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Case Report

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Therapy of resistant hypertension in patients with chronic kidney disease complications of anemia in hemodialysis: A case report

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Abstract: Chronic Kidney Disease (CKD) is closely related to hypertension. Increasing the severity of CKD is associated with more difficult blood pressure control. Appropriate therapeutic management is needed to prevent complications due to uncontrolled hypertension. We report the case of a 78-year-old female patient with a diagnosis of hypertension and end-stage CKD with a history of undergoing hemodialysis for 4 years. The patient has been taking antihypertensive drugs such as Angiotensin Receptor Blockers, Calcium Channel Blockers and Diuretics. However, the administration of three antihypertensive drugs still could not help achieve the expected blood pressure target where the systolic blood pressure was still above 160 mmHg. The patient also has anemia as a common complication of chronic kidney disease. Appropriate management of therapy with fourth-line therapy and hemoglobin repair is necessary to achieve improved clinical outcomes and reduce renal worsening.

Keywords: Hypertension, Chronic Kidney Disease, Anemia, Hemodialysis.

INTRODUCTION

Chronic Kidney Disease (CKD) is characterized by renal structural abnormalities or a progressive and irreversible decline in renal function.[1] CKD is defined as kidney damage lasting for ≥ 3 months due to structural or functional anomalies, with or without a reduction in Glomerulus Filtration Rate (GFR) to <60 mL/min/1.73 m².[2–4] CKD significantly contributes to hypertension development.[5,6] Chronic kidney dysfunction escalates blood pressure through mechanisms encompassing impaired sodium excretion, decreased baroreceptor sensitivity, heightened sympathetic nerve activity, and activation of the renin-angiotensin-aldosterone system.[7] The prevalence of hypertension increases proportionally with the severity of CKD stages.[2,8]

Hypertension emerges as a pivotal cardiovascular comorbidity among end-stage CKD patients undergoing hemodialysis.[9] Underlying pathophysiology

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revolves around excessive extracellular volume and kidney function alterations, influencing heightened vascular resistance and cardiac output.[10] Compared to healthy individuals, hemodialysis patients exhibit reduced urine volume, predisposing them to excess extracellular volume.[11,12] This fluid surplus drives changes in cardiac output and vascular resistance, key regulators of blood pressure.[13,14] Even with reduced GFR, renal renin secretion persists, triggering angiotensin II production and sodium retention, exacerbating extracellular volume expansion. As glomerular mass declines, sympathetic nerve overactivity ensues, contributing to increased cardiac output and vascular resistance.[15,16]

Hypertension management principles in hemodialysis patients involve preventing excess extracellular volume through antihypertensive diuretic therapy.[17,18] Inappropriate diuretic selection can lead to resistant hypertension. Regimen modification, including diuretic addition, dose escalation, or utilization of diuretics with distinct mechanisms, is viable.[2,19] Loop diuretics are preferred for GFR < 30 ml/min/1.73 m^2.[20] Kidney Disease: Improving Global Outcomes (KDIGO) recommends loop diuretics from CKD stage 4.[21] If tolerated, first-line Angiotensin-Converting Enzyme Inhibitors (ACE Inhibitors) or Angiotensin Receptor Blockers (ARBs) are also suggested for CKD patients with or without proteinuria due to their renoprotective benefits and ability to mitigate cardiovascular and renal event risks.[22–25]

CASE REPORT

A 78-year-old female elderly patient was admitted to the hospital with a diagnosis of grade II hypertension, stage 5 chronic kidney disease (CKD), anemia, constipation, and meteorism. The patient had been undergoing hemodialysis (HD) for the past 4 years. She presented with moderate nausea, abdominal pain, and black stools three days prior to admission. Vital signs revealed a heart rate of 84 beats per minute, systolic blood pressure above 160 mmHg, and SpO2 at 96%. Laboratory results indicated a hemoglobin level of 7.6 g/dL (L), PCV (*packed cell volume*) 23,5%(L), RBC 2,74 x 10^6 sel/µL (L), MCV 85,5 fl (N), MCH 27,7 pg (N), MCHC 32,5% (N), serum creatinine of 1.82 mg/dL, BUN of 10 mg/dL, urea of 22 mg/dL, and albumin of 5.03 g/dL. Stool examination revealed the presence of bacteria, leukocytes, and erythrocytes. On the second day of hospitalization, a repeat kidney function test showed an increase in serum creatinine to 3.28 mg/dL. Radiological findings indicated cardiomegaly with HHD configuration and aortosclerosis.

During her 9-day hospital stay, the patient received two units of blood transfusion, 14 TPM Kidmin, 1x8 mg ODR, 1x40 mg omeprazole, 3x500 mg Kalnex for 2 days, 3x1 15 mL Nucral syrup, 3x1 Dulcolax tablets, and Lactulax syrup. Initial antihypertensive therapy included furosemide 1x40 mg, which was discontinued after two days of use. The medication was switched to candesartan 1x16 mg and bisoprolol 1x5 mg. On the third day of medication use, these were halted, and amlodipine 1x5 mg was administered for a day. With the initiation of candesartan, blood pressure decreased from 180/83 mmHg to 155/88 mmHg. However, on the subsequent day, blood pressure rose again above 160 mmHg. The patient was discharged with amlodipine 1x5 mg, bisoprolol 1x5 mg, ranitidine 2x150 mg, and 3x1 15 mL Lacons syrup for home use.

RESULTS AND DISCUSSION

Uncontrolled hypertension is associated with increased risks of cardiovascular events, hospitalization, and mortality.[5] Thus, appropriate blood pressure control is essential for patients with chronic kidney disease (CKD) and hypertension to prevent adverse clinical outcomes. In this case report, we present a patient with end-stage CKD who experienced uncontrolled blood pressure despite treatment with three different classes of antihypertensive medications, a

condition known as resistant hypertension. According to the European Society of Cardiology (ESC) 2018 guidelines, resistant hypertension is defined as failure to lower systolic or diastolic blood pressure to values below 140 and 90 mmHg, respectively, despite combination therapy with an ACE inhibitor or ARB, calcium channel blocker (CCB), and thiazide or thiazide-type diuretic.[26,27]

In the double-blind crossover PATHWAY-2 study, spironolactone was compared to placebo, bisoprolol, and doxazosin. The results demonstrated that low-dose spironolactone (12.5-50 mg) led to greater reductions in both systolic and diastolic blood pressure compared to other therapies and placebo.[28] Based on these findings, ESC recommends managing uncontrolled hypertension in CKD with a combination of ARB, CCB, diuretic, and the addition of an aldosterone antagonist.[27] The American Heart Association (AHA) also shares a similar recommendation, suggesting spironolactone as the fourth-line treatment for resistant hypertension, followed by beta-blockers, alpha and beta-blockers, clonidine, or diltiazem).[29] If contraindicated, spironolactone may be substituted with bisoprolol and doxazosin.[26,27]

Anemia, a complication of CKD due to erythropoietin deficiency, can also occur. Research reports that CKD patients with a history of hypertension may experience anemia. Anemia is associated with hypertension, affecting the increase of endothelin-1 as a vasoconstrictor or increasing the sensitivity of angiotensin II. Hence, antihypertensive therapy is often accompanied by erythropoietin-stimulating agents (ESA) administration.[23] Subcutaneous erythropoietin administration can increase blood pressure by up to 10 mmHg in patients with chronic kidney disorders.[30]

The Kidney Disease Outcomes Quality Initiative (KDOQI) recommends a systolic blood pressure target of 140 mmHg before dialysis and ≤130 mmHg after dialysis. The JNC 8 guidelines suggest a more lenient target, recommending systolic and diastolic blood pressure below 150 mmHg and 90 mmHg, respectively).[24] Monitoring serum creatinine and BUN for adverse effects is essential when using ARB therapy.[25] Several studies have shown that the use of valsartan, captopril, and lisinopril can increase serum creatinine by 20–30%. In cases of persistent hyperkalemia, discontinuing ARB may be considered. Patient education regarding dietary and lifestyle modifications, as well as medication adherence, is crucial upon hospital discharge.

CONCLUSION

Based on the above case reports, the management of patients with chronic kidney disease complicated by hypertension is carried out in achieving appropriate blood pressure control targets and reducing the risk of kidney deterioration as well as cardiovascular events. Combination antihypertensive therapy consisting of ACE inhibitors or ARBs, calcium channel blockers, diuretics and spironolactone can be a therapeutic approach in patients with resistant hypertension.

AUTHORS' CONTRIBUTIONS

Yenry Sumarlim and Emilia Gan took research data and wrote this journal. Desantika Wuryana, M. Hari Pristantiningtyas, Herya Putra Dharma and Muhammad Muchlis chose cases in the hospital that could be used as case reports, as well as guiding the writing of this journal. Jainuri Erik Pratama, Adji Prayitno Setiadi and Marisca Evalina Gondokesumo reviewed and supervised the journal. All authors have read and approved the final journal.

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