INTRODUCTION

Diabetes insipidus (DI) is a polyuric polydipsic syndrome that can be of central or nephrogenic origin. Patients with DI have a urinary output of more than 50mL per Kg in 24 hours and usually consume more than 3L of water per day. Nephrogenic DI is associated with the inability of the kidney to respond to the neuropeptide vasopressin. Vasopressin is secreted in the posterior hypothalamus (paraventricular and supraoptic nuclei) in response to hypovolemia or osmolality shifts and acts in the receptor V2 of the principal cells of the conducting duct, allowing the reabsorption of water through the regulation of the aquaporin 2 water channel (AQP2).

Nephrogenic DI can be congenital, detected in the early stages of life, or acquired, associated with drugs, systemic disease, or electrolyte abnormalities. Lithium was once one of the most used and efficacious treatments of type 1 bipolar disease, but the emergence of serious side effects concerning nephrotoxicity led to its obliviation. Nephrogenic DI associated with Li usually appears after longer periods and with higher cumulative doses. Other factors include female gender, age, and other risk factors for chronic kidney disease.

Renal side effects are mostly associated with the action in the principal cells of the distal tubules and collecting ducts. Li enters through the epithelial sodium channel in the cell and accumulates there, interfering with the traffic of AQP2 and allowing the loss of a great quantity of water through dilute urine and leading to the clinical picture of polyuria, polydipsia, and hypernatremia.
Lithium, an Old Friend and a Forgotten Enemy

**Response to the administration of D-amino D-arginine vasopressin allows differentiating the nephrogenic type from the central DI.** The diagnostic algorithm accuracy is only around 70%, which led to the proposal of a direct test that includes the measurement of serum vasopressin levels after osmotic stimulation failed to enter clinical practice. There is increasing evidence for new markers such as copeptin that likely increase the accuracy of the etiology of the polyuric polydipsic syndromes. Imaging tests like MRI do not appear to have a role in the diagnosis of DI.

Nephrogenic DI associated with lithium is seen rarely nowadays since its use as a mood stabilizer decreased dramatically. The treatment requires stopping the therapy, hydration, and sometimes thiazidic diuretics to restore the hydric balance by increasing the amount of sodium and water reabsorbed in the proximal tubules. Other possibilities are the prostaglandin synthesis inhibitors and acetazolamide, with the last not approved yet.

The prognosis is usually good when the cessation of the Li therapy is tolerated by the patient, and nephrogenic DI can sometimes completely resolve.

**Conclusion**

The diagnosis of polyuric polydipsic syndromes is still a challenge in clinical practice, although it seems to be evolving to more accurate techniques. Although Li is now rarely used in clinical practice, clinicians must be aware of the possible side effects of prolonged treatments and ideally anticipate their appearance in order to prevent organ damage.

**Author’s Contribution**

All authors have contributed equally to the work.

**Learning points**

- Lithium therapy, despite its great effectiveness, is now rarely used in clinical practice due to its side effects;
- Whenever there is a suspicion of a polyuric polydipsic syndrome, all causes must be excluded since nephrogenic DI can have many causes;
- Early recognition and management of this syndrome can prevent life-threatening complications.
RESUMO

INTRODUÇÃO: O diabetes insípido nefrogênico faz parte das síndromes poliúricas polidipsicas e pode ter múltiplos fatores causais.

CASO CLÍNICO: Mulher de 69 anos, com doença bipolar medicada com lítio 400 mg por dia durante 12 anos. A doente foi internada, após descompensação da doença bipolar, por hipernatremia não responsiva a fluidoterapia hipotônica endovenosa. O diagnóstico de DI foi realizado com base no elevação da osmolaridade plasmática, baixa osmolaridade urinária e níveis elevados de hormona antidiurética. Verificou-se recuperação clínica completa com suspensão do lítio, hidratação e clorotalidona.

DISCUSSÃO: Apesar do seu uso frequente no passado, o lítio (Li) é hoje em dia raramente utilizado na prática clínica por períodos prolongados pelos seus efeitos potencialmente devastadores. Os médicos devem ter em conta os potenciais efeitos secundários de forma a prevenir lesão de órgão em doentes com doença bipolar de difícil controlo com outra terapêutica.

PALAVRAS-CHAVE: Transtorno bipolar. Lítio. Diabetes insípido nefrogênico.

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