Combined desmopressin (DDAVP) and chlorpropamide therapy for diabetes insipidus with absent thirst[1]

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A patient with neurogenic diabetes insipidus and defective thirst regulation due to a craniopharyngioma is described who responded to a combination of desmopressin (DDAVP) and chlorpropamide with improved thirst regulation and decreased urine output. When DDAVP was discontinued he became hypernatremic. This patient required both DDAVP and chlorpropamide to maintain normonatremia.

Index terms: Brain neoplasms • Chlorpropamide • Craniopharyngioma • Desmopressin (DDAVP) • Diabetes insipidus
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The clinical picture of neurogenic diabetes insipidus in combination with defective thirst mechanisms is sometimes seen in patients with hypothalamic damage.[1,2] Management is difficult because both renal and behavioral mechanisms for regulating water balance are nonfunctional. Although desmopressin (DDAVP) alone promptly restores the ability to conserve water,[3] there may be wide swings in plasma osmolality and sodium concentration. Patients with this syndrome are hypodipsic and therefore may develop severe hypernatremia without experiencing thirst. Home intake and output monitoring and calculation of appropriate water intake to replace insensible and renal losses is one method of treatment, which, although theoretically elegant, may allow large shifts in plasma osmolality. Chlorpropamide increases vasopressin release.[4] Some patients with absent thirst have responded to chlorpropamide with resumption of drinking and needed no further treatment with vasopressin.[5–7] We describe a patient with diabetes insipidus and absent thirst due to a craniopharyngioma who required both chlorpropamide and DDAVP to prevent hypernatremia.

Case report

The patient was seen at 14 years of age for diplopia and severe bifrontal headaches. He had been in good health previously. Funduscopic examination showed papilledema. There were no pubertal changes in hair or genitalia. Brain computerized tomography (CT) scan revealed a large mass above the sella confirmed on surgical exploration to be a large craniopharyngioma, which had invaded the anterior hypothalamus. Removal was believed at the time of surgery to be total. Postoperatively, diabetes insipidus with lack of thirst was noted, and at one time serum sodium was 169 mEq/L. He responded to DDAVP, 2.5 mcg/day, with a dramatic decrease in urine output, but during the next 2 years he had a slightly elevated serum osmolality of 310–315 mOsm/L and a serum sodium in the low 150s(mEq/L). Cortisol, thyroid, and testosterone replacement were also required.

Two years later, follow-up CT scan showed a subarachnoid cyst above the sella, and a further defect in visual fields was noted. A drain was placed in the cyst under CT observation and left in place. Preoperatively, electrolytes showed a serum sodium of 156 mEq/L, a serum chloride of 126 mEq/L, a serum potassium of 3.7 mEq/L, and blood urea

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nitrogen (BUN) of 14 mg/dl. Postoperatively the patient experienced polyuria but did not increase his water intake. Several hours later serum sodium was reported as greater than 160 mEq/dl. By giving increased amounts of free water this was brought down to the mid 150s (mEq/dl). The patient continued to require careful intake and output monitoring and needed to be encouraged to drink water. He complained about being asked to drink even when hypernatremic at 155 mEq/L. Increased doses of DDAVP did not alleviate this. Chlorpropamide, 250 mg/day, was started, and by the third day the patient began to ask for water and maintained a serum sodium level of 150 mEq/L or less without fluids being forced. The patient was discharged on this regimen and did well with no further episodes of hypernatremia for nine months. Mild leg edema occurred but responded to furosemide, 80 mg twice daily, without interruption of the DDAVP or chlorpropamide. Because of the patient's concern about fluid retention and edema, DDAVP was decreased to every other day without any change in serum sodium. However, when DDAVP was discontinued, serum sodium rose to 155 mEq/L. When DDAVP was restarted, serum sodium rose to the patient's more usual range of 145–150 mEq/L.

Discussion

This patient had a craniopharyngioma, a brain tumor known to be associated with the extremely difficult clinical problem of diabetes insipidus with impaired thirst.[1,7–9] Before the appearance of the subarachnoid cyst in the second surgical procedure, he was in a chronic mild hypernatremic state, which appeared to be tolerated and stable, although drowsiness was a problem. Postoperatively, serum sodium became more elevated, and forcing fluids orally was necessary to avoid potentially fatal hypernatremia. After chlorpropamide was added, the patient drank voluntarily and maintained a stable high normal serum sodium. When an attempt was made later to discontinue the DDAVP, but not the chlorpropamide, hypernatremia again developed.

In previous reports, chlorpropamide restored thirst but also restored concentrating ability so that DDAVP was no longer necessary.[5–8] This patient differs in showing only a partial response, that is, his thirst was increased by the chlorpropamide, but not enough to enable him to compensate for an increased urine flow. The patient did not report polyuria when the DDAVP was discontinued, suggesting that he might have a partial response to this effect of chlorpropamide as well.

The use of chlorpropamide in diabetes insipidus and other disorders with impaired thirst has been reported by Bode[6,7] and Mahoney.[5] To our knowledge, however, this is the first patient who showed only a partial response and required both DDAVP and chlorpropamide to maintain normonatremia.

The combination of diabetes insipidus and impaired thirst may lead to brain damage or death, because rapid shifts of large magnitude in plasma osmolality are difficult to avoid even with home or hospital intake and output monitoring. Osmotic shifts and hypernatremia itself cause alterations in mental status and impair quality of life. The excellent result obtained in this patient leads us to suggest that patients with this syndrome who do not respond adequately to chlorpropamide or DDAVP alone may benefit from a trial of both drugs in combination. The patient described here had considerable improvement in well-being and returned to school and increased physical activity as a result of his treatment. He reported feeling much better when his hypernatremia was controlled. We recommend further trials of this combination for patients with this disorder.

References

1. Randall RV, Clark EC, Dodge JW Jr, Love JG. Polyuria after operation for tumors in the region of the hypophysis and hypothalamus. J Clin Endocrinol Metab 1960; **20:**1614–1621.
2. Stuart CA, Neelon FA, Lebovitz HE. Disordered control of thirst in hypothalamic-pituitary sarcoidosis. N Engl J Med 1980; **303:**1078–1082.
3. Robinson AG. DDAVP in the treatment of central diabetes insipidus. N Engl J Med 1976; **294:**507–511.
4. Hayes JS, Kaye M. Inappropriate secretion of antidiuretic hormone induced by chlorpropamide. Am J Med Sci 1972; **263:**137–141.
5. Mahoney JH, Goodman DA. Hypernatremia due to hypodipsia and elevated threshold for vasopressin release. Effects of treatment with hydrochlorothiazide, chlorpropamide and tolbutamide. N Engl J Med 1968; **279:**1191–1196.
6. Bode HH, Harley BM, Crawford JD. Restoration of normal drinking behavior by chlorpropamide in patients with hypodipsia and diabetes insipidus. Am J Med 1971; **51:**304–313.
7. Bode HH. Disorders of the posterior pituitary. [In] Kaplan SA, ed. Clinical Pediatric and Adolescent Endocrinology. Philadelphia, Saunders, 1982, pp. 49–68.
8. Brezis M, Weiler-Ravell D. Hypernatremia, hypodipsia and partial diabetes insipidus: a model for defective osmoregulation. Am J Med Sci 1980; **279:**37–45.
9. Schaad U, Vassella F, Zuppinger K, Oetliker O. Hypodipsia-hypernatremia syndrome. Helv Paediatr Acta 1979; **34:**63–76.