ADEQUATE BLOOD PRESSURE CONTROL AND ASSOCIATED FACTORS AMONG DIALYSIS NAIVE CHRONIC KIDNEY DISEASE PATIENTS IN NORTH WEST NIGERIA

¹Makusidi AM, ¹Yakubu A, ¹Liman HM, ¹Isah MD, ²Adamu NA, ²Chijioke A,

¹Department of Medicine, Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria

²Department of Medicine, University of Ilorin Teaching Hospital, Ilorin, Nigeria

ABSTRACT

Background: Majority of chronic kidney disease patients have systemic hypertension, which is an independent risk factor for progression to end stage renal disease and cardiovascular events. The importance of lowering BP and inhibiting the RAAS as specific goals for renal and cardiovascular protection has not been studied in our environment.

Objectives: We assessed pattern of BP control and associated factors to determine influence of drug combination that included RAAS inhibitors.

Methods: Records of 167 CKD patients were studied. Information on bio-data, aetiology of CKD, pattern of BP control, antihypertensive drug usage and social behavior were categorized and documented. CKD was defined as estimated GFR < 60ml/min/1.73m² and/or presence of dipstick proteinuria for > 3 months. Adequate target treatment goal was taken as BP ≤ 130/80mmHg.

Results: Majority of the CKD patients were in the third and fourth decades and the commonest aetiology was hypertension. Commonest drug class combination which achieved target goal was ACEI, ARB, CCB with diuretic, followed by ARB, CCB with diuretic. The use of multiple drugs including ACEI and ARB was associated with better control of BP.

Conclusions: Adequate target BP control is achievable with combination of drugs that include ARB, ACEI and diuretics but the major impediment was that of poverty and high cost of drugs. We recommend aggressive use of three or more drugs including ARB and ACEI. Health education on regular clinic attendance and compliance with medication should be vigorously pursued.

Key Words: BP control, Renin-Angiotensin Inhibitors, CKD, Nigeria

Correspondence:
Dr MA Makusidi,

Department of Medicine, Usmanu Danfodiyo
University Teaching Hospital, Sokoto, Nigeria
E-Mail: makusidi1@yahoo.com
Tel +2348036057382, +2348055088223

INTRODUCTION

Systemic Hypertension (HTN) is a cause and complication of chronic kidney disease (CKD).^{1,2} It increases the risk of loss of kidney function and end-stage renal disease (ESRD), early development and accelerated progression of cardiovascular disease and premature death.^{3,4} An increased pressure load to renal microvasculature leads to damage of capillaries and mesangial cells which activate the renin-angiotensin-aldosterone system, culminating in elevated sympathetic tone and fluid overload.⁵ The nephron damage leads to loss of ability to auto regulate glomerular filtration flow, resulting in hyperfiltration that manifests as proteinuria.^{5,6} An interplay of increased sympathetic tone, fluid overload and proteinuria activate repair

responses mediated by fibrinogenetic cytokines and angiotensin II which compound progression of hypertension and nephron loss.^{6,7} The crucial role of adequate blood pressure (BP) control in reduction of cardiovascular risks and progression of CKD is increasingly being recognized.^{8,9}

Studies have demonstrated benefits of BP control in slowing progression of kidney disease.^{6,8,10,11} Angiotensin converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB) which preferentially lower intraglomerular pressure and reduce proteinuria are more effective than other antihypertensive drugs in preventing progression of kidney disease.^{6,8,10,11} A combination of both ACEI and ARB drugs has been found to be more effective than treatment with either drug alone in reducing BP and

microalbuminuria but carries risk of a drop in GFR and mild elevation in serum creatinine and potassium.^{12, 13} The importance of both lowering BP and inhibiting the renin-angiotensin system as specific goals for renal and cardiovascular protection in CKD have been emphasized.^{3,14} There is paucity of information on BP control and associated factors among CKD patients in our environment especially with increasing use of ACEI and ARB in relation to other classes of antihypertensive drugs. The foregoing reasons prompted this study.

MATERIALS AND METHODS

It is a retrospective cross-sectional study. The case notes of renal patients who were either attending or discharged from Usmanu Danfodiyo University Teaching Hospital, Sokoto (UDUTH) within January 2003 and December 2013 were retrieved from the medical records. Patients that met criteria for CKD¹⁵ but are yet to commence renal replacement therapy were studied. Information obtained from case files included bio-data, blood pressure at first presentation, BP during subsequent visits, antihypertensive medication and social habits. CKD was defined by estimated GFR $<60\text{ml/min/1.73m}^2$ and/or presence of dipstick proteinuria for greater than 3 months. The aetiological diagnosis of CKD followed the process of a previous study in our environment (16). Adequate BP control was defined as BP $\leq 130/80\text{mmHg}$ in at least three preceding clinic visits, following published guidelines for disease specific definitions of BP control.¹⁷ Resistant hypertension (RHT) was taken as persistent elevation of BP above $130/80\text{mmHg}$, while isolated systolic hypertension (SHT) and isolated diastolic hypertension (DHT) were taken as $>130/\leq 80\text{mmHg}$ and $\leq 130/>80\text{mmHg}$ respectively, despite regular use of maximal tolerated doses of three antihypertensive drugs including a diuretic for at least one month.¹⁸

It is the practice in our centre to measure BP after at least 3 minutes rest, using standard

mercury sphygmomanometer and appropriate cuff size. The cuff is usually applied to exposed right upper arm and rapidly inflated to 30mmHg above level at which the pulse disappears and then deflated gradually. Phases 1 and 5 of Korotkoff sound was taken as systolic and diastolic BP respectively. An average of two readings of BP measured in the patient was taken for the purpose of this study. Patient was said to be compliant if regular on medication and clinic attendance in the preceding four scheduled clinic visits and those with 75% attendance were regarded to be adherent to treatment.

Data analysis was done using statistical software SPSS version 16. Mean $\pm$ standard deviation was used for continuous data, student t test for comparison of means while comparison of proportion was by chi-square test. The level of statistical significance was taken as $p < 0.05$.

RESULTS

A total of 167 CKD patients were studied. Majority were in the third and fourth decades of life (Fig 1). The aetiology of CKD (Fig 2) showed that the commonest cause was systemic hypertension (HTN) followed by chronic glomerulonephritis (CGN) and diabetic nephropathy (DN). The categories of BP control are demonstrated in figure 3. Majority of the patients had poor control (54%) while 46% had good control. The pattern of drug utilization shows that 42% were non-compliant on treatment and the commonest drug class combination which achieved the highest number of good control was ACEI, ARB, calcium channel blockers (CCB) with diuretic, followed by ARB, CCB with diuretic and CCB and ACEI with diuretic. Resistant HTN was commonest among patients that used CCB with diuretic alone. Patients with aetiological diagnosis of HTN and CGN had highest frequency of poor BP control accounting for 35.6% and 33.3% respectively. There was positive correlation between poor BP control and body mass index ($p < 0.05$), but no correlation with age, alcohol intake and smoking habit ($p > 0.2$).

DISCUSSION

Majority of patients with CKD have HTN which is an independent risk factor for progression of kidney disease and cardiovascular events.³ Prevalence of HTN increases with declining GFR and documented rates are 30%, 48%, 60%, and 84% for patients with stage 1, stage 2, stage 3, and stages 4 to 5 CKD respectively.¹⁹ The risk for a major cardiovascular event in these patients also increases progressively as the renal function declines ranging from 1.4 fold for patients with GFR of 45ml/min/1.73m² to 3.4 fold for patients with GFR < 15ml/min/1.73m² relative to people with normal renal function. Adequate control of BP to evidence based target with appropriate antihypertensive agents can prevent serious consequences of CKD.^{19, 20} The markedly lowered BP threshold for kidney damage necessitates lowering of BP to normotensive range in order to prevent progressive kidney damage.

Majority of CKD patients in this study were in the third and fourth decades of life in contrast with fifth and sixth decade in developed nations.²¹⁻²⁴ The disparity is linked with pattern of disease causing CKD in both populations.^{16,21,22,24,25} The relatively young age at which CKD patients present in the tropics is ascribed to a variety of infective agents implicated in the aetiology of CGN that are prevalent in endemic proportions.^{21, 22, 25} Hypertension was the commonest aetiology of CKD followed by CGN and DN in our study. This is in accord with findings from some tropical and temperate countries which show that much of excess risk of ESRD in blacks is due to high rate of renal disease from systemic hypertension.²⁶⁻²⁸ It contrasts with reports from earlier studies in the tropics which revealed CGN as the commonest prevalent cause of CKD.^{16,21,25} However, with current trend of transition from communicable to non-communicable disease, it is expected that the latter will equal or even exceed the former in developing nations; thus resulting in double burden.^{25, 29}

Majority of these patients (54%) had uncontrolled BP categorized into resistant hypertension (39%), isolated systolic hypertension (7%) and isolated diastolic hypertension (8%). Factors that contributed to poor BP control include lack of primary care providers, high rate of non-adherence to medication and non-compliance with dietary guidelines. Major contributing factors to non-adherence to medication from this study were ignorance, poverty, and high cost of newer antihypertensive drugs. Risk factors for poor BP control from other studies include lack of understanding of the importance of BP control in preventing progression and complications of CKD, cognitive difficulties associated with CKD, intolerance of drug side effects and high cost of medication.³⁰⁻³¹ Our findings on target BP control are comparable with observation from similar studies in United States of America, in which 37% of patients achieved target goal.²⁸ It however contrasts with our observation among those with uncontrolled hypertension in which 12% versus 59% had systolic hypertension, while 16% versus 7% had diastolic hypertension respectively. The disparity in uncontrolled systolic hypertension may be due to older age of patients with advanced CKD in developed countries as recent data has documented high rate of systolic hypertension among elderly CKD patients.^{32, 33}

The commonest drug class combination that achieved the highest number of target control was ACEI, ARB, CCB with diuretic (38%), followed by ARB, CCB with diuretic (25%) and CCB, ACEI with diuretic (16%). Our finding that the use of multiple drugs including ACEI and ARB is associated with better control of BP is in accord with previous studies that alluded to the fact that rennin-angiotensin-aldosterone system (RAAS) inhibitors have emerged as leading drugs in the treatment of hypertension among CKD patients.^{33, 34} These drugs slow progression of kidney disease and reduce risk of cardiovascular events independent of their BP lowering effects.^{14, 33} It is instructive to note from our study that a

combination which involved ARB and ACEI achieved better target control than those combinations which included either ARB or ACEI and the risk of hyperkalaemia was not increased.

We therefore recommend judicious use of ARB/ACEI in addition to CCB and diuretic among our CKD patients. Despite the paucity of elevation in serum creatinine and potassium in our findings, these parameters should be monitored one to two weeks after initiation of combined ARB and ACEI therapy. Our observation that cigarette smoking and alcohol intake did not influence pattern BP control is difficult to explain since both habits are risk factors for cardiovascular events and progression of chronic kidney disease. It may be due to very low prevalence of both social behaviors among our CKD patients which could have blunted any relationship with BP control. Our CKD patients with aetiological diagnosis of HTN and CGN had the highest rate of poor BP control in contrast with DN and chronic pyelonephritis. The disparity in the

pattern of BP control may be related to differences in the mechanism involved in genesis of hypertension in these conditions.

Fig 3: Categories of BP Control

In conclusion, BP control was inadequate in majority of our CKD patients using the newer control guidelines. Adequate target BP control is achievable with combination of drugs that include ARB, ACEI and diuretics. The main contributory factors to poor BP control were ignorance, poverty, high cost of newer antihypertensive drugs and non-compliance to medication as many of these patients with resistant hypertension could neither afford nor sustain use of ARB and ACEI. We recommend aggressive use of three or more drugs including ARB and ACEI especially among those having HTN and CGN aetiologies. Health education with emphasis on regular clinic attendance and compliance with medication should be vigorously pursued in a bid to reduce burden of ESRD.

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