Hypokalemia in patients on dialysis and supplementation with potassium

Reviewed by:

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Introduction

Chronic kidney disease (CKD) is a global public health issue and has a strong link with conditions like cardiovascular disease and diabetes. A systematic review and analysis published in 2022 estimated the prevalence of CKD in Asia and noted the absolute number of individuals with CKD in India to be up to 140.2 million.[1] Kidneys are involved in regulating fluid and electrolytes in the body. Conditions like CKD and end-stage renal disease (ESRD) are associated with potassium derangements, metabolic acidosis, etc.[2]

The extracellular fluid has only 2% of the total potassium while the intracellular fluid has most of the body's potassium (98%). Kidneys maintain the body's potassium homeostasis and remove the excess potassium. However, in patients with ESRD undergoing hemodialysis, non-renal potassium excretion and dialytic removal play a crucial role in potassium balance as renal excretion is decreased.[3] Potassium derangements, including hyperkalemia and, to a lesser extent, hypokalemia, can be seen in patients with CKD.[2]

This article focuses on hypokalemia in CKD and dialysis patients and management of hypokalemia, including the role of potassium supplementation.

Hypokalemia in CKD and hemodialysis patients

Altered potassium excretion from the kidneys results in hyperkalemia; however, hypokalemia can also be observed in patients with CKD.[2]

Potassium level in the serum of <3.5 mEq/L is considered hypokalemia. The potassium reduction could be caused by excess excretion or deficient intake of potassium. It could also be due to potassium shift in the extracellular to intracellular space.[3] Some causes of hypokalemia are summarized in Figure 1.[4]

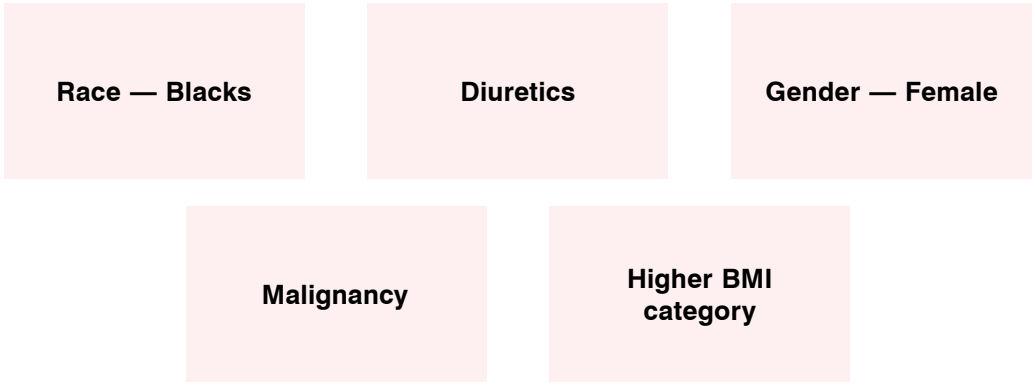
Hypokalemia in CKD could be attributed to the loss of potassium from the gastrointestinal tract or renal loss on account of diuretics (non-potassium sparing).[2] Severe potassium depletion could be associated with ileus, paralysis, and arrhythmias.[2] Hypokalemia is linked to an accelerated deterioration in kidney function among patients with CKD. This occurs as a result of hypokalemic nephropathy.[5] Key risk factors for hypokalemia in CKD patients are summarized in Figure 2.[6] Hypokalemia-induced cardiac arrest is particularly seen in patients who have a cardiac condition and in patients who are on digitalis.[3] At serum potassium levels below 3 mEq/L, the patient may develop generalized weakness and at levels below 2.5 mEq/L, there can be necrosis of muscles and rhabdomyolysis. As hypokalemia advances, one can have ascending muscle paralysis followed by respiratory failure and arrest.[3]

A study evaluated the relationship between serum potassium and the combined outcome of death and start of renal replacement therapy among older patients with CKD stages 4-5. During the 8-year follow-up, 24% of the patients died before starting replacement therapy and 35% started replacement therapy. The hazard ratios (HR) for combined outcome of death or kidney replacement therapy were shown to rise considerably when serum potassium dropped to 4.5 mmol/L or below and increased above 5.4 mmol/L (lowest HR at a potassium level of about 4.9 mmol/L).[5] It is important to prevent both hypokalemia and hyperkalemia in CKD patients.

Figure 1. Causes of hypokalemia

Loss of potassium	Deficient potassium intake	Transcellular shift
• Loss from gastrointestinal tract • Drugs — Diuretics, steroids, laxatives • Renal loss — Mineralocorticoid excess, renal tubular acidosis, osmotic diuresis, etc. • Dialysis • Hypomagnesemia	• Starvation • Anorexia • Total parenteral nutrition • Dementia	• Drugs — Decongestants, overdose of insulin, β_2- sympathomimetics, amphotericin B, etc. • Alkalosis • Thyrotoxicosis • Hypothermia • Familial hypokalemic periodic paralysis • Refeeding syndrome • Enhanced β_2-adrenergic stimulation

Figure 2. Risk factors for hypokalemia in CKD patients



BMI: Body mass index

The prevalence of hypokalemia among those undergoing hemodialysis is estimated at 1-2%. It appears to be more frequent among those on peritoneal dialysis at around 5-22%.[7] The major causes of hypokalemia in dialysis patients include use of low potassium dialysate, inadequate intake of potassium, and malnutrition. Hypokalemia-related mortality risk is greater as compared to hyperkalemia-related risk. This holds true even for CKD patients and dialysis patients.[7] A link has been suggested between hypokalemia following dialysis and fatal arrhythmias as well as sudden cardiac death, which is a major cause of mortality among dialysis patients.[2]

Use of low potassium dialysate results in a huge potassium shift across the membranes. This is regarded as a key factor contributing to cardiac events. Additionally, using low potassium dialysate and greater fluid removal could be tied to atrial fibrillation and premature ventricular beats.[2] Patients having a predialysis serum potassium level of 4 mmol/L or below have been reported to have around 1.4 times stronger death risk compared to a level of 5.1 mmol/L (optimum level).[8]

Even though there is a vulnerability to develop hyperkalemia, patients on hemodialysis can have low levels of intracellular potassium. Additionally, those having a low potassium level prior to dialysis may have longer or severe hypokalemia following dialysis. Low predialysis potassium also indicates malnutrition. These could explain the increased risk of death in these patients.[8]

Considering the impact of low potassium dialysate, ≥3 K* dialysate should be used in patients having a pre-dialysis potassium level of below 5 mmol/L.[2]

*Potassium

Management of hypokalemia

The aims of hypokalemia treatment include:[3,7,9]

- Reduce loss of potassium
- Replenish potassium
- Ascertain the cause
- Assess toxicity
- Prevention of cardiac arrhythmia and neuromuscular weakness, without leading to hyperkalemia.

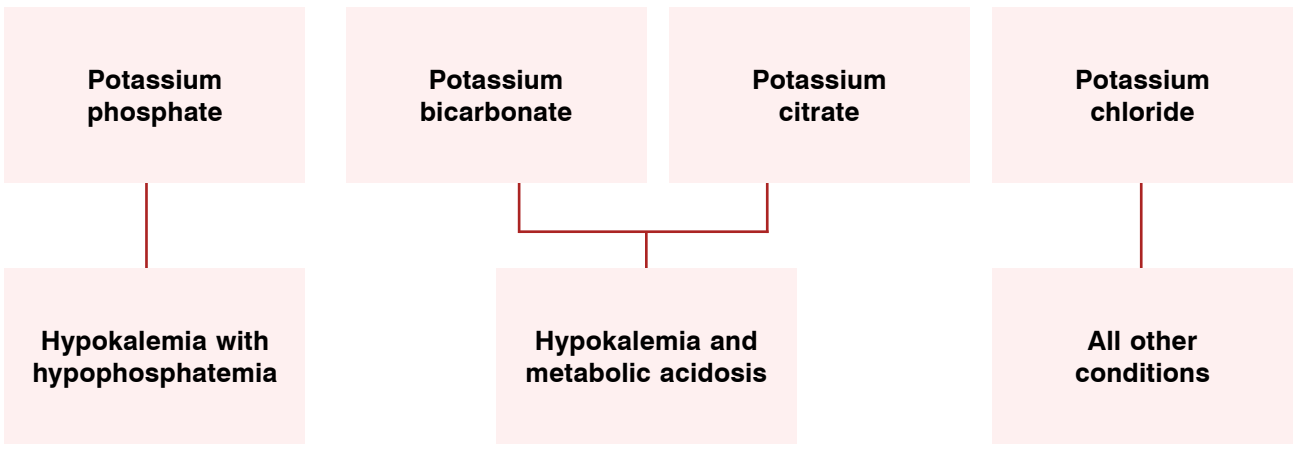
Presence of symptoms, abnormalities on electrocardiogram (ECG), and the severity of hypokalemia guide treatment.[7] Every 100 mEq reduction in total body potassium corresponds to a reduction in plasma potassium concentration by roughly 0.3 mEq/L.[3]

One must determine the underlying cause and treat it. This could be achieved by appropriate treatment of diarrhea and vomiting, stopping laxatives, giving potassium-sparing diuretics in patients requiring diuretic therapy, managing hyperglycemia, etc.[9]

Treatment of hypokalemia also involves potassium supplementation often given through the oral route. The preparations for potassium supplementation include potassium phosphate, potassium bicarbonate, potassium citrate, and potassium chloride (Figure 3).[3]

The route of potassium replacement is usually oral. Intravenous (IV) replacement can be considered in patients with severe hypokalemia with respiratory or cardiac instability.[3] Oral potassium supplementation is better taken with meals or afterwards.[9]

Figure 3. Potassium preparations



IV potassium is administered at a rate of up to 20 mEq/hr in order to reduce the risk of iatrogenic hyperkalemia. Peripheral administration of high potassium chloride concentrations can be detrimental as it may lead to pain or sclerosis.[3,7] Additionally, on account of the potential to cause increased sodium, potassium replacement should be done cautiously among those who have associated severe hyponatremia.[7] Caution must also be exercised while using IV potassium in patients with arrhythmia with rapid ventricular response, arrhythmia from digoxin toxicity, paralysis, severe diarrhea, and those having severe myopathy along with necrosis of muscles.[3]

Oral potassium chloride	IV potassium chloride
20 to 80 mEq/day Divided doses	Up to 20 mEq/hr Cardiac monitoring required Serum potassium to be checked after infusion of 60 mEq

A randomized study allocated peritoneal dialysis patients having hypokalemia to protocol-based potassium supplementation (oral potassium chloride to maintain 4-5 mEq/L serum potassium) or conventional supplementation (reactive supplementation at levels below 3.5 mEq/L) for a duration of 52 weeks. A total of 85 patients were given protocol-based treatment and 82 received conventional treatment (time-averaged serum potassium 3.33±0.28 mEq/L). In the protocol-based treatment group, there was a rise in serum potassium to 4.36±0.70 mEq/L (Conventional group 3.57±0.65 mEq/L). A significantly longer median time to first episode of peritonitis was noted in the protocol-based group (223 days compared to 133 days).[10]

Potassium chloride is effective in common causes that lead to potassium depletion. It is an efficient method to replenish acute potassium loss and oral potassium is the best way, given over days to weeks. While a 20 mEq/day dose may suffice for preventing hypokalemia, treatment may be achieved with 40 to 100 mEq/day.[11]

Conclusion

Potassium level in the serum of <3.5 mEq/L is considered hypokalemia. Though less common, hypokalemia can be seen in patients with CKD. There are various factors associated with potassium depletion, such as inadequate intake of potassium, excessive removal, potassium shifts, and gastrointestinal and renal losses.

Hypokalemia is linked to adverse outcomes and must be prevented and appropriately treated. Besides managing the underlying conditions, potassium supplementation is also used to treat hypokalemia. The severity of hypokalemia guides the route of potassium administration. Oral route is commonly used; however, patients with severe hypokalemia having respiratory or cardiac instability may need IV administration. Of the available potassium preparations, potassium chloride can be beneficial in a majority of causes that are known to result in potassium depletion.

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