

Acute symptomatic hyponatraemia associated with valerian extract supplement use

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Abstract

An 81-year-old woman was referred by her GP to the Acute Medical Unit due to hyponatraemia and $\text{Na}^+ = 122$. The patient reported symptoms of dizziness and tiredness. The patient had no causative comorbidities and was not taking any prescribed medications to hyponatraemia. There was no history of alcohol excess. History taking revealed regular use of a valerian supplement for stress relief. Her sodium normalised after stopping the supplement and undergoing a short period of fluid restriction. Her symptoms resolved and did not recur.

Keywords

acute medical unit; hyponatraemia; ocular migraines

Background

Stress and sleeping disturbances are very common problems in modern Western societies [1]. For that reason, a large number of products have been released onto the market and are sold over-the-counter. However, many of these agents have not undergone rigorous scientific testing and therefore, may have unknown side effects or interactions with other medications. In this case-report, we present the case of an older female who developed symptomatic hyponatraemia due to the consumption of such an agent.

Case Description

An 81-year-old female was referred by her GP to the Acute Medical Unit due to hyponatraemia. The patient visited her GP due with a 3 week history of dizziness and fatigue. The GP performed blood tests which showed: serum $\text{Na}^+ = 122$ mmol/L, $\text{K}^+ = 4.7$ mmol/L, Urea = 4.7 mmol/L and Creatinine = 69 umol/L. Her full blood count and liver function were unremarkable with a CRP of 1 mg/L. Sodium two months prior was 134 mmol/L (Normal range $\text{Na}^+ = 133 - 145$ mmol/L).

She had a past medical history of ocular migraines, hypertension, previous breast cancer and bilateral total hip replacements. She had been admitted in the past, to another hospital with severe hyponatraemia and a seizure which were attributed to bendroflumethiazide. After the culprit diuretic was stopped, her sodium levels had returned to normal. Unfortunately, the serum sodium levels from that admission were not available to us. Her main symptoms had been tiredness and a subjective feeling of imbalance and unsteadiness. She denied recent angina, dyspnoea, cough, fevers, abdominal pain, diarrhoea, vomiting, nausea, polyuria, oliguria, dysuria and headaches. Her admission. Her regular prescription included atenolol 25mg OD, amlodipine 5mg OD, doxazosin 4mg BD and colecalciferol 800 units OD. Her daily oral fluid intake included various beverages like water, tea and juices but it was not excessive and she denied experiencing excessive thirst. She drank alcohol occasionally, usually 1 small glass of wine and there was no previous history of alcoholism. She had never smoked and had never used recreational drugs. Upon further questioning, the patient reported daily use of an over-the-counter hops and valerian root supplement (Trademark name KALMS, <https://www.kalmsrange.com/>) to help her with anxiety and insomnia. She had been using that supplement for several weeks and took the maximum dose of its daytime version KALMS DAY (two tablets three times a day) and the maximum dose of its night time version (four tablets before bed time) called KALMS night.

On examination, she was alert with a GCS = 15/15. She had normal heart sounds with no murmurs and her pulse was regular. Her lungs were clear on auscultation and resonant on percussion. The abdomen was soft, non-tender with present bowel sounds. There were no rashes and no peripheral oedema. Her neurological examination was unremarkable.

Her ECG showed a sinus rhythm of 67 beats per minute. Her CXR was unremarkable. Her urine dip was negative.

A full work up for hyponatraemia was arranged. Bloods were taken including urea, creatinine and electrolytes, full blood count, liver function tests, serum osmolality, thyroid function tests and a random cortisol test. Her urine was checked for urine sodium concentration and urine osmolality.

Blood tests are shown in table 1 including older serum sodium measurements. On the day of the admission, her thyroid function tests and cortisol levels were normal. Her full blood count, magnesium levels and liver function tests were all normal. Her serum sodium was 122 mmol/L, potassium was 4.7 mmol/L, urea was 4.7 mmol/L and creatinine was 69µmol/L. The serum osmolality was 258mmol/Kg (low), urine osmolality was 552 mmol/Kg (high) and urine sodium concentration was 21 mmol/L (higher than expected for the levels of serum sodium).

Table 1: Patient’s blood results and sodium levels

	14/06/2016	16/10/2017	05/04/2019	16/06/2019	17/06/2019	18/06/2019	19/06/2019	25/06/2019	28/06/2019	05/07/2019	25/07/2019
SERUM Na ⁺	133	134	134	122	124	126	130	131	131	134	134
Urine Sodium				21							
Serum Osmolality				258							
Urine Osmolality				552							
Random Cortisol				315							
Free T4				15.3							
TSH				1.48							

UNITS OF MEASUREMENT: SERUM Na⁺ in mmol/L, Urine sodium in mmol/L, Serum Osmolality in mmol/Kg, Urine osmolality in mmol/Kg, Random Cortisol in mmol/L, Free T4 in pmol/L, TSH in mU/L. **Normal Range of sodium = 133 - 145 mmol/L**

Differential Diagnosis

Hyponatraemia is classically categorised in hypovolaemic, hypervolaemic and euvolaemic with different conditions under each category. In our case, this lady had euvolaemic hyponatraemia. The main diagnoses considered were pharmacogenic hyponatraemia, primary polydipsia, hypothyroidism and syndrome of inappropriate anti-diuretic hormone secretion (SIADH). Since she reported normal oral fluid intake, her thyroid function tests were normal and was not on any drug that could cause hyponatraemia, SIADH was the most likely diagnosis.

SIADH per se has various aetiologies including thoracic and head trauma, malignancy, infection, haemorrhage and medications. However, none of these could be identified in this patient. Her breast cancer had been treated many years ago and there was no evidence of any recurrence. Chest XRAY and chest examination were both unremarkable. Since she had no neurological symptoms and there was no history of brain metastases or other intracranial pathologies, CT head and MRI head were not performed. The patient also did not have any known endocrine problems which could indicate pituitary or hypothalamic lesion and her thyroid function tests were normal.

Since there was lack of any obvious aetiology for her SIADH, a quick online literature search was performed regarding any connection between the use of hops or valerian extracts and hyponatraemia. Two case reports were found. One of them described a possible contribution of valerian extracts to hyponatraemia in the context of primary polydipsia. The other described a direct connection between valerian supplements and hyponatraemia [2,3].

Given the above, the patient was advised to completely stop taking the valerian root extract supplement and was advised to stay in hospital for serum sodium levels monitoring to ensure that they would not go down further. She was put on a 1.5 litre fluid restriction, while an inpatient. She had daily serum sodium measurements which revealed a progressive improvement as shown in table 1. After 3 days,

her serum sodium had risen to 130 mmol/L and she was therefore discharged.

Discharge & Follow-up

A week after discharge her sodium had risen to 131 mmol/L. The patient had not restarted her valerian supplement and her symptoms of tiredness and imbalance had resolved completely.

Nine days after discharge, the patient was re-admitted with palpitations and was found to be in atrial fibrillation with a fast ventricular response. She was managed with bisoprolol and was started on anticoagulation (apixaban). Her blood tests showed persistent mild hyponatraemia with Na^+ 131 mmol/L. She was discharged with advice to keep her fluid intake to 1.5 litres per 24 hours and to have further monitoring in primary care. Her latest sodium was 134 mmol/L (normal). Subsequently, the fluid restriction was stopped. Her symptoms of headache, instability and nausea have not recurred and she is feeling well at the time of writing of this case report.

Discussion

Hyponatraemia is the commonest electrolyte abnormality identified in inpatients and it is also one of the commonest reasons for admission and investigation [4].

As mentioned above, differential diagnosis can be broad and it is not uncommon for hyponatremia to be multifactorial. In the case of this elderly female patient, there was no evidence of any of the well-known pathologies that are associated with hyponatraemia. A quick online search revealed the two [2,3] similar cases in the literature connecting valerian supplements with hyponatraemia. The supplement containing valerian extract does have a list of potential side effects and interactions on its box but hyponatraemia is not mentioned. Another online literature search was conducted but no results came up regarding any interaction of valerian extracts with the hypothalamus, hypophysis or renal cells. It is possible that hyponatraemia is an extremely rare side effect of using such supplements; therefore it has not been documented frequently and has not been investigated thoroughly.

The main learning point from the management of this patient was that asking for over-the-counter supplements, medications or herbal agents and recreational drugs can be the key to answering difficult diagnostic questions. It needs to be kept in mind that many over-the-counter substances claim to offer health benefits but they do not have sufficient scientific evidence behind them or on occasion no evidence at all. Patients should be aware and informed when purchasing such supplements and it is advisable that they consult their GP or regular physician when considering taking them.

Learning points

- Patients must always be asked about over-the-counter/non-prescribed substances that they are using when taking their medical history.
- This is the third case report connecting valerian root extract and hyponatraemia and it could be

potentially a very rare side effect that doctors should be aware of.

- Valerian root has now been suspected in two cases associated with severe, life-threatening hyponatraemia and healthcare professionals should be vigilant to this.
- Hyponatraemia caused by valerian root extract may take several days to completely resolve.

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