Abstract: The introduction of dialysis for the treatment of end-stage renal disease (ESRD) during the middle of the last century has completely changed the prognosis of ESRD patients helping to prevent several deaths from uremia, pulmonary edema and electrolyte disturbances. Nevertheless mortality rates remains extremely high and several risk factors contribute to such scenario, including the high prevalence of traditional risk factors as diabetes and hypertension, but also due risk factors related do chronic kidney disease and eventually to new risk factors introduced when a dialysis modality is initiated.

Potassium disturbances are common and frequently associated with negative outcomes. In this paper we will focus on potassium disturbances in peritoneal dialysis patients. Particularly, we will discuss the role of hypokalemia in this population, comparing its prevalence in both dialysis modality and exploring the results of some important observational studies that investigated the negative association of low serum potassium levels with clinical outcomes including overall, cardiovascular and infectious mortality.

Keywords: Serum Potassium, Hypokalemia, peritonitis

Introduction:

The introduction of dialysis for the treatment of end-stage renal disease (ESRD) during the middle of the last century has completely changed the prognosis of ESRD patients. Dialysis prevented several deaths from uremia, acute pulmonary edema and severe electrolytic disturbances, of which hyperkalemia is considered one of the most important and frequent. Nevertheless the life expectancy of patients with chronic kidney disease (CKD) stage 5D remains significantly reduced despite efforts from the nephrology community. Several risk factors seems to contribute to such high mortality rates, ranging from traditional risk factors as diabetes and hypertension, to non-traditional risk factors as inflammation, uremia and dialysis related risk factors. In this paper we will focus on potassium disturbances, particularly in the important impact of hypokalemia in clinical outcomes.

Prevalence of hyper/hypokalemia

The prevalence of potassium disturbances varies considerably between dialysis modalities. Patients on hemodialysis (HD) are more likely to present hyperkalemia whilst peritoneal dialysis (PD) patients are more prone to develop hypokalemia. Actually some reports have shown that the prevalence in PD can be as great as 60% in some single centers.
studies but in average ranges from 5 to 10% of the whole PD population (2-10). Such differences are not unexpected because the dynamics of each modality: in intermittent HD, patients are normally submitted to rapid changes in their electrolyte pool followed by a interdialytic period of 48 to 72 hours that may lead to fluctuating serum potassium levels\(^\text{[11]}\). In contrast, PD provides continuous removal of potassium as a 24h-long therapy (except for nocturnal intermittent peritoneal dialysis - NIPD) and its solution does not contain any potassium. In addition, the constant glucose absorption from the peritoneal cavity may also promote a shift of extracellular potassium into the cells as a consequence of insulin secretion.

**Impact on clinical outcomes**

**Mortality**

Whilst hyperkalemia is considered of the most feared electrolyte disorders in the setting of CKD due its known association with cardiac arrhythmias and cardiovascular death (12), the impact of hypokalemia on mortality rates were until recently under-recognized(13). Nevertheless, hypokalemia is also associated with cardiovascular events in dialysis patients (2,7). One of the possible mechanisms underlying this association is the effect of potassium depletion on reducing the permeability of the cell membrane, delaying repolarization and thus increasing the refractory period of the cell leading to a higher predisposition to arrhythmias through a reentry mechanism. In addition, hypokalemia has been repeatedly reported as a surrogate marker of malnutrition and inflammation (4,14).

Several cohort studies from the past decades have shown that mortality rates are similar between HD and PD even for cardiovascular mortality and despite the myocardial stunning observed in the former (15-18). Therefore some authors hypothesized that the higher prevalence of hypokalemia in PD could be counterbalancing the negative impact of myocardial stunning observed in HD. In fact, a large cohort study shown that hypokalemia is not only more frequent in patients on PD as their contribution to the risk of mortality seems to be disproportional of the risk of hyperkalemia. Analyzing data of more than 120,000 dialysis patients (which approximately 10,000 on PD), found that the population-attributable risk for all-cause mortality was 3.6% for hypokalemia and 1.9% for hyperkalemia (2) . The authors found hypokalemia to be associated with all-cause mortality, cardiovascular mortality and even infectious mortality. All these associations were recently confirmed outside North America by the BRAZPD II, which is the largest cohort in Latin America (7,19).

The concern that hypokalemia could be only a surrogate marker was minimized with the study from the BRAZPD II cohort. Its difference from the previous studies was the use of a propensity score to match patients for several known risk factors suggesting that hypokalemia may have a direct impact on mortality(7). One interesting finding was that the association with infectious mortality was confirmed in the Brazilian cohort. Such association is not related to peritonitis but to sepsis not related to PD suggesting that hypokalemia may also directly influence the hemodynamic response of patients being treated for severe sepsis.

**Peritonitis**

Peritonitis remains the main cause of technique failure worldwide (19,20). Hypokalemia has been described as a risk factor for this complication (21) and the suggested link between hypokalemia and peritonitis is the translocation of intestinal bacteria to the peritoneal cavity. It is known that low serum potassium levels affect gastrointestinal motility leading to bacterial overgrowth increasing the chance of bacterial translocation. To support this idea, a study looking at 140 CAPD patients over 2 years of follow-up found a significant
association between peritonitis caused by Enterobacteriaceae and hypokalemia (22). Such effect of hypokalemia may be more intense, although not studied in PD yet, in the presence of malnutrition and inflammation since both conditions can influence the intestinal permeability to bacteria (23).

Conclusion

In summary hypokalemia is more prevalent in PD patients, has a greater impact in PD patients compared to HD patients in term of mortality and is associated with enteric peritonitis. Intervention studies are necessary to determine whether correction of hypokalemia is able to improve outcome in PD patients and commercial PD solutions could be also available with small contents of potassium to reduce the occurrence of hypokalemia after begging of PD.

References


