

Review Article

Water, Sodium and Potassium Imbalance in Peritoneal Dialysis Pediatric Patients

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Abstract

Water, sodium and potassium regulation is usually altered in end-stage renal disease patients, particularly in frail individuals such as pediatric and elderly people. In this review article, pathophysiology of water, sodium, and potassium imbalance in peritoneal dialysis pediatric patients is in detail described. Understanding the etiological mechanisms of dysnatremia and dyskalemia in this group is crucial for their proper diagnosis and treatment.

INTRODUCTION

One of the main renal functions consists of regulation of water, sodium and potassium metabolisms. Therefore serum sodium and potassium levels can be seriously affected, resulting in the appearance of dysnatremias or dyskalemias, respectively, in end-stage renal disease patients, particularly in pediatric patients on dialysis [1-3]. In the present article, the pathophysiology of water, sodium, and potassium imbalance in peritoneal dialysis pediatric patients is analyzed in detail, in order to facilitate its understanding, and consequently the implementation of an adequate therapeutic approach.

Salt & water imbalance: its pathophysiology

Serum sodium level usually results from the relation between salt and water (Na:H₂O) body content, thus a low Na:H₂O ratio can induce hyponatremia (serum sodium < 135 mmol/L), and a high Na:H₂O ratio can induce hypernatremia (serum sodium > 145 mmol/L) (Table 1). Additionally, there are other factors which can modify Na:H₂O ratio, and induce hyponatremia, such as [4-12]: (A) Low body potassium content: Potassium intracellular depletion induces hyponatremia at least by two mechanisms: • by inducing sodium shift into the intracellular space, •by inducing inadequate vasopressin release. Edelman summarized this concept in the following equation [1]: Serum sodium = body (exchangeable) sodium + body (exchangeable) potassium / total body water (B) Excessive free water retention: Free water retention induced by inadequate vasopressin secretion secondary to drugs (opioids, psychotropic medications), endocrinopathies (hypothyroidism, hypoaldosteronism), and

other diseases: neurological, pulmonary, or paraneoplastic. (c) Excessive water intake: A water income which overcomes renal free water excretion capability can induce hyponatremia even in a context of fully suppressed vasopressin secretion. This type of hyponatremia has been documented in patients who suffered from primary polydipsia. (D) Low intracellular phosphate content: Low cellular phosphate can lead to intracellular hypo-osmolarity and consequently to water shift into extracellular compartment. (E) Reset osmostat: Reset osmostat hyponatremia is induced by a change in the set point for serum sodium tonicity. This sort of hyponatremia is usually found in malnourished chronically-ill patients, and it should be a diagnosis of exclusion. Regarding hyponatremia, it is classically classified depending on patient's plasma tonicity and patient's extracellular fluid (ECF) status (Table 2).

Altered serum sodium in peritoneal dialysis

Hyponatremia is a prevalent electrolyte problem in peritoneal dialysis patients; and this disturbance is mainly induced in anuric peritoneal dialysis patients by different mechanisms [1,12-14]: (A) Low sodium / water ratio secondary

Table 1: Salt & water imbalance characteristics.

	volume contraction	volume overload
imbalance	negative	positive
magnitude	mild to severe	mild to severe
clinical manifestation	axillary dryness orthostatism, hypotension,	hypertension, peripheral edema, lung congestion

Table 2: Hyponatremia clinical classification.

Hypotonic Hyponatremia PO: <280 mOsm/L	Normotonic Hyponatremia PO: 280-300 mOsm/L	Hypertonic Hyponatremia PO: >300 mOsm/L
increased free water body content eg: classical hyponatremia	normal free water body content eg: important paraproteinemia or dyslipidemia	increased free water intravascular content eg: hyperglycemia
Hypotonic Hyponatremia	Hypotonic Hyponatremia	Hypotonic Hyponatremia
low ECF axillary dryness, orthostatism hypotension	normal ECF normal clinical exam	high ECF hypertension, peripheral edema, lung congestion
Abbreviations: PO: Plasma Osmolarity; ECF: Extracellular Fluid		

to a high oral water intake (water in excess of sodium), and/or low water excretion (insufficient ultrafiltration). This situation occurs with an increase in body weight, as well as clinical signs of volume overload. (B) Low sodium / water ratio secondary to an extracellular fluid sodium deficit due to a low intake (low sodium diet), and/or excess sodium loss (excessive ultrafiltration). (C) Low potassium body content due to low potassium intake [low potassium diet], and/or excessive potassium loss (diarrhea). Intracellular potassium depletion induces sodium to shift from the extracellular compartment to the intracellular one, in order to keep body compartments electrically neutral. The flux of sodium from the extracellular fluid to the intracellular compartment, leads to extracellular volume contraction. This scenario presents with a reduction in body weight and there may be clinical signs of hypovolemia, but not always hypokalemia. (D) Intracellular phosphate deficit due to malnutrition which induces shift of water into the intravascular compartment. This mechanism of dilutional hyponatremia presents itself with reduced body weight (lean mass reduction) but without signs of volume contraction. Regarding peritoneal dialysis patients who have a significant residual renal function (RRF): GFR: 15-20 ml/min/1.73 m², such as those who start peritoneal dialysis earlier due to refractory hyperkalemia or concomitant cardiac failure (incremental dialysis), they can also suffer from hyponatremia induced by free water retention due to an inadequate vasopressin secretion. This hyponatremia presents itself without edema or body weight change. When evaluating hyponatremic patients, first of all you should rule out the presence of non hypotonic hyponatremia, either normotonic hyponatremia (pseudohyponatremia), as it is documented in cases of severe paraproteinemia or dyslipidemia; or hypertonic hyponatremia, as it is documented in hyperglycemia, or icodextrin use. Secondly, evaluate the serum potassium level, and nutritional status. If the patient presents hypokalemia, or intracellular potassium depletion is strongly suspected, potassium should be administered cautiously and with close monitoring of the serum potassium level. If the patient is malnourished, adequate nourishment should be provided, but not before assuring the normal serum potassium and phosphorus levels, as well as monitoring them during this process in order to avoid re-feeding syndrome. Finally, regarding hypotonic hyponatremia, the extracellular volume should be evaluated. If extracellular volume is high: negative volume balance should be induced. For this purpose, dextrose-based solutions (removal by osmosis) may be better than icodextrin (removal by colloid osmosis) since they remove water in excess of sodium, particularly with exchanges of shorter duration. If extracellular

volume is low: salt supply should be delivered (orally or intravenously, depending on the acuity of the situation); and if extracellular volume is normal with significant residual renal function: consideration should be given to antidiuretic hormone - driven renal water retention; in those without significant residual renal function, it could be interpreted as an osmostat reset [13]. Hyponatremia is usually associated with intermittent peritoneal dialysis which consists of a dialytic schedule based on frequent exchanges at 30-60 minutes intervals. This sort of dysnatremia occurs more commonly when high dialysate glucose concentration is used to achieve ultra filtration [14]. At least three mechanisms for the development of hypernatremia have been proposed [14-16]: • Dialysate hypertonicity, which induces salt and water loss in excess of water. •Dialysis induced hyperglycemia which causes osmotic diuresis (if residual diuresis is preserved) and consequently increases the serum sodium level. •Shorter exchanges have a lower outflow dialysate sodium concentration and because of that are more likely associated with hypernatremia.

Salt & water imbalance in peritoneal dialysis pediatric patients

Fluid and electrolyte requirements in children vary according to their primary kidney disease, degree of residual kidney function, and method of kidney replacement therapy. Supplementation or restriction of fluid, sodium, and potassium intake is individualized and influenced by the volume of urine output and the ability to concentrate urine, hydration status, and the presence or absence of hypertension or hyperkalemia. Body composition also differs considerably in children as compared to adults. Total body water is 75 % in newborns, 60 % in infants and adolescents and 50 % in elderly men [17,18]. The primary cause of chronic kidney disease needs to be considered. Although restriction of sodium and/or fluids is appropriate in children with chronic nephropathy associated with sodium and water retention, the most common causes of renal disease in children are associated with excessive loss of sodium and chloride. Infants and children with obstructive uropathy or renal dysplasia have polyuria, polydipsia, and difficulty conserving sodium chloride. Dehydration frequently occurs in these children in association with gastroenteritis. So it has to be taken into consideration that CKD children may develop a salt-wasting state and required salt supplementation. Sodium depletion seriously affects extracellular volume, muscle development, mineralization of the bone and growth [17,19]. Infants on peritoneal dialysis therapy

Table 3: Main electrolytes alterations in peritoneal dialysis pediatric patients.

	mechanism
Dehydration	high ultrafiltration low water income diarrhea
Hypotonic Hyponatremia	high dialysis dose low sodium income
Hypokalemia	high dialysis dose low potassium income
Hyperkalemia	low dialysis dose drugs catabolism metabolic acidosis cytolysis

are predisposed to substantial sodium losses too, even when anuric. Higher ultra filtration requirements per kilogram of body weight as compared to adults result in removal of significant amounts of sodium chloride. This high ultra filtration is needed to achieve adequate nutrition. But on the other hand, breast milk or standard commercial infant formulas have a low sodium content (160 mg/L or 7 mmol/L and 160 to 185 mg/L or 7 to 8 mmol/L respectively). In such children, ultrafiltration related convective solute transport is considerable and addition of oral sodium chloride supply is often required to prevent a reduce body sodium content, hypotension and neurological sequel [19,20]. Consequences of hyponatremia include cerebral edema and blindness, and therapy should be individualized based on clinical symptoms, including hypotension, and a degree of hyponatremia. Sodium balance measurements, determined from dietary and medication intake and dialysate effluent losses, should be considered every 6 months concurrent with the measurement of dialysis adequacy. More frequent measurement is indicated after significant changes to the dialysis prescription or clinical status (Table 3) [19-21].

Potassium imbalance: its pathophysiology

Total body potassium is mostly located in the intracellular compartment, especially in muscles, erythrocytes, and liver. Conversely, the extracellular space contains the minority of this cation. This uneven distribution reflects the large potassium concentration gradient between the intracellular (K_i : 150 mmol/L) and extracellular (K_e : 4 mmol/L) fluid compartments, which is generated by Na-K-ATPase pump activity (Figure 1) [22]. Potassium has two balances: the external balance between organism and environment, and the internal balance between extracellular and intracellular compartments within the organism [23]. Regarding the external balance, it normally depends on nutrition, renal (80%) and colonic (20%) potassium excretion, and this renal excretion depends on GFR and potassium distal tubule secretion, which is mainly stimulated by aldosterone [23]. In regards with the internal balance, it depends on the potassium shifts between intracellular and extracellular compartments. Insulin and the adrenergic system are the main stimuli for its intracellular shift along with metabolic alkalosis, plasma hypotonicity and beta-adrenergic sympathetic tone, while the main stimuli for its extracellular shift are glucagon, metabolic acidosis, plasma hypertonicity, and alpha-adrenergic sympathetic

tone [22-24]. Potassium retention is one of the dangers associated to advanced chronic renal failure, especially when glomerular filtration rate falls below 20 ml/min/1.73 m² [22]. Potassium imbalances can leads to either hypokalemia (serum potassium < 3.5 mmol/L) or hyperkalemia (serum potassium > 5.5 mmol/L); and the pathophysiology of dyskalemias depends on an altered external or internal balances (Table 4) [22-24]:

Serum potassium alteration in peritoneal dialysis

Despite physical principles applied in peritoneal dialysis and hemodialysis are the same ones, the rate of potassium removal is markedly slower in the former [25,26]. Peritoneal clearance for potassium averages about 17 ml/minute for intermittent peritoneal dialysis, and approximately 7 ml/minute for continuous ambulatory peritoneal dialysis (CAPD). These values are between those for urea and creatinine clearances. Interestingly, during the first hour of a dwell, potassium clearance is higher (24 ml/minute) than that of the remaining period and the most probable explanation for these high values is the release of potassium from the cells that line the peritoneal cavity. This release may be promoted by the initial low pH and/ or by the hyperosmolality of the instilled dialysate. Some additional potassium can also be removed by ultra filtration [25-27]. Contrary to patients on hemodialysis, peritoneal dialysis patients have normal or even high intracellular potassium content, especially those on CAPD. This phenomenon is probably related to the continuous glucose absorption from the dialysis solutions and the subsequent stimulation of intracellular uptake of potassium, mediated by insulin release [27]. Hyperkalemia is considerably less common in stable CAPD patients contrary to those on chronic hemodialysis [28]. The main causes that can induce hyperkalemia in peritoneal dialysis patients are: a high potassium diet, hyperkalemia generating drugs [angiotensin converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), low dialysis dose, or an internal fount of potassium release (potassium shift from the intracellular space to the intravascular one): rbdomyolysis, gross haematoma, hemolysis, bulky tumour necrosis, or acute hepatitis [24-28]. Since it has been documented that peritoneal dialysis patients were not able to handle an acute potassium overload, it takes a prolonged dialysis (by automatic peritoneal or hemodialysis) to normalize their plasma potassium levels avoiding a hyperkalemic

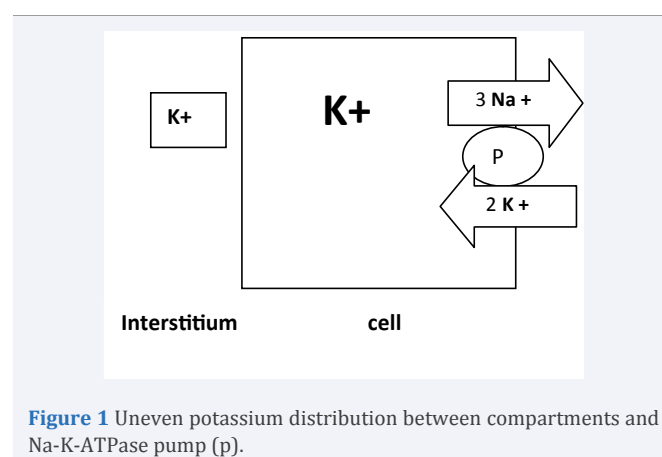


Figure 1 Uneven potassium distribution between compartments and Na-K-ATPase pump (p).

	Dyskalemia
negative external balance	hypokalemia
positive external balance	hyperkalemia
internal balance (shift into the cells)	hypokalemia
internal balance (shift out of the cells)	hyperkalemia

rebound in the post-dilaytic period [28]. Regarding hypokalemia in CAPD patients, 10-36% of them require potassium supplementation for hypokalemia, and it has been reported that patients on continuous cycling peritoneal dialysis (CCPD) have significantly lower serum potassium levels compared to CAPD patients. Since CCPD uses a greater number of exchanges with shorter dwell times and does not allow for equilibration to occur, there is always a concentration gradient difference between the dialysate and the plasma allowing more potassium to be transported into the dialysate fluid [26-28]. Poor nutritional status associated with intracellular potassium depletion, which can lead to flux of extracellular sodium and potassium into the cells, resulting in hyponatremia and hypokalemia. Additionally, as it was mentioned above, the stimulation of insulin secretion by absorption of glucose in the dialysis fluid may drive potassium into cells and cause hypokalemia. Potassium supplementation should be performed with caution in dialysis patients in order to avoid iatrogenic hyperkalemia [27].

Potassium imbalance in peritoneal dialysis pediatric patients

Children on peritoneal dialysis rarely need dietary potassium restriction and may actually develop hypokalemia. This risk of hypokalemia is due to greater potassium excretion in peritoneal dialysis. Pediatric dialysis patients with low serum potassium may experience muscle weakness, abdominal distention, and irregular heart contractions [17, 30-32]. Normokalemia may be achieved through counseling and frequent reinforcement of a high potassium diet, potassium supplements or potassium-sparing diuretics (spironolactone, amiloride) prescription, although the latter therapeutic alternative has been described in middle-age peritoneal dialysis patients. Sometime addition of potassium to the dialysate may be needed [15,33]. When hyperkalemia develops, strict adherence to dietary potassium restriction is required. Non dietary causes of hyperkalemia such as spurious values, hemolysis, metabolic acidosis, other exogenous potassium sources, constipation, inadequate dialysis, medications (angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, nonsteroidal anti-inflammatory agents, and potassium-sparing diuretics), and tissue destruction due to catabolism, infection, surgery, or chemotherapy should be investigated further [26,34]. Energy- dense feeds may be needed in infants on peritoneal dialysis with oligoanuria, and formulas can be concentrated. This can lead to hyperkalemia and hyperphosphatemia. Moderate to severe hyperkalemia may require treatment with a potassium binder (Table 3) [30].

CONCLUSION

Knowledge of the pathophysiology of electrolyte disorders in pediatric patients on peritoneal dialysis is crucial for their proper diagnosis and treatment.

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