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Case Report

Hypernatraemia and polyuria due to high-dose colchicine in a suicidal patient

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Introduction

Hypernatraemia is a relatively common electrolyte disturbance with high mortality rates ranging from 42 to 70% [1]. It appears to be particularly common at the extremes of age, i.e. in children and in the elderly. Hypernatraemia developing in non-hospitalized adults is predominantly a disease of the elderly, and may reflect inadequate nursing care of patients in chronic care facilities. However, hospital-acquired hypernatraemia occurs in a wider range of patients, with an age distribution more similar to the general hospitalized population [1]. We present here an unusual case of hypernatraemia and polyuria in a healthy young person resulting from ingestion of a high dose of colchicine. To our knowledge, the consequences of ingestion of large amounts of colchicine on water metabolism have not been described before in humans.

Case

A 30-year-old female suicidal patient who ingested a high dose of colchicine was admitted to the emergency room with diffuse abdominal pain, severe nausea, vomiting, headache and dizziness. Her past medical history was unremarkable. On initial evaluation, she was in rather poor clinical condition. Her blood pressure was 100/70 mmHg, pulse 108/min and body temperature 35.6°C. Physical examination was unremarkable except for localized epigastric tenderness on deep palpation. Haematological studies revealed a haemoglobin level of 14.6 g/dl and a leukocyte count of 12 600/mm^3. Serum biochemistry results were as follows: BUN, 28 mg/dl; creatinine, 1.0 mg/dl; glucose, 62 mg/dl; Na, 136 mEq/l; K, 3.8 mEq/l; Cl, 92 mEq/l; total protein, 6.8 g/dl; albumin, 3.6 g/dl; uric acid, 6.2 mg/dl; Ca, 9.8 mg/dl; and P, 4.2 mg/dl. Serum transaminases were within normal limits. The results of urinalysis were glucose (−), protein (−) and no pathology on microscopic examination. Within 2 h, the patient was confused, sweating and tachypnoeic. The patient was given a rapid infusion of i.v. 5% dextrose in 0.9% sodium chloride. During follow-up within 6 h, restoration of blood pressure and body temperature and a general improvement were seen.

However, 1 day later, after admission, the patient developed progressive hypernatraemia (up to 160 mEq/l) and a minor increase in BUN concentration, combined with normal plasma creatinine. While the patient remained haemodynamically stable, massive polyuria (up to 8 l) developed. Osmolality of serum and urine were 336 and 186 mOsm/kg, respectively. Serum glucose and screening test results for cortisol and thyroid hormone levels were within normal limits. Plasma vasopressin (AVP) level was 2.4 pg/ml (normal: 1.3–4.1 pg/ml). The urine osmolality was 212 mOsm/kg while plasma osmolality was 332 mOsm/kg after fluid deprivation (3% loss of body weight). The urine osmolality did not rise with subsequent injection of vasopressin. The plasma AVP level increased to 6.2 pg/ml after fluid deprivation. These findings suggested that hypernatraemia and polyuria were due to responsiveness to AVP at the level of the renal tubule in this patient (nephrogenic diabetes insipidus). The patient received hypotonic saline solution (0.45% sodium chloride). She was then given a low-salt diet in combination with low-dose thiazide diuretic therapy. Within 1 week after her admission, her urine volume reduced gradually, and plasma osmolality, urine osmolality and electrolyte values returned to normal (Table 1, Figure 1).

Discussion

Sodium is the most important osmolyte in the extracellular compartment. Its concentration is regulated within narrow limits. An elevation of the serum sodium concentration above the normal range (136–145 mmol/l) is indicative of a deficit in body water

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Table 1. Laboratory findings of the patient during the follow-up period

Day	Plasma sodium (mmol/l)	Plasma osmolality (mOsmol/kg)	Urine osmolality (mOsmol/kg)	Urine volume (ml)
1	136	286	436	1550
2	152	312	296	4300
3	160	336	186	8120
4	156	314	212	6835
5	152	302	278	4270
6	146	290	346	3850
7	139	286	390	2785
8	138	285	428	2250
9	136	286	430	1965
10	136	288	430	1820

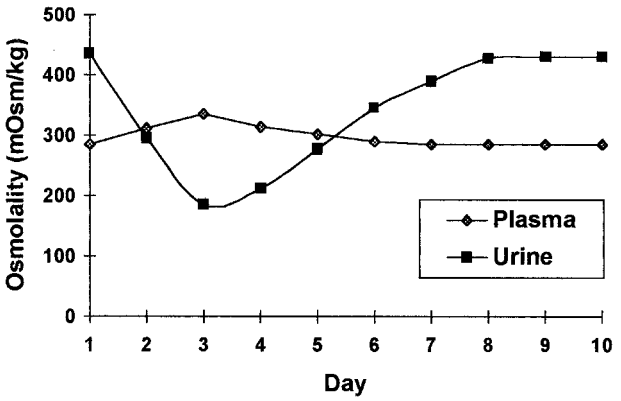

Fig. 1. Values of the plasma and urine osmolality.

relative to sodium. The increase in plasma osmolality, induced by a rising plasma sodium concentration, results in water movement out of the cells into the extracellular fluid, and the resultant cellular dehydration of brain cells is responsible for the dominant clinical symptoms (lethargy, seizures, coma). The severity of hypernatraemic symptoms is related primarily to the rate of rise in plasma osmolality rather than to the absolute degree of hypernatraemia [2].

Impairment of AVP production, release or action can lead to profound water deficits and to polyuria and hypernatraemia. Various drugs impair the end-organ response to AVP and thus cause a renal concentrating defect. The drugs most commonly associated with polyuria and hypernatraemia are lithium and demeclocycline. These drugs, whose mechanism of actions have been studied extensively in humans and in animal models, inhibit the increase in cAMP generation after AVP stimulation and also block events distal to cAMP generation [3].

On the other hand, it was shown that colchicine and vinblastine, which disrupt intracellular microtubules, inhibited AVP- and cAMP-mediated water flows of the mammalian kidney [4]. The integrity of cytoplasmic microtubules in cells of the distal nephron is required for the antidiuretic action of vasopressin, probably at steps distal to cAMP generation. To date, similar defects in AVP responsiveness have not been reported with the use of these agents in humans, and the clinical significance of the above *in vitro* observation has not been determined. The present case was remarkable because of the ingestion of high-dose colchicine was associated with hypernatraemia and polyuria in a human; to our knowledge, no such case has been reported before. The exact pathomechanism by which colchicine interfered with tubular water reabsorbtion could not be investigated specifically in the present patient. We definitively could not identify any other factor potentially responsible for the hypernatraemia and polyuria other than the high-dose colchicine ingestion. However, we acknowledge that a chance association cannot be excluded.

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