Evidence for a Direct Adverse Reaction of Neuroleptics in Self-Induced Water Intoxication of Psychiatric Patients

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Summary: A mentally retarded patient who developed polydipsia and hyponatremia following the long-term use of neuroleptics is described. Before the investigation, he was treated with a combination of five drugs: diazepam, propericiazine, carbamazepine, lithium carbonate and trihexyphenidyl. The treatment was switched to diazepam alone; to propericiazine, trihexyphenidyl and diazepam; to carbamazepine and diazepam; and finally to lithium carbonate with diazepam. Under the five drug treatment protocols, his weight gains during the day were monitored, every day as an index of the water he drank in the day time. The combination of the five drugs caused the greatest weight differences per day and the other drug regimens, except diazepam alone, seemed to increase the weight differences to some extent. These findings indicate that a drug combination such as the neuroleptics, lithium and carbamazepine used for emotional stabilization must be carefully monitored to avoid the induction of compulsive drinking.

Key Words: Mental retardation—Polydipsia—Hyponatremia—Neuroleptics—Lithium—Carbamazepine

Introduction

Polydipsia and hyponatremia occur occasionally in psychiatric patients (Illowsky and Kirch, 1988). However the etiology of these symptoms has not been elucidated. polydipsia can occur in psychiatric patients who are not taking medications. Some observers have cited the anticholinergic effects of many psychoactive medications as a possible exacerbating factor in overdrinking, noting the dry mouth that these medications can induce (Winstead, 1976). Others have proposed that neuroleptics may directly stimulate hypothalamic thirst centers (Rao et al. 1975).

It is difficult to investigate the etiological role of drugs on polydipsia in schizophrenic patients because the withdrawal of neuroleptics can aggravate their psychotic symptoms. This report describes a mentally retarded patient with aggressive behavior who developed polydipsia and hyponatremia following the long-term use of neuroleptics. Such a case may produce an explanation of the etiology of this disease.

Case Report

Mr. A. is a 38 year-old man who is severely mentally retarded. He had exhibited frequent outbursts of violent or self-injurious behavior which necessitated neuroleptic therapy at the age of 22 years. It was noted that he drank excessive
amounts of water at the age of 38, because of an incontinence of urine or vomiting of water. He was admitted to Seiwakai Nishikawa Hospital to examine the etiology of the polydipsia.

The physical and neurological examinations were normal. Admission serum values included sodium, 127 mEq/L; potassium, 5.1 mEq/L; chloride, 96 mEq/L; antidiuretic hormone (ADH), 0.1 pg/mL; blood urea nitrogen, 4.7 mg/dL; creatinine, 1.1 mg/dL; glucose, 81 mg/dL; and calcium, 4.5 mEq/L. The thyroid function tests, serum cholesterol and triglycerides, serum protein, electrocardiogram, chest roentgenogram, and computed tomographic brain scan were normal.

Before his admission to the hospital, diazepam, 15 mg, propericiazine, 75 mg, carbamazepine, 600 mg, lithium carbonate, 1200 mg, and trihexyphenidyl, 6 mg, had been prescribed for eight months. After admission, the patient's body weight was checked every day at bed-time and on awakening to estimate the volume of water he drank. His weight gain during the day was regarded as his water intake. Fig. 1 shows the weight differences per day (weight gain) for the following five treatment protocols. The five drug regimen was switched to diazepam alone; to propericiazine, trihexyphenidyl, and diazepam; to carbamazepine and diazepam and finally to lithium carbonate and diazepam. An analysis of variance performed on the effects of the drug mixtures on weight yielded significant dif-

![Fig. 1. Effects of five drug treatment protocols on day-time weight gains.](image-url)
ferences \( F(4, 140) = 25.52, P<0.01 \) between the five treatment protocols. The combination of five drugs induced the greatest weight differences per day and all the other drug combinations, except diazepam alone, seemed to increase the weight to some extent.

After the study was completed, the patient was treated with diazepam (30 mg) for five years. This medication controls both the psychic symptoms and the polydipsia.

Discussion

Several research groups have reported that diurnal weight gain is an index of polydipsia and hyponatremia in chronic psychiatric patients (Delva et al. 1988; Vieweg et al. 1988). Furthermore, under the circumstances used to examine body weight, only water was given ad libitum. For this reason, weight differences can be regarded as an index of the water consumed each day.

Clinical examination of the patient eliminated other known causes of polydipsia and polyuria, such as diabetes mellitus, diabetes insipidus, chronic renal failure, hypocalcemia, and hypokalemia. Moreover, the syndrome of inappropriate secretion of ADH (SIADH) was also eliminated, because the serum ADH concentration was low. Hyponatremia in this case may have developed from drinking too much water and from other dysfunctions of the osmotic regulatory centers, such as the "reset osmostat" proposed by Hariprasad et al. (1980).

Many drugs including carbamazepine and neuroleptics can induce SIADH and thereby impair the renal excretion of free water. Lithium was reported to be effective for the treatment of SIADH (White and Fetner, 1975). However the present data indicates that propericazine, carbamazepine and lithium stimulate thirst either centrally or peripherally; because the ingestion of large amounts of water occurred immediately after the administration of these drugs.

The best hypothesis for the etiology of polydipsia is the dopaminergic supersensitivity hypothesis (Smith and Clark, 1980; Shen and Sata, 1983), which is similar to the dopamine hypothesis for schizophrenia and the dopamine supersensitivity hypothesis of tardive dyskinesia. It appears from animal experiments that a hyperdopaminergic state is associated with increased fluid intake and that dopamine depletion is associated with decreased fluid intake (Dourish, 1983). According to this hypothesis, the sudden withdrawal of neuroleptics should cause a supersensitivity of the dopaminergic neurons and should increase compulsive drinking. The present data did not support this hypothesis.

The current findings indicate that a drug combination, such as a neuroleptic, lithium and carbamazepine used for emotional stabilization, must be carefully monitored to avoid the induction of compulsive drinking. Furthermore, a high dose of diazepam (Beckmann and Hass, 1980) should be used for maintenance therapy of schizophrenics who have self-induced water intoxication.

References


Illowsky, B.P. and Kirch, D.G. (1988). Polydipsia and hyponatremia in psychiatric pa-