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Chronic Renal Failure and Arterial Hypertension

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Abstract: ***Hypertension is a frequent and early component in the uremic syndrome. Extracellular volume expansion causes hypertension in approximately 75% of patients with chronic renal failure and therefore is responsive to hemodialysis. The other major cause of hypertension in uremic patients is hyperreninemia. The degree of hypertension in this small group of patients is more extreme, is not responsive to volume manipulations by dialysis, and often will require bilateral nephrectomy. The route of excretion and drug-dosage alteration in hypertension treatment before initiation of dialysis are important. Indications for hemodialysis and bilateral nephrectomy for complicated hypertension and in preparation for renal transplantation vary in different programs. The increased incidence of cardiovascular death in chronic hemodialysis patients should modify these indications to obtain earlier and better control of hypertension.***

Keywords: chronic renal disease, hypertension, treatment, prevention

1. Introduction

Chronic kidney disease (CKD) is increasingly prevalent, with an estimated 26 million adults with CKD in the US (1). Hypertension is the most common comorbidity in chronic kidney disease. At least 85% of patients with stage 3 CKD or greater have hypertension, making parenchymal kidney disease the most common 'secondary' form of hypertension. Treatment of hypertension can often be challenging, as these patients often have severe hypertension requiring the use of multiple medications to achieve target blood pressure (BP) goals. Target BP goals are lower in patients with CKD than in the general population. Ideally, BP should be less than 130/80mmHg and less than 125/75mmHg if patients also have significant proteinuria (>1g/24 hours). Hypertension is very common in CKD, with more than 80% of CKD patients having coexistent hypertension. Patients with more severe CKD are more likely to have more severe hypertension that is more difficult to control, requiring a greater number of medications. Conversely, patients with more severe hypertension are more likely to develop CKD (2). The type of renal disease also influences the likelihood of hypertension, and classically tubulo-interstitial diseases have had less prevalence of elevated BP than glomerular diseases. A large and growing number of factors influence BP regulation in CKD. Most of the increase in BP results from a subset of three primary systems, which include: salt retention, renin–angiotensin–aldosterone axis activation and sympathetic nervous system activation (4). These factors are all potentially treatable and the physician should take these into account when selecting medications in CKD patients. Volume expansion is common in hypertension of CKD. As renal function declines, so does the ability to excrete sodium. If heart failure occurs, this adds to the challenge of maintaining euvolemia. Sodium increases BP, so as kidney function declines it does so to an even greater extent than simple volume expansion would predict at the lowest levels of kidney function (5). This finding suggests that the effect of salt intake on BP as further kidney function loss occurs is likely to be enhanced by the CKD milieu. Moreover, salt administration is well known to abet the pro-hypertensive effects of angiotensin-II and norepinephrine. The renin–angiotensin system plays a major role in hypertension, especially in patients with CKD. This is clear in the antihypertensive response to both ACE inhibitors and angiotensin II receptor blockers (ARBs) in patients with CKD. Aside from the hemodynamic consequences of renin activation, the excess angiotensin II produced probably contributes to progressive renal function loss and other target organ damage. It does this through its stimulation of aldosterone release, potentiation of the effects of various growth factors, and, in particular, its stimulating effects on the fibrogenic cytokine transforming growth factor-β (6). Some of the increase in renin system activation may be the result of sympathetic input into the juxtaglomerular apparatus through the β1-adrenoreceptor. The sympathetic nervous system also appears to be overactive in CKD.10 Like the renin–angiotension system, the kidney is both the source and the recipient of neurogenic activity (7). There is a fairly extensive network of sensory nerve fibers in the kidney, and many laboratory data indicate that sympathetic activation plays a role in hypertension in CKD through direct vascular constriction and the aforementioned interactions with renin and salt. The recent investigation showing that renal sympathetic nerve ablation improves BP control in drug-resistant hypertension is further evidence of the importance of this system (8). Several other systems are also active to a pathological degree in some patients with CKD. Among those amenable to potential drug treatment are endothelin and aldosterone. Finally, there is also some progress on the genetic front. Several rare phenotypes in which the kidney and hypertension are linked have been described, shedding light on important intra-renal BP regulation pathways. Aside from diagnostic value, there has been little benefit achieved to date from genetic studies with respect to guiding intervention (9).

2. Material and Methods

One hundred and thirty six patients with CKD treated at regional hospital of Fier, between January 2013, and December 2015, were considered for the study. This was a prospective observational study. Inclusion criteria were: Newly diagnosed cases of CKD based on Kidney Disease Improving Global Outcome 2012 criteria, including CKD patients on hemodialysis; Age ≥18 years. Exclusion criteria:

Those not willing to participate in the study; Age <18 years; Valvular heart diseases; Congenital heart diseases; Pulmonary obstructive and restrictive diseases; HIV-infected patients; Chronic liver disease; Connective tissue diseases; Hypothyroidism and hyperthyroidism.

3. Results

The study included 145 patients with average age of 59.9 + 13.2 years. 65 (44.8%) of the sample were females and 80 (55.2%) males (table 1). The mean uricemia value in females was 5.68+ 1.40 mg/dl, while in males was 6.45 + 1.66 mg / dl, with a statistically significant difference between them (p=0.01). Kendal correlation coefficient was analyzed for relation of uricemia with other variables, from which a statistically significant, positive relationship was found between with gender (p=0.02), urea (p=0.02) and and VLDL (p=0.04). There was no significant difference in systolic and diastolic blood pressure according to the stages of dialysis (fig. 1). PH remained an underestimated issue in CKD patients until the very recent years. In our study, majority of the patients in all the three echocardiography had moderate PH. This is consistent with other studies. PH in CKD can occur through multiple mechanisms, including PH of WHO Group 1–5 (pulmonary arterial hypertension, left-sided heart disease, chronic pulmonary disease and hypoxia, chronic thromboembolic disease, and unexplained PH, respectively) (10). The evaluation of patients with hypertension and CKD requires some additional consideration aside from the standard hypertensive work-up suggested by JNC-716, in the following ways: In addition to the usual history taken for determining primary versus secondary hypertension, target organ damage, and presence of other cardiovascular risk factors, historical details should focus on prior drug therapies and why they were stopped (11).. This should include issues such as drugs that caused hyperkalemia, worsening renal function, edema or dyspnea, and intolerable side effects. In addition to the usual exam findings that may suggest secondary forms of hypertension, document the presence of rales, presence of an S3, pedal edema, and carotid bruits. These findings are more common in CKD patients, and their subsequent clinical course may guide diuretic management. In addition to the standard lab tests (detailing target organ damage, suggesting secondary hypertension, or reflecting drug side effects), consider checking for presence/degree of anemia (12). Proteinuria should also be quantified since erythropoietin (which can raise BP) may be necessary and because the antihypertensive benefits and treatment goals of intervention are more impressive and lower, respectively, when proteinuria is present. Both proteinuria and reduction of GFR have been associated with increased cardiovascular morbidity and mortality (13,14). This association is so strong and clinically relevant that the diagnosis of CKD places a patient into the highest cardiovascular risk level, irrespective of stratification according to traditional cardiovascular risk factors (14,15). The high mortality among CKD patients on renal replacement therapy, which for the ages between 25 and 35 years may rise up to 375-fold compared to the general population, is derived predominantly from cardiovascular causes (16,17). This cardiovascular morbidity occurring in patients with CKD is called cardiorenal syndrome type 4, which reflects tight interlink between the heart and kidney (18).

4. Conclusion

Most kidney diseases worsen progressively over time. Antihypertensive therapy affects several modifiable key factors related to the progression of kidney disease, including hypertension, proteinuria, and other mechanisms, such as increased acitivity of the reninangiotensin system (RAS). Several large, controlled trials have examined the effect of antihypertensive therapy on the progression of kidney disease in patients with and without hypertension. While these trials have provided important answers about therapy, the relationships among these “progression factors” are complex, and many questions remain unanswered, especially regarding the mechanisms underlying the therapeutic benefit of the interventions

References

[1] Bello AK , Levin A , Tonelli M , et al . Assessment of Global Kidney Health Care Status. JAMA 2017;317:1864–81.doi:10.1001/jama.2017
[2] Taler SJ, Agarwal R, Bakris GL, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for management of blood pressure in CKD. Am J Kidney Dis. 2013;62(2):201-213.
[3] Lilitkarntakul P, Dhaun N, Melville V, Blackwell S, Talwar DK, Liebman B, *et al*. Blood pressure and not uraemia is the major determinant of arterial stiffness and endothelial dysfunction in patients with chronic kidney disease and minimal co-morbidity. Atherosclerosis 2011;216:217-25.
[4] National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. Am J Kidney Dis 2002;39 2 Suppl 1:S1-266.
[5] Tonelli M, Wiebe N, Culleton B, House A, Rabbat C, Fok M, *et al*. Chronic kidney disease and mortality risk: A systematic review. J Am Soc Nephrol 2006;17:2034-47.
[6] Vanholder R, Massy Z, Argiles A, Spasovski G, Verbeke F, Lameire N; European Uremic Toxin Work Group. Chronic kidney disease as cause of cardiovascular morbidity and mortality. Nephrol Dial Transplant 2005;20:1048-56.
[7] US Renal Data System: USRDS 2009 Annual Data Report: Reference Tables. Patient Characteristics Bethesda, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2009.
[8] House AA, Anand I, Bellomo R, Cruz D, Bobek I, Anker SD, *et al.* Definition and classification of Cardio-Renal Syndromes: Workgroup statements from the 7th ADQI Consensus Conference. Nephrol Dial Transplant 2010;25:1416-20.
[9] madi J, Zolfaghari H, Firoozi R, Ardalan MR, Toufan M, Shoja MM, *et al.* Unexplained pulmonary hypertension in peritoneal dialysis and hemodialysis patients. Rev Port Pneumol 2012;18:10-4.
[10] Ramasubbu K, Deswal A, Herdejurgen C, Aguilar D, Frost AE. A prospective echocardiographic evaluation

of pulmonary hypertension in chronic hemodialysis patients in the United States: Prevalence and clinical significance. Int J Gen Med 2010;3:279-86.
[11] Wu HY, Huang JW, Peng YS, et al. Microalbuminuria screening for detecting chronic kidney disease in the general population: a systematic review. *Ren Fail* 2013; 35:607–614.
[12] Saran R, Li Y, Robinson B, et al. US Renal Data System 2014 Annual Data Report: epidemiology of kidney disease in the United States. *Am J Kidney Dis* 2015; 66 (1 suppl 1):S1–S305.
[13] Anderson AH, Yang W, Townsend RR, et al; Chronic Renal Insufficiency Cohort Study Investigators. Time-updated systolic blood pressure and the progression of chronic kidney disease: a cohort study. Ann Intern Med. 2015;162(4):258-265.
[14] McClellan WM, Flanders WD. Risk factors for progressive chronic kidney disease. *J Am Soc Nephrol* 2003; 14:S65–70.
[15] O'Seaghdha CM, Hwang SJ, Bhavsar NA, et al. Lower urinary connective tissue growth factor levels and incident CKD stage 3 in the general population. *Am J Kidney Dis* 2011; 57:841–849.
[16] Shankar A, Sun L, Klein BE, et al. Markers of inflammation predict the long-term risk of developing chronic kidney disease: a population-based cohort study. *Kidney Int* 2011; 80:1231–1238.
[17] K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis*2002; 39 (2 suppl 1):S1–266.
[18] Wells GA, Shea B, O'Connell D, et al.. The Newcastle–Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses, 2016.

Table 1: Sociodemographic and clinical characteristics of patients

Variables	Data
Age (years)	
M (SD)	59.9 (13.2)
range	18-84
Gender n (%)	
Females	65 (44.8)
Males	80 (55.2)
Hypertension	
Systolic	137.8 (18.2)
Diastolic	79.9 (13.8)
Duration of Hypertension (years)	
<10	120 (82.8)
10-15	17 (11.7)
>15	8 (5.5)
Duration of CKD (weeks)	
M (SD)	36.5 (42.7)
range	0-351

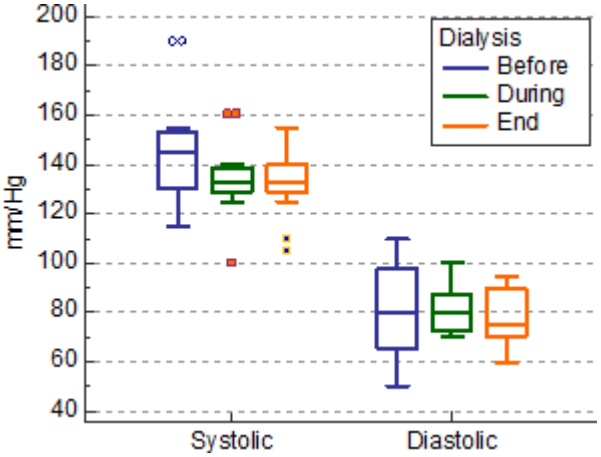

Figure 1: Comparison of systolic and diastolic blood pressure according to dialysis