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Hyponatraemia and Clomipramine Therapy

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The fortuitous detection of SIADH is described in a patient receiving clomipramine therapy.

A wide variety of drugs have been implicated as causing hyponatraemia via the syndrome of inappropriate antidiuretic hormone secretion (SIADH). No particular type of drug appears to be implicated and no mechanism has been elucidated. A number of reports (Garson, 1979; Madahusoodanan & Osnos, 1981; Abbott, 1983) have implicated psychoactive drugs and most patients have been emergency admissions to hospital. We report a patient in whom the condition was fortuitously detected before this situation arose.

Case report

The patient was a 64-year-old married woman with a long history (19 years) of treatment for depression and anxiety. Previous treatment had included a range of benzodiazepine and tricyclic drugs (Table I). None of these, nor carbamazepine and temazepam used later, were beneficial. In lieu, she commenced clomipramine (25 mg t.d.s.) on 20 October 1986. The possibility of future lithium treatment was suggested at this stage, and routine serum electrolytes and creatinine clearance were requested. Apart from the psychological problems mentioned, the patient was asymptomatic.

TABLE I
Drugs prescribed over the course of psychiatric disturbance before this presentation

Benzodiazepines	*Tricyclic drugs*	*Other*
Chlordiazepoxide	Trimipramine	Trisilate
Diazepam	Amitriptyline	Flupenthixol
Flurazepam	Butriptyline	Mianserin hydrochloride
Ketazolam	Nortriptyline	Orphenadrine citrate
Clorazepate dipotassium	Dothiepin	Trazadone hydrochloride
Temazepam		Carbamazepine
Prazepam		Tryptophan
Alprazolam		
Oxazepam		
Triazolam		

Initial serum electrolytes were measured on 22 October and, following the finding of hyponatraemia, a repeat specimen was requested to confirm this finding (23 October). The course of biochemical measurements is charted in Table II.

A provisional diagnosis of SIADH secondary to tricyclic therapy was made and the patient was instructed to cease taking the tricyclic on 27 October. The biochemical picture in the following two days appeared little improved and on closer questioning it appeared that the patient had been recommenced on clomipramine by the deputising service of the general practitioner, who was unaware of a possible SIADH.

The importance of stopping this drug was again emphasised to the patient on 30 October and electrolyte levels a week later showed a normal pattern.

One month later, the patient was asymptomatic and not feeling particularly depressed, in spite of ceasing tricyclic therapy.

Discussion

A wide variety of drugs has been implicated in the development of SIADH, including a number of psychoactive drugs (Streeton *et al*, 1980). While the occurrence of SIADH in a psychiatric setting is recognised, the actual incidence is unclear from the literature. Jose & Perez-Cruet (1979) concluded that the incidence of water intoxication in chronic psychiatric patients was of the order of 3–5%. Sandifer (1983) estimated that two to three cases associated with psychotropic drugs per year may be

TABLE II
Biochemical results

	Serum								*Urine*	
Date: 1986	*Na: mmol/l*	*K: mmol/l*	*Cl: mmol/l*	*HCO_3: mmol/l*	*Urea: mmol/l*	*Creatinine: mmol/l*	*Osmolality: mOsm/kg*	*Na: mmol/l*	*K: mmol/l*	*Osmolality: mOsm/kg*
22 October		124	4.5	88	5.6	60	—	—	—	—
23 October	123	4.5	—	—	4.5	—	253	77	61	613
28 October	124	4.5	90	24	3.7	—	255	18	46	404
29 October	126	5.0	90	27	5.2	68	259	67	71	628
6 November	133	4.5	95	25	5.2	54	269	—	—	742

expected in a tertiary-care hospital, while Ananth & Lin (1986) referenced over 30 cases of SIADH induced by psychotropic drugs reported in the literature over a six-year period.

No definitive mechanism has been found for the syndrome, although a number of possibilities have been advanced: compulsive drinking of water seen in some psychotic patients (Sandifer, 1983); increased fluid intake to counter dryness of the mouth (possibly caused by the anticholinergic effects of neuroleptics) (Lewis, 1971); increased sphincter tonus of the urinary bladder; and a local anaesthetic effect and a central antidiuretic effect (Appel *et al*, 1971).

The patient under discussion had previously been prescribed a number of drugs known to have this side-effect, without any apparent problems, although serum electrolytes had not been measured on these occasions. As these drugs had been taken for a long time, it is unlikely that serious hyponatraemia would have gone unnoticed. Apparent sensitivity to one particular drug (amitriptyline) has been recognised in this context previously (Madahusoodanan & Osnos, 1981).

Although measurement of antidiuretic hormone was not made, the criteria for diagnosis of SIADH were met – hyponatraemia, hypo-osmolality, lack of maximal urinary sodium retention and urinary osmolality greater than serum osmolality. These findings were not accompanied by evidence of volume depletion, cardiac failure, renal failure or hypothyroidism.

A previous case of SIADH on clomipramine was reported by Garson (1979), whose patient was referred as an emergency by her family practitioner. It was fortuitous that our patient had her electrolyte levels checked several days after clomipramine therapy had commenced, as there was no clinical indication of a problem at that time.

A number of lessons stem from this case. The fact that a patient has not previously suffered electrolyte disturbance whilst on tricyclic therapy is no indication that this situation will appertain if the drug regime is altered.

As the initial symptoms of hyponatraemia (confusion, weakness, etc.) may mimic the psychiatric condition, clinical impression may not be a good guide.

It is impossible to predict which patients will be affected. An argument can be made for single measurement of serum and urine electrolyte levels on those patients whose symptoms are suggestive of possible SIADH following commencement or change of tricyclic therapy. It is hoped that this will prevent the full sequalae of SIADH developing in patients at risk.

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