de imágenes más precoz[9]. Además, se realza la diferenciación respecto del tejido normal adyacente, pues la médula adrenal sana no capta el radiotrazador[6,9], una característica que algunos autores han propuesto optimizar mediante el tratamiento previo con carbidopa[10].

Es interesante recordar, no obstante, que, dada la heterogeneidad y baja prevalencia de los feocromocitomas y paragangliomas, establecer la mejor prueba diagnóstica es difícil, pues vendrá determinada por las características individuales del paciente en relación al perfil secretor, la localización de sospecha, las características histológicas de diferenciación celular, el comportamiento biológico y la posible asociación con una mutación genética[6,11].

Es necesario adaptarse a la modernización de las técnicas de imagen y plantear la posibilidad de que en aquellos centros en los que esté disponible, la ^{18}F-DOPA-PET podría remplazar, al menos en parte, a la ^{123}I-MIBG, por su mayor precisión, comodidad de realización y menores efectos adversos para el paciente, si bien serán necesarios estudios de coste-efectividad que evalúen su utilización.

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Ana María Ramós-Leví[a,*], Ángel Molino[b], Santiago Ochagavía[c] y Ángel Díaz Pérez[a]

[a] *Servicio de Endocrinología y Nutrición, Hospital Clínico San Carlos, Madrid, España*
[b] *Servicio de Medicina Interna, Hospital Clínico San Carlos, Madrid, España*
[c] *Servicio de Cirugía General, Hospital Clínico San Carlos, Madrid, España*

[*] Autor para correspondencia.
Correo electrónico: ana_ramoslevi@hotmail.com (A.M. Ramós-Leví).

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Acute severe hyponatremia induced by aceclofen in a male patient with central diabetes insipidus

Hiponatremia aguda grave inducida por aceclofeno en un paciente varón con diabetes insípida central

Introduction

The side effects of desmopressin are headache, lethargy, obtundation and seizures all of which are due to severe and rapid hyponatremia caused by water intoxication. These symptoms have been described in patients treated with this drug for central diabetes insipidus, primary nocturnal enuresis and nocturnal polyuria.

Non-steroidal anti-inflammatory drugs (NSAIDs) in combination with desmopressin can induce symptomatic hyponatremia, though this effect is very rare and has seldom been described in the literature.

In this report, we describe the case of a 46-year-old man with central diabetes insipidus undergoing long-term treatment with a constant dose of desmopressin who developed acute severe symptomatic hyponatremia when desmopressin was combined with aceclofen.

Case report

A 46-year-old man was admitted to the Emergency Department of the Dr. Peset University Hospital (Valencia, Spain) with lethargy, obtundation and loss of consciousness. He had been diagnosed with central diabetes insipidus at the age of 28 and was being treated with desmopressin at a dose that

he denied having altered. Three days prior to admission the patient had experienced dizziness, headache, nausea and vomiting.

A physical examination revealed normal blood pressure (130/80 mmHg), pulse rate of 90 bpm and body temperature of 36.9 °C. A neurological examination gave a Glasgow coma score of 14 (E4 V4 M6) and otherwise normal results.

On admission, the most relevant laboratory parameters were as follows: sodium (Na) 113 mequiv./L (reference value 135–145 mequiv./L); potassium (K) 4.3 mequiv./L (reference value 3.5–5 mequiv./L); creatine phosphokinase (CPK) 3576 UI/L (reference value 30–200 UI/L); creatinine 0.68 mg/dl (reference value 0.7–1.20 mg//dl); urea 31 mg/dl (reference value 19–50 mg/dl); and normal blood count. Urine analysis showed Na 200 mequiv./L (reference value 40–220 mequiv./L) and K 101 mequiv./L (reference value 25–125 mequiv./L).

A brain CT scan revealed no signs of intracranial bleeding or other abnormalities.

Further information indicated that the patient had not altered the prescribed dose of desmopressin (10 μg per day of intranasal solution administered divided in two doses) and had not experienced any previous complications. Additionally, several previous blood chemistry controls revealed that his plasma sodium concentration was within a normal range (the last, performed 45 days before hospital admission, showed a result of 139 mequiv./L). At the time of admission, the patient had also been taking 200 mg of aceclofen per day for one week as a pain killer for lumbar pain caused by weight lifting.

Desmopressin treatment was discontinued and the patient was treated with hypertonic saline infusion. The symptoms disappeared within 24 h. Serum sodium concentration increased to 123 mequiv./L 24 h later and to 136 mequiv./L on the second day after admission. On the third day desmopressin treatment was reinstated at the usual dosage and normonatremia persisted (discharge sodium concentration 139 mequiv./L). One month later, the patient's blood sodium concentration continued within the normal range (141 mequiv./L).

Discussion

Headache, dizziness, nausea, vomiting and uneasiness are mild, non-specific initial symptoms of hyponatraemia. Severe symptoms do not usually appear until blood sodium levels fall below 125 mequiv./L or drop abruptly. In such conditions, patients can experience loss of consciousness, seizures, obtundation and progressive lethargy.

Desmopressin is a structural analog of vasopressin (antidiuretic hormone) that increases water reabsorption via vasopressin V2 receptors in the renal tubules, thereby increasing urine osmolality and decreasing urine volume. This results in an increase of intravascular volume and a decrease in plasma osmolality, effects that last between 6 and 24 h.

This drug is more potent and much longer-acting than human vasopressin, and has several indications (central diabetes insipidus, nocturnal enuresis, haemophilia A and mild-to-moderate von Willebrand disease). Water intoxication with severe hyponatraemia is a potential risk of intravenous or intranasal administration of desmopressin. This adverse effect often occurs on initiation of therapy, until the appropriate daily dosage is determined.

Renal prostaglandins are important regulators of urinary dilution, as they partially antagonize the antidiuretic effects of vasopressin in the collecting tubules and impair sodium reabsorption in the loop of Henle and cortical collecting tubule.[1] By inhibiting glomerular cyclooxygenase, NSAIDS diminish renal synthesis of prostaglandins, thus increasing urinary concentrating ability. In patients with diabetes insipidus, the net effect can be a 25–50 per cent reduction in urine output, leading to water retention and consequent hyponatremia.[2,3] However, despite the well-known renal effect of these drugs and their frequent use, hyponatraemia as a result of water intoxication has seldom been described.[1,4,5]

To our knowledge only one other case of severe symptomatic hyponatremia as a result of the combination of non-steroidal anti-inflammatory drugs and desmopressin has been reported to date.[6]

The fact that our patient had been taking the same dosage of intranasal desmopressin for 18 years without developing clinical symptoms of hyponatraemia pointed to an additive effect of co-administration with aceclofen. It is well known that non-steroidal anti-inflammatory drugs constitute a widely used pharmacologic group, and are consumed with medical prescription and also through self-medication. In fact, in recent years, NSAID consumption has increased considerably. For instance, in 2008 ibuprofen was the third most prescribed drug in the Spanish Public Health System, while nearly 30 million persons worldwide are currently using non-steroidal anti-inflammatory drugs on a daily basis.[7]

The use of these agents is not free of risks: the most frequent adverse reactions are gastrointestinal (perforation, ulcer, bleeding), but there are many other potential complications and pharmacologic interactions that must be considered, especially in patients with comorbidities in whom NSAIDs may cause acute decompensation, thus leading to hospital admission, increasing mortality and morbidity rates and putting extra pressure on the resources of health systems.[8]

Hyponatremia can be induced by any NSAID, although it is proposed that with a low dose of aspirin (about 40 mg per day) the inhibition of glomerular cyclooxygenase is partial and transient, avoiding a significant reduction in glomerular prostaglandins.[8] Sulindac, another non-selective non-steroidal anti-inflammatory agent, appears to be safer than other NSAIDs, since some studies suggest that it spares prostaglandins by inhibiting cyclooxygenase to a lesser degree.[9] However, careful monitoring is recommended in all cases.

To conclude, although non-steroidal anti-inflammatory drugs are not contraindicated in central diabetes insipidus patients treated with desmopressin a priori, doctors should be aware of the potential risks in prescribing them and take the necessary precautions.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Marina Teresita Bergoglio[a,*], Eva Solá Izquierdo[a,b], Silvia Veses Martin[a], Antonio Hernández Mijares[a,b]

[a] *Servicio de Endocrinología y Nutrición, Hospital Universitario Doctor Peset, Valencia, Spain*
[b] *Departamento de Medicina, Universitat de Valencia, Spain*

[*] Corresponding author.
E-mail address: drabergoglio@gmail.com (M.T. Bergoglio).

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Colestasis disociada: una complicación infrecuente del tratamiento con tionamidas

Dissociated cholestasis: An uncommon complication of thioamide therapy

Introducción

El hipertiroidismo se debe a una síntesis y/o secreción inadecuada de hormonas tiroideas por diferentes causas, situándose su prevalencia en torno al 1%. La causa más frecuente de tirotoxicosis es el hipertiroidismo primario de etiología autoinmune (enfermedad de Graves), en donde la estimulación por parte de los anticuerpos antirreceptores de tirotropina (TRAb) condiciona un incremento de la producción de hormonas tiroideas. En Europa, el tratamiento de primera elección de la enfermedad de Graves son las tionamidas, siendo el tratamiento con radioyodo y la cirugía terapias de segunda línea. El metimazol, junto con el carbimazol y el propiltiouracilo, pertenece a la familia de las tionamidas y es uno de los principales fármacos empleados en el tratamiento del hipertiroidismo[1].

Al igual que con cualquier otro fármaco, se han descrito efectos adversos de diferente gravedad con los antitiroideos. Entre estos, como efectos adversos más frecuentes y leves se encuentran las reacciones cutáneas (4-6%), las artralgias (1-5%) y las alteraciones gastrointestinales (1-5%). En cuanto a los efectos adversos graves que se han descrito con mayor frecuencia están la agranulocitosis (0,1-0,5%) y la hepatotoxicidad (0,1-0,2%). Se supone que las alteraciones leves anteriormente descritas son dosis dependientes en el caso del metimazol y carbimazol, mientras que la hepatotoxicidad en estos 2 fármacos, al contrario que en el caso del propiltiouracilo, es idiosincrásica[2–5].

La prevalencia de hepatitis aguda secundaria a antitiroideos se sitúa en torno a 0,1-1%, y la mayoría de los casos descritos en la literatura son secundarios a propiltiouracilo. Datos de 2003 reportaban un total de 83 casos descritos de hepatitis aguda secundaria a propiltiouracilo, aunque se ha llegado a sugerir que hasta el 1,2% de los pacientes tratados con dicho fármaco pueden presentarla[3,7].

A día de hoy, se han descrito en la literatura menos de 40 casos de hepatitis aguda secundaria a metimazol o carbimazol[6]. Los casos descritos corresponden en su mayoría a una hepatitis aguda colestásica[4–6], a excepción de un caso en que predominaba un patrón de citolisis[8], un caso de hepatitis granulomatosa[9] y un caso de esteatosis hepática[10].

Observación clínica

Se trataba de un varón de 68 años, exfumador, sin hábito alcohólico, hipertenso, dislipémico, cardiópata isquémico y con una miocardiopatía dilatada secundaria. El paciente era portador de un marcapasos desde el 2008 por un síndrome bradicardia-taquicardia. Desde entonces había presentado numerosos episodios de flutter y fibrilación auricular (FA), motivo por el cual se inició tratamiento con amiodarona 200 mg/día 3 años antes del inicio del cuadro. Su tratamiento habitual era: bisoprolol 5 mg, olmesartan 20 mg, fluvastatina 80 mg, ezetimiba 10 mg, ácido acetilsalicílico 100 mg, parches de nitroglicerina 5 mg, acenocumarol 1 mg, omeprazol 20 mg y escitalopram 15 mg.

En un ingreso hospitalario en mayo de 2011, por un nuevo episodio de fibrilación auricular, se consultó al Servicio de Endocrinología por hallazgos analíticos compatibles con un hipertiroidismo primario: T4L 4,21 ng/dl (0,89-1,76), T3L 6,59 pg/ml (2,3-4,2), TSH 0,009 mcU/ml (0,55-4,78). Se interrogó al paciente, que no relataba otros síntomas sugestivos de hiperfunción tiroidea. La palpación de la región cervical anterior fue anodina, así como el resto de la exploración física. La autoinmunidad tiroidea mostró unos anti-TPO de 60,6 U/ml (0-60), antitiroglobulina de 213 U/ml (0-60) y anti-TSI negativos. Se solicitó una ecografía tiroidea, en la que no se objetivaron alteraciones significativas. En conjunto se orientó como un hipertiroidismo