ESPN Research Grant Application final report

european society for paediatric nephrology

Title of the project:

The role of Copeptin as a biomarker of volume status in pediatric polyuric tubulopathies.

Principal investigator	**Year of award**
Angela Ferrulli Leire Madariaga	2022

Please provide an overall summary of the project (max 500 words)

This project investigated the role of copeptin as a biomarker of volume status in children affected by polyuric tubulopathies, including nephrogenic diabetes insipidus, Bartter syndrome, Dent disease, cystinosis, and related disorders. These rare inherited kidney diseases are characterized by impaired tubular handling of water and electrolytes, frequently leading to chronic polyuria, dehydration risk, and long-term kidney damage. Accurate assessment of intravascular volume status in affected children remains challenging in routine clinical practice, as currently available surrogate markers—such as plasma osmolality, blood pressure, and diuresis measurements—are limited in reliability and feasibility, particularly in pediatric populations.
Arginine vasopressin (AVP) plays a central role in regulating renal water reabsorption and maintaining fluid homeostasis; however, its short half-life and analytical instability limit its use as a clinical biomarker. Copeptin, a stable peptide secreted in equimolar amounts with AVP, represents a promising surrogate marker reflecting vasopressin activity. Although copeptin has demonstrated diagnostic utility in disorders of water balance and chronic kidney disease, its role in pediatric polyuric tubulopathies had not previously been systematically evaluated.
This multicenter prospective cohort study enrolled pediatric patients (0–18 years) with genetically confirmed polyuric tubulopathies and preserved kidney function (eGFR ≥60 ml/min/1.73 m^2). Participants underwent clinical and biochemical assessment at three time points over a one-year follow-up period. Blood and urine samples were collected to measure serum copeptin together with markers of kidney function and fluid-electrolyte homeostasis, including serum sodium, osmolality, renin, aldosterone, urinary aquaporin-2 (AQP2), and urinary cyclic AMP. These parameters were analyzed to determine correlations between copeptin concentrations and clinical indicators of hydration status, tubular function, and disease severity.
The primary objective of the project was to evaluate whether copeptin could serve as a reliable biomarker of circulating volume status in children with polyuric tubulopathies. Secondary objectives included assessing its relationship with renal function parameters, hormonal activation of the renin–angiotensin–aldosterone system, urinary concentrating mechanisms, and growth outcomes. Statistical modeling of repeated measurements allowed exploration of longitudinal associations while accounting for intraindividual variability.
By establishing the clinical utility of copeptin in this patient population, the project aimed to provide clinicians with a practical and minimally invasive tool to improve monitoring of hydration status, guide therapeutic strategies, and better understand disease progression. Ultimately, incorporation of copeptin measurement into routine clinical practice may support earlier identification of chronic volume depletion, optimize individualized fluid management, and contribute to improved long-term renal outcomes and quality of life in children with inherited polyuric tubulopathies.

How was the grant used for the project? (max 200 words)

The ESPN research grant supported the multicenter implementation of this study investigating copeptin as a biomarker of volume status in pediatric patients with primary polyuric tubulopathies. The funding was used for sample processing, shipment of biological material between participating centers, centralized biochemical analyses (including serum copeptin, renin, aldosterone, urinary cAMP, and urinary AQP2), and statistical analyses.
Biological samples were collected from pediatric patients fulfilling the inclusion criteria across several collaborating European centers, including Spain, Turkey, the Netherlands, and France. The grant enabled standardized handling, storage, and laboratory assessment of samples, ensuring consistency and reliability of biomarker measurements across sites.
All planned laboratory determinations have been completed. The funded statistical analyses are currently being performed to evaluate associations between copeptin levels and clinical and biochemical markers of hydration status, kidney function, and tubular response to vasopressin. Data interpretation is ongoing, and a scientific manuscript is in preparation. Overall, the grant was essential for supporting international coordination, laboratory investigations, and statistical evaluation required to achieve the project's objectives.

Please list all publications completed, with links to open access publications where available

Madariaga L, Ferrulli A, García-Alonso M. Copeptin in the diagnosis and management of renal tubular disorders. Pediatr Nephrol. 2026 May;41(5):1249-1258. doi: 10.1007/s00467-025-06941-9. Epub 2025 Sep 9. PMID: 40924182; PMCID: PMC13008999.

Are any other publications planned?

Yes. A scientific publication reporting the results of the study is currently in preparation.

Please list all presentations relating to the project

Madariaga L. Role of copeptin in salt losing disorders. ESPN Annual Meeting 2024, Valencia, Spain (presentation of the ongoing project during the meeting of the Inherited Kidney Diseases working group)