A. S., Jones, C., Klag, M. J. 2001. Prevalence of high blood pressure and elevated serum creatinine level in the United States: findings from the third National Health and Nutrition Examination Survey (1988-1994). Archives of internal medicine, 161(9):1207–1216.

Duan, J., Wang, C., Liu, D., Qiao, Y., Pan, S., Jiang, D., Zhao, Z., Liang, L., Tian, F., Yu, P. 2019. Prevalence and risk factors of chronic kidney disease and diabetic kidney disease in Chinese rural residents: a cross-sectional survey. Scientific Reports, 9(1):10408.

Forouzanfar, M. H., Alexander, L., Anderson, H. R., Bachman, V. F., Biryukov, S., Brauer, M., Burnett, R. 2013. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and metabolic risks or clusters of risks in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study. The Lancet, 386:2287–2323.

Hallan, S. I., Coresh, J., Astor, B. C., Åsberg, A., Powe, N. R., Romundstad, S., Hallan, H. A., Lydersen, S., Holmen, J. 2006. International Comparison of the Relationship of Chronic Kidney Disease Prevalence and ESRD Risk. Journal of the American Society of Nephrology, 17(8):2275–2284.

Hildebrandt, F. 2010. Genetic kidney diseases. The Lancet, 375(9722):1287–1295.

Kidney International Supplements 2013. K/DOQI clinical practice guidelines for the evaluation and management of chronic kidney disease. Official journal of the international society of nephrology, 3(1):136–150.

Lekp, F., Kamdem, F., Doualla, M., Nouga, Y., Sontsa, O., Temfack, E., Kingue, S. 2017. Prevalence and risk factors of chronic kidney disease in newly diagnosed and untreated hypertensive patients in cameroon: A cross-sectional study. Saudi Journal of Kidney Diseases and Transplantation, 28(5):1144–1144.

Levey, A. S., de Jong, P. E., Coresh, J., Nahas, M. E., Astor, B. C., Matsushita, K., Gansevoort, R. T., Kasiske, B. L., Eckardt, K.-U. 2011. The definition, classification, and prognosis of chronic kidney disease: a KDIGO Controversies Conference report. Kidney International, 80(1):17–28.

National Kidney Foundation 2002. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. American Journal of Kidney Diseases : The Official Journal of the National Kidney Foundation, 39(2 Suppl 1):1–266.

Ojji, D. B., Ajayi, S. O., Mamven, M. H., Atherton, J. 2009. Prevalence of dyslipidemia in normoglycemic subjects with newly diagnosed high blood pressure in Abuja, Nigeria. Journal of Clinical Lipidology, 3(1):51–56.

Park, J. I., Baek, H., Jung, H. H. 2011. Prevalence of Chronic Kidney Disease in Korea: the Korean National Health and Nutritional Examination Survey. Journal of Korean Medical Science, 31(6):915–923.

Ridao, N., Luño, J., de Vinuesa, S. G., Gómez, F., Tejedor, A., Valderrábano, F. 2001. Prevalence of hypertension in renal disease. Nephrology Dialysis Transplantation, 16(suppl_1):70–73.

Rysz, J., Franczyk, B., Ciałkowska-Rysz, A., Gluba-Brzózka, A. 2017. The Effect of Diet on the Survival of Patients with Chronic Kidney Disease. Nutrients, 9(5):495–495.

Shankar, A., Klein, R., Klein, B. E. K. 2006. The Association among Smoking, Heavy Drinking, and Chronic Kidney Disease. American Journal of Epidemiology, 164(3):263–271.

Tannor, E. K., Norman, B. R., Adusei, K. K., Sarfo, F. S., Davids, M. R., Bedu-Addo, G. 2019. Quality of life among patients with moderate to advanced chronic kidney disease in Ghana - a single centre study. BMC Nephrology, 20(1):122–122.

Tozawa, M., Iseki, K., Iseki, C., Kinjo, K., Ikemiya, Y., Takishita, S. 2003. Blood Pressure Predicts Risk of Developing End-Stage Renal Disease in Men and Women. Hypertension, 41(6):1341–1345.

Walker, R., Whittlesea, C. 2015. Clinical Pharmacy and Therapeutics E-Book (Walker, Clinical Pharmacy and Therapeutics). page 1000. Churchill Liv-
Wang, L., Zhao, J., Liu, B., Shi, D., Zou, Z., Shi, X. 2012. Antihypertensive Effects of Olmesartan Compared with Other Angiotensin Receptor Blockers. *American Journal Cardiovascular Drugs*, 12(5):335–344.