of urinary concentration and serum sodium level are important to quickly diagnose and treat drug-induced AVP-R.

I have no potential conflict of interest to disclose.

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WCN26-6657

KLOTHO DEFICIENCY AND IMPAIRED POTASSIUM HOMEOSTASIS: INVOLVEMENT OF MTORC1 SIGNALING

(Article No. 103842)

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Introduction: Hyperkalemia is a common electrolyte disturbance associated with poor prognosis. It frequently occurs in patients with chronic kidney disease, particularly in older adults, and is linked to reduced levels of the anti-aging factor Klotho. This study aims to investigate the relationship between hyperkalemia and Klotho deficiency.

Methods: In Klotho heterozygous knockout (KLKO) mice, we measured serum potassium levels, urinary potassium excretion, and the membrane expression of renal outer medullary potassium channel 1 (ROMK1), as well as cleaved α- and γ-subunits of the epithelial sodium channel (ENaC). Plasma aldosterone concentration (PAC) and phosphorylated S6 kinase (p-S6K), a downstream target of mechanistic target of rapamycin complex 1 (mTORC1), were also evaluated.

Results: KLKO mice exhibited mild but significant hyperkalemia and reduced urinary potassium excretion, along with decreased membrane ROMK1 expression. Aldosterone production was elevated, as shown by increased PAC and adrenal Cyp11b2 expression, accompanied by enhanced cleavage of α- and γ-ENaC. Severe hyperkalemia was induced by administration of the ENaC inhibitor amiloride. Renal p-S6K expression was elevated in KLKO mice. Treatment with rapamycin or Klotho supplementation restored ROMK1 expression and serum potassium levels, while suppressing Cyp11b2 expression, PAC, and ENaC activation.

Conclusion: Klotho deficiency activates renal mTORC1 signaling, leading to ROMK1 downregulation and impaired urinary potassium excretion, thereby contributing to hyperkalemia. In parallel, increased aldosterone production and ENaC activation partially compensate for the impaired potassium excretion and mitigate the elevation in serum potassium levels. Thus, ENaC inhibition under Klotho deficiency can provoke severe hyperkalemia. These findings suggest that Klotho supplementation and mTORC1 inhibition may represent potential therapeutic strategies for preventing hyperkalemia in Klotho-deficient states.

I have no potential conflict of interest to disclose.

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WCN26-6812

RECURRENT HYPOKALEMIA: THE HIDDEN FOOTPRINT OF AN AUTOIMMUNE DISTAL RENAL TUBULAR ACIDOSIS. CASE REPORT

(Article No. 103843)

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Introduction: Distal renal tubular acidosis (dRTA) is an uncommon cause of hypokalemia and metabolic acidosis, especially among young adults. When associated with autoimmune diseases, it may represent the first manifestation of systemic involvement, as occurs in systemic lupus erythematosus (SLE) and Sjögren's syndrome.

Methods: Case presentation

Results: Case presentation: We report the case of a 22-year-old woman with recurrent episodes of hypokalemic paralysis since 2022, presenting with progressive weakness of the lower limbs leading to inability to walk. Laboratory evaluation revealed severe hypokalemia and metabolic acidosis with a normal anion gap and inappropriately alkaline urinary pH, findings consistent with dRTA. Antinuclear antibodies were positive (1:320, speckled pattern), Anti-Ro antibodies were positive (>400), subnephrotic-range proteinuria was present, renal biopsy showed no parenchymal alterations, and minor salivary gland biopsy revealed a Focus Score of 1.2. Application of the ACR–EULAR criteria confirmed the diagnosis of systemic lupus erythematosus associated with Sjögren's syndrome. The patient received potassium and bicarbonate replacement followed by methylprednisolone pulses and maintenance therapy with azathioprine, hydroxychloroquine, and prednisone, achieving full recovery of muscle strength and stable serum potassium levels upon follow-up.

Conclusion: his case highlights the importance of pathophysiological reasoning and comprehensive renal assessment in patients with recurrent hypokalemia. Autoimmune distal renal tubular acidosis should be suspected in young women presenting with unexplained episodes of muscle weakness and metabolic acidosis.

I have no potential conflict of interest to disclose.

I did not use generative AI and AI-assisted technologies in the writing process.

WCN26-6955

WHEN LESS IS MORE: INSIGHTS INTO SODIUM AND PHOSPHATE HOMEOSTASIS FROM A MICROVILLUS INCLUSION DISEASE PATIENT ON CHRONIC PARENTERAL NUTRITION

(Article No. 103844)

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Introduction: Microvillus inclusion disease (MVID) is a rare form of congenital secretory diarrhea caused by pathogenic MYO5B variants. We present a 2-year-old girl with MVID referred to Nephrology for persistent severe hypophosphatemia. Paradoxically, serum phosphate (PO4) decreased despite graded increases in PO4 supplementation. Her electrolyte profile was otherwise unremarkable aside from mild hypokalemia and hypochloremia. Typical of patients with MYO5B-MVID, nutrition was solely through intravenous supplementation (∼0.5L of 0.9% for 6h and ∼1.1L of parenteral nutrition (PN) for 12h). Severe hypophosphatemia has been described in other MVID patients on PN: it was hypothesized to be due to proximal tubular dysfunction related to the pathogenic MYO5B genotype because MYO5B is expressed in proximal tubule cells.

Methods: To elucidate the physiology of phosphate wasting and solute handling, the patient underwent a 24-hour metabolic balance study during alternating periods with and without PN and intravenous fluids, with serial paired serum, urine and stool electrolyte measurements. After discharge, serial paired studies were continued for twenty-four months.

Results: A 24h balance study (on/off PN) revealed that tubular reabsorption of phosphate (TRP) was the lowest (49%), and fractional excretion of sodium (FENa) highest (∼2%), while on PN. These values improved after 6 hours without PN. Concurrent stool and urine electrolyte analysis confirmed that the negative PO4 balance was exclusively due to renal losses, without other evidence of a proximal tubulopathy. It also confirmed that 100% of chloride losses were from stool, and 85% of potassium losses were from urine. We reasoned that the combination of high PN and IV fluid PO4 and sodium (Na) loads caused an obligate phosphaturic response by upregulating parathormone (PTH: 115 ng/L ref 16-63) and fibroblast growth factor 23 (FGF23: 452 RU/mL ref <230). We first corrected the hypokalemia and hypochloremia (allowing urine chloride to be detectable) while also reducing PN Na by 13% over a 4-week period. This resulted in a moderate improvement in her serum PO4, TRP values and FENa. Then, we