Drug-induced syndrome of inappropriate antidiuretic hormone secretion (SIADH)

Sanja Klobučar Majanović, Čedomir Zorić, Nenad Bićanić, Neven Franjić, Željka Crnčević Orlić
Department of Endocrinology, Diabetology and Metabolic Disorders
University Hospital Centre Rijeka

Introduction

Hyponatraemia is one of the most common electrolyte abnormalities that may be drug-induced either as a result of inappropriate antidiuretic hormone secretion (SIADH) or excessive sodium loss[1]. SIADH is diagnosed on the basis of low plasma osmolarity associated with inappropriately concentrated urine. Essential criteria for the diagnosis of SIADH are shown in Table 1.

Table 1 Essential criteria for the diagnosis of SIADH

Hyponatraemia with serum sodium < 135 mmol/L
Decreased measured plasma osmolality < 275 mOsm/kg
Inappropriately concentrated urine > 100 mOsm/kg
Clinical euvolaemia - No clinical signs of contraction of extracellular fluid (eg. no orthostasis, tachycardia, decreased skin turgor, or dry mucous membranes) - No clinical signs of expansion of extracellular fluid (eg., no oedema or ascites)
Urinary sodium > 20 mmol/L with normal dietary sodium intake
Normal thyroid and adrenal function

Case report

A 67-year-old woman was admitted to hospital because of progressive confusion and perseveration. Her medical history included bipolar disorder, arterial hypertension and gastritis. Her drug therapy on admission was chlorpromazine (Prazine), sertaline (Zoloft), fluphenazine (Moditen), lisinopril (Laaven) and pantoprazole (Controloc). On physical examination the patient appeared euvolemic without evidence of congestion or dehydration. The CT scan of the brain and chest X-ray were normal. Laboratory tests revealed severe hyponatraemia (111 mmol/L) and the infusion of a 3% saline was administered. Approximately 24 hours after admission the patient's serum sodium increased to 120 mmol/L and her mental status improved. Hyponatraemia, low serum osmolarity (258 mOsm/kg), high urine osmolarity (398 mOsm/kg), high urine sodium (64 mmol/L) together with normal renal, thyroid and adrenal function, all supported diagnosis of SIADH. Therefore, fluid restriction was instituted and her chronic drug therapy suspended. Serum sodium level increased progressively and low doses of new psychotropics re-initiated (risperidone and escitalopram). At the time of hospital discharge, serum sodium level was 133 mmol/L. A follow up serum sodium three weeks after discharge was within the limits of normal range. Diagnostic approach and clinical management in this particular case are shown in Figures 1 and 2.

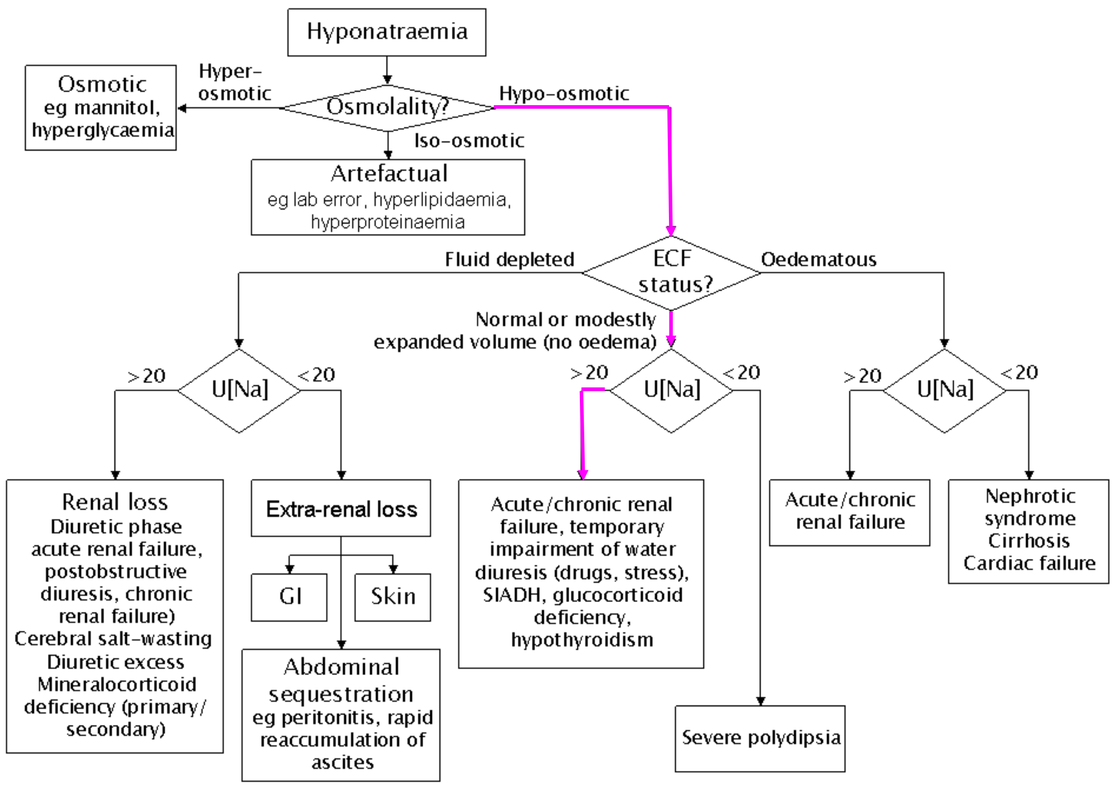

Figure 1. Diagnostic approach to the patient with hyponatraemia

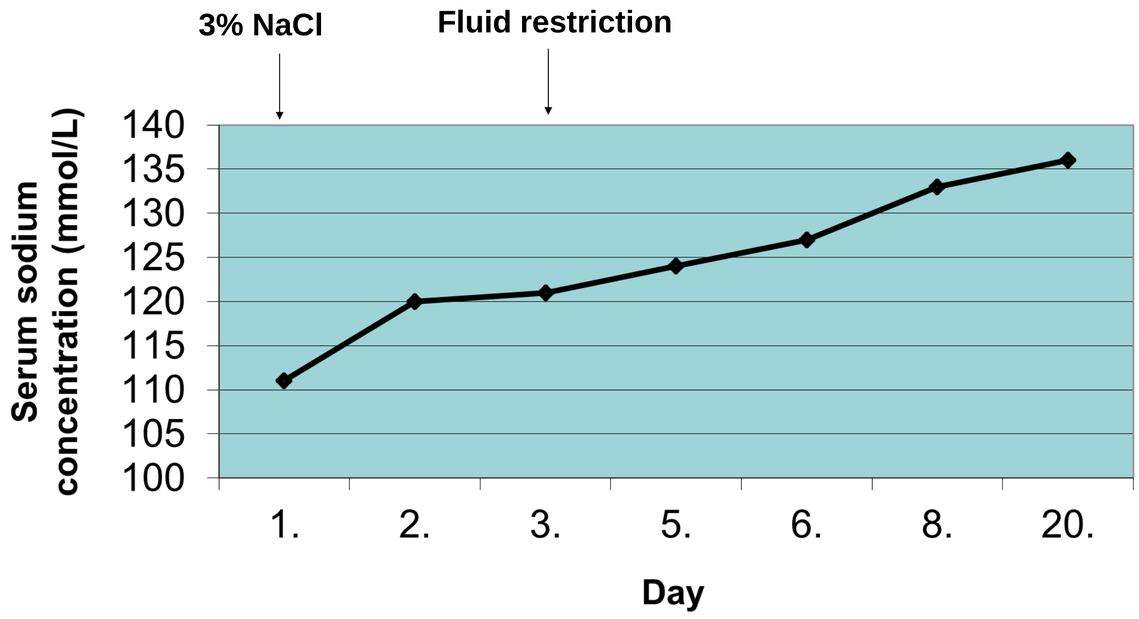

Figure 2. Clinical management

Table 2 Drugs that may cause SIADH

ADH analogues	Antineoplastics	Cardiovascular agents	Psychotropics
Desmopressin (DDAVP)	Alemtuzumab	ACE inhibitors -- cilazapril -- enalapril -- lisinopril -- ramipril	Antipsychotics -- chlorpromazine -- haloperidol -- fluphenazine -- risperidone
Oxytocin	Chlorambucil	Amiodarone	Lorazepam
Vasopresin	Carboplatin	Clofibrate	SSRIs -- sertaline
Analgesics	Cisplatin	Clonidine	Duloxetin
Diclofenac	Cyclophosphamide	Methyldopa	Tricyclic antidepressant
Fentanyl	Etoposide	Phenoxybenzamine	Venlafaxine
Ibuprofen	Melphalan	Propafenone	Viloxazine
Antiparkinson agents	Rituximab	Thiazides	Other
Amantadine	Vidarabine		IFN-α
Levodopa	Vincristine	Anti-infectives	MDMA (ecstasy)
Anticonvulsants	Vinblastine	Azithromycin	Nicotine
Carbamazepine	Hypoglycemic agents	Miconazole	Omeprazole
Oxcarbazepine	Glimepiride	Rifabutin	Tacrolimus
Valproic acid	Metformin		Theophylline

Conclusion

Hyponatremia may develop in the course of treatment with drugs used in every-day clinical practice (Table 2)[3,4]. Patients may receive complex drug regimens containing several candidates as the cause of hyponatremia. Effective clinical management of drug-induced SIADH can be handled through understanding of the underlying pathophysiologic mechanisms and awareness of the adverse effects of certain pharmaceutical compounds on serum sodium levels. Withdrawing the suspect drug(s) and restricting fluid intake is generally recommended. However, in patients with severe symptomatic hyponatremia hypertonic saline should be administered but the daily correction rate should not exceed 8-10 mmol/L [4,5].

References

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