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LITHIUM-INDUCED NEPHROGENIC DIABETES INSIPIDUS RESPONSIVE TO DESMOPRESSIN

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Abstract

Nephrogenic diabetes insipidus (NDI) is the most common renal side effect seen with lithium therapy. Persisting cases after the cessation of the therapy may be seen when lithium therapy is continued for too long. Although desmopressin treatment is not one of the accepted treatment modalities for NDI, there are few reports using desmopressin treatment in unresponsive cases. Herein, we reported the fourth lithium-induced NDI case in the literature responsive to desmopressin therapy.

Key words: desmopressin, diabetes insipidus, lithium, nephrogenic.

Dear Editor,

Lithium, used to treat bipolar disorder, may cause multiple endocrinopathies. Nephrogenic diabetes insipidus (NDI) is the most common renal side effect seen with lithium therapy (1). Although NDI is accepted to be reversible when lithium treatment is discontinued, persisting cases are reported after the cessation of the therapy (2). Despite the known treatment modalities, the management of NDI may sometimes be difficult. Herein, we presented a case of lithium-induced NDI case responsive to l-deamino-8-D-arginine vasopressin (DDVAP) treatment. A 55-year-old female patient was admitted due to hypernatremia, polyuria and polydipsia. Her medical history revealed bipolar disorder of 39 years' duration. She had been treated with lithium for 37 years. The lithium treatment was stopped and switched to ketiapin two years ago due to the increase in creatinine levels. On physical examination, she was normotensive and not edematous. Her laboratory findings at the time of admission are shown in Table 1. In addition to hypernatremia, patient's results revealed subclinic hyperthyroidism (absent thyrotropin receptor antibodies, absent radioiodine uptake) due to prolonged lithium use. Based on the medical history and laboratory results, the patient was diagnosed with lithium-induced nephrogenic diabetes insipidus and indapamid (1.5mg) plus indomethacin (50mg) treatment was started. Since the patient's serum sodium level was 150mEq/L, we could not do water deprivation test could not be performed. Hypotonic solution was started for hydration. Mild decrease was seen in the patient's sodium levels but her polyuria continued in spite of the hydration with hypotonic solutions, non-steroidal anti-inflammatory drug (NSAID) and diuretic use, so she was admitted to our inpatient clinic (Table 1). On the 3rd day of her admission, her sodium level and urinary output (5600 mL/24h) were still high so a single dose of DDVAP (10mcg) was administered. Although urine osmolality did not change (580mOsm/kg and 600mOsm/kg before and after DDVAP, respectively), which confirmed the diagnosis of NDI, serum sodium level and urinary output of the patient decreased (Table 2). Computed tomography and magnetic resonance imaging of the brain as well as anterior pituitary hormones were evaluated in order to rule out central diabetes insipidus. They did not reveal any pathology. The patient was started DDVAP 120 μg. On the 7th day of the treatment serum sodium level was 145 mEq/L. NSAID and diuretic treatment was stopped. On the 15th day of the treatment the patient was prescribed 180 mcg DDVAP therapy and discharged with serum sodium level of 143 mEq/L with urinary output of 2500 mL/24h.

DISCUSSION

Lithium therapy can cause many endocrinopathies; hypothyroidism/hyperthyroidism, nephrogenic diabetes insipidus (NDI) and hypercalcemia. Although the mostly seen renal disease with lithium therapy is chronic tubulointerstitial nephritis, NDI is seen in 20 to 40% of the patients (3). Lithium interferes with renal collecting tubules and generates cyclic adenosine monophosphate in response to antidiuretic hormone secretion, which then results in a reduction of the kidneys' capacities to preserve water leading to polyuria (4). Another mechanism causing lithium-induced NDI is down-regulation of

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Table 1. Sequential serum and urine measurements of the patient

Factor	Normal Range	At the time of consultation	3rd day	4th day	5th day
Bun (mg/dL)	<21	9	9	11	14
Creatinine (mg/dL)	0.50-1.11	0.87	0.83	0.85	1.11
Sodium (mmol/L)	134-145	151	149	148	148
Serum osmolality (mOsm/kg)	280-300	311	306	304	306
Urine volume (mL/24h)	1000-2000Ş	6000	5000	4500	4600

ªunder normal dietary conditions.

Table 2. Serum and urinary findings of the patient after DDVAP therapy

Factor	Normal Range	6th day	7th day	11th day	15th day
Bun (mg/dL)	<21	19	16	10	10
Creatinine (mg/dL)	0.50-1.11	1.13	0.96	0.83	0.73
Sodium (mmol/L)	134-145	146	145	140	143
Serum osmolality (mOsm/kg)	280-300	304	301	289	293
Urine volume (mL/24h)	1000-2000Ş	2800	3000	2800	2500

ªunder normal dietary conditions.

aquaporin-2 expression which is accepted reversible with the cessation of the therapy (5). However, Guirguis *et al.* reported eight cases of lithium-induced NDI persisting after the cessation of lithium carbonate therapy (2). They related this continuous lithium effect to slow recovery from urinary concentrating defects and prolonged exposure to the drug (>10 years), as seen in our patient. She was treated with lithium for 37 years and the side effects of the drug were persisting in spite of the cessation of the therapy for two years.

The accepted treatments of NDI are amiloride, thiazide diuretics and NSAID, especially indomethacin and ibuprofen. There are two case reports pointing out the importance of DDVAP in the treatment of NDI with indomethacin (6, 7). Stasior *et al.* reported the mechanism under this combination as; indomethacin blocking the production of prostaglandin and potentiating the effect of DDVAP (6). They gained this result with 6 mcg DDVAP. On the other hand, Kamath *et al.* reported a case of lithium-induced NDI unresponsive to amiloride, thiazides and ibuprofen in combination (8). High doses of DDVAP therapy alone caused reduction in the urine output by 50%. We were also able to decrease the urine output with 180mcg DDVAP therapy. Although there is not enough evidence about the use of DDAVP in NDI, in the light of early studies we tried oral desmopresin therapy and gained successful results. The most likely explanation to this condition may be as the defective vasopressin receptor and aquaporin-2 axis in the renal tubular cells in lithium-induced NDI causing partial vasopressin resistance which may be overcome by high doses of desmopressin therapy (9).

Herein, we mentioned a case of nephrogenic diabetes insipidus responsive to desmopressin therapy which is to our knowledge is the fourth case in the literature. Physicians should try oral desmopressin when the management of lithium-induced NDI becomes challenging. There should be detailed studies done to enlighten the underlying mechanism.

Conflict of interest

The authors declare that they have no conflict of interest.

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