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Review Article

Ten common pitfalls in the evaluation of patients with hyponatremia

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ABSTRACT

Hyponatremia is the most common electrolyte disorder in hospitalized patients associated with increased morbidity and mortality. On the other hand, inappropriate treatment of hyponatremia (under- or mainly overtreatment) may also lead to devastating consequences. The appropriate diagnosis of the causative factor is of paramount importance for the proper management and avoidance of treatment pitfalls. Herein, we describe the most common pitfalls in the evaluation of the hyponatremic patient, such as failure to exclude pseudohyponatremia or hypertonic hyponatremia (related to glucose, mannitol or glycine), to properly assess urine sodium concentration and other laboratory findings, to diagnose other causes of hyponatremia (cerebral salt wasting, reset osmostat, nephrogenic syndrome of inappropriate antidiuresis, prolonged strenuous exercise, drugs) as well as inability to measure urine osmolality or delineate the diagnosis and cause of the syndrome of inappropriate antidiuretic hormone secretion. Clinicians should be aware of these common clinical practice pitfalls, which could endanger patients with hyponatremia.

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Hyponatremia is the most common electrolyte disorder in hospitalized patients, with an incidence ranging from 10 to 30% [1–3]. Acute (<48 h) and chronic hyponatremia are both associated with increased morbidity and mortality [4,5]. On the other hand, inappropriate treatment of hyponatremia could also have devastating consequences, including the osmotic demyelination syndrome that leads to major neurologic disabilities or even death [4–6]. The appropriate diagnosis of the causative factor is of paramount importance for the proper management and avoidance of treatment pitfalls, which can lead to under or mainly overtreatment of hyponatremia.

Herein, we describe the ten most common pitfalls in the evaluation of the hyponatremic patient (Table 1).

1. Failure to exclude pseudohyponatremia

Patients with pseudohyponatremia exhibit non-hypotonic hyponatremia with normal values of plasma osmolality (Posm 275–290 mOsmol/kg), measured with an osmometer. However, since an osmometer is not invariably available, the suspicion of pseudohyponatremia should be raised upon a case of hyponatremia in an entirely asymptomatic patient. Pseudohyponatremia is observed in patients with hyperproteinemia (as seen in multiple myeloma and other monoclonal gammopathies or with intravenous immunoglobulin administration) and severe hypertriglyceridemia [7–9]. Severe hypercholesterolemia, mainly due to primary biliary cirrhosis, is also a cause of pseudohyponatremia [10]. Serum levels of total proteins and lipid parameters (total cholesterol and triglycerides) should be always measured in patients with low serum sodium levels. It is worth mentioning that pseudohyponatremia is observed when indirect potentiometry with diluted samples is used to determine serum sodium levels. The analysis of electrolyte concentrations with indirect ion-selective electrodes is preceded by a dilution step of the sample. Thus, the dilution step and the subsequent calculation of concentration lead to a falsely low sodium concentration, when water concentration has been altered by increased lipid or protein levels [11]. In patients with suspected pseudohyponatremia, measurement of sodium levels with a direct potentiometer (using one of the most modern blood gas analyzers), which does not include a dilution step, could reveal the true serum sodium concentration [9,12].

2. Failure to exclude hypertonic hyponatremia

Hypertonic hyponatremia (normal/increased Posm > 280 mOsm/kg) is related to the presence of an osmotically active substance in the circulation [9]. In this case, free water is osmotically moved from intracellular environment to intravascular space leading to decreased serum sodium levels. The diagnosis of hypertonic hyponatremia can be easily achieved when an osmometer is available. In the absence of an osmometer,

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Table 1
Common pitfalls in the evaluation of hyponatremic patients.

Pitfall	Associated conditions that could be missed and/or clues to diagnosis
Failure to exclude pseudohyponatremia	Hyperproteinemia (multiple myeloma, other monoclonal gammopathies, intravenous immunoglobulin administration), severe hypertriglyceridemia and hypercholesterolemia
Failure to exclude hypertonic hyponatremia (measurement of Posm)	Elevated levels of glucose, administration of mannitol, glycine, hyperosmolar radiocontrast media administration
Inability to measure and properly evaluate the urine osmolality (Uosm)	Primary polydipsia (Uosm <100 mOsm/kg), beer-potomania syndrome, tea and toast diet
Failure of assessment of urine sodium concentration in a random urine specimen	Low effective arterial blood volume (urine sodium <30 mEq/l), SIADH (>30 mEq/l)
Failure to properly evaluate other laboratory findings in hyponatremic patients	Serum uric acid levels: <4 mg/dl →SIADH, >5 mg/dl →hypovolemia.
	FEUA: <4% →hypovolemia, 4–11% →reset osmostat or primary polydipsia, >11% → SIADH
	Urea levels (<10 mg/dl) with increased FEurea (>55%) →SIADH
Diagnosis of SIADH without exclusion of other causes of hyponatremia	Hypothyroidism, adrenal insufficiency, pituitary insufficiency
Inability to delineate the cause of SIADH	Drug-associated hyponatremia, malignancy, temporal arteritis, Walderstrom macroglobulinemia
Failure to diagnose the underlying cause of hyponatremia in patients with neurological diseases: Differential diagnosis between SIADH and cerebral salt wasting (CSW)	Serum urea levels: increased in CSW. Central venous pressure: low in CSW. Administration of NaCl 0.9%: increase in serum sodium in CSW. FEUA: >11% in CSW after restoration of normonatremia
Failure to recognize other causes of hyponatremia not usually considered in the evaluation of hyponatremic patients	Reset osmostat syndrome, nephrogenic syndrome of inappropriate antidiuresis, strenuous exercise
Failure to realize the supreme role of a growing list of medications associated with decreased sodium levels	Thiazides, selective serotonin reuptake inhibitors (SSRIs), norepinephrine reuptake inhibitors (SNRIs), carbamazepine, oxcarbamazepine, ecstasy

SIADH = syndrome of inappropriate antidiuretic hormone secretion; FE = fractional excretion

hypertonic hyponatremia should be suspected in patients with elevated levels of glucose [13]. In these cases, it is imperative to calculate the serum sodium corrected for the degree of hyperglycemia by increasing the measured serum sodium level by 1.4 to 2.4 mEg for every 100 mg/dl of blood glucose increase above normal [14]. In these cases, patient's management should proceed according to the corrected serum sodium levels [15,16]. Hypertonic hyponatremia is also observed with the administration of mannitol, glycine (for example during transurethral resection of the prostate or gynecological procedures), or even with hyperosmolar radiocontrast media administration [9,17]. A careful and thorough history can reveal the cause of hyponatremia in such cases.

3. Inability to measure and properly evaluate the urine losmolality (Uosm)

Uosm (measured with an osmometer) is useful for the determination of urine diluting ability, which actually reflects vasopressin (antidiuretic hormone, ADH) activity. A value below 100 mosmol/kg suggests that kidneys' ability to excrete maximally diluted urine remains intact. In this case, the cause of hyponatremia is either primary polydipsia or other underlying psychiatric disorders, such as schizophrenia, which are associated with massive water intake [18]. However, hyponatremia with decreased Uosm can also be observed in individuals who consume large amounts of fluid but small amounts of salt and protein. This results in a limited amount of solutes to be excreted and leads to decreased water excretion. This phenomenon has been reported in ill-nourished heavy drinkers (beer potomania syndrome) but also in elderly with increased water and low solute intake (for example, tea and toast diet) [19–22]. Psychiatric patients with increased water intake (partially due to drug-associated xerostomia) and impaired renal diluting ability (underlying renal disease, volume depletion, decreased solute intake or drugs affecting water homeostasis such as thiazide diuretics) may exhibit hyponatremia with relatively dilute urine but with Uosm > 100 mosm/kg (usually between 100 and 300 mosm/kg) [6]. It has also been reported that acute psychosis results in increased ADH secretion and water retention [23]. Finally, low urine osmolality is similarly observed after rehydration with saline solutions in patients with hyponatremia attributed to hypovolemia. In hypovolemic hyponatremia, the restoration of euvolemia rapidly reverses the defect in water excretion (hypovolemia-induced ADH increase) and may lead to brisk aquaresis and rapid correction of hyponatremia (autocorrection). In this case frequent measurement of serum sodium concentration and appropriate limitation of the rate of correction are mandatory [6,24]. It is worth mentioning that patients with severe kidney disease exhibit decreased urine diluting ability and are prone to develop hyponatremia [25].

4. Failure of assessment of urine sodium concentration in a random urine specimen

The estimation of urine sodium concentration is mandatory for the etiologic diagnosis of hyponatremia. Values of less than 30 mEq/l are suggestive of low effective arterial blood volume due to either true hypovolemia or to edematous states, such as congestive heart failure or ascites [26–28]. On the contrary, a value of >30 mEq/l points toward to the diagnosis of the syndrome of inappropriate antidiuretic hormone secretion (SIADH) [29]. However, it should be mentioned that increased urine sodium levels are frequently observed in several clinical conditions associated with the development of hyponatremia, such as renal failure, salt losing nephropathy, primary adrenal insufficiency, thiazide administration, glucosuria and metabolic alkalosis [30]. In the case of metabolic alkalosis, a useful clue is the identification of low urine chloride concentration (<30 mEq/l), which points toward extracellular volume depletion [31]. On the other hand, low urine sodium levels can be found in patients with chronic SIADH on a low salt diet or anorexia.

5. Failure to properly evaluate other laboratory findings in hyponatremic patients

Other laboratory parameters that should be assessed in patients with hyponatremia include:

i.) Serum uric acid levels: values <4 mg/dl are commonly encountered in SIADH, while values >5 mg/dl are mainly observed in patients with hypovolemia [32]. It is worth mentioning that the determination of serum uric acid levels is also useful in patients with thiazide-associated hyponatremia, since it can be used in the differential diagnosis between the two distinct subgroups of patients with thiazide-associated hyponatremia, namely patients with extracellular volume depletion (serum uric acid >5 mg/dl) and patients with a SIADH-like picture (serum uric acid levels <4 mg/dl) [33].

ii.) Fractional excretion of uric acid (FEUA): The fractional excretion of a molecule is calculated by the formula

$$FEmolecule = \frac{urine\ molecule \times serum\ Creatinine}{serum\ molecule \times urine\ Creatinine} \times 100.$$

Increased levels of FEUA (>12%) indicate SIADH even in patients under thiazide diuretics [34,35]. A more recent practical algorithm for determining the underlying cause of hyponatremia proposed that FEUA >11% is suggestive of SIADH, while patients with volume depletion and adrenal insufficiency exhibit values <4% [36].

iii.) Levels and fractional excretion of urea: Low urea levels (<10 mg/dl) with increased FEurea (>55%) point to SIADH [37].

6. Diagnosis of SIADH without exclusion of other causes of hyponatremia

SIADH should be diagnosed only when other common causes of hyponatremia have been carefully excluded. Thus, the essential criteria in the diagnosis of SIADH include hypotonic hyponatremia (Posm < 275 mosm/kg), inappropriate urine concentration (Uosm > 100 mosm/kg), clinical euvolemia defined by the absence of signs of either hypovolemia or hypervolemia, increased urine sodium concentration (>30 mEq/l) and absence of other potential causes of euvolemic hyponatremia, including thiazide administration [38,39]. In this setting it should be emphasized that endocrine disorders, like adrenal insufficiency, pituitary insufficiency or severe hypothyroidism, are rather common causes of euvolemic hyponatremia and thus a morning cortisol and TSH concentration are necessary in the diagnostic workup of hyponatremic patients [40]. Supplemental criteria for the diagnosis of SIADH include low serum uric acid levels with uricosuria, low urea levels with increased FEurea, FENa >1%, increased ADH levels and abnormal water load test [4,6,30]. Finally, nausea, pain, stress or hypoxia, which are commonly observed in hospitalized patients, leads to exaggerated ADH secretion and water retention resulting to hyponatremia [4–6,30,41,42]. In equivocal cases, the therapeutic criterion can also be used in the differential diagnosis between SIADH and hypovolemia without evident clinical signs: Volume expansion with 1–2 L of Normal Saline solution (NaCl 0.9%) is associated with an increase in serum sodium levels in patients with hypovolemia, while no significant change or even a decrease in serum sodium levels can be observed in SIADH. On the contrary, in many asymptomatic patients with SIADH, fluid restriction may be sufficient to increase serum sodium levels [30].

7. Inability to delineate the cause of SIADH

In patients with SIADH every effort should be undertaken to reveal the underlying cause. Thus, a detailed medical history including infections, endocrine disorders and malignancies with a special focus in drugs and diseases affecting water homeostasis, a thorough physical examination and appropriate laboratory investigation, including an x-ray of the chest, a CT scan of the thorax (especially in smokers) and even an MRI of the brain in patients with suspected neurological disease, are necessary. Furthermore, rare causes of the syndrome such as temporal arteritis or Walderstrom macroglobulinemia can be considered in suspected cases [4–6,30,40–43]. However, the delineation of the cause of SIADH is difficult in many cases. The prevalence of idiopathic SIADH (i.e. SIADH with no evident cause) has been reported to be up to 40% in a geriatric population[11].

8. Failure to diagnose the underlying cause of hyponatremia in patients with neurological diseases: differential diagnosis between SIADH and cerebral salt wasting (CSW)

Patients with intracranial disorders commonly exhibit hyponatremia mainly due to SIADH. However, some patients, mostly with subarachnoid hemorrhage, may present with hyponatremia due to salt wasting leading to hypovolemia, increased non-osmotic ADH secretion, water retention, and decreased serum sodium levels. These patients, in contrast to those with SIADH, exhibit signs of extracellular volume depletion (such as orthostatic hypotension) [44]. However, in patients with neurological diseases clinical assessment of fluid status is difficult. Furthermore, both groups of patients may present with low serum uric acid levels, uricosuria and natriuresis (urine sodium > 30 mEq/l) [45,46]. Serum urea levels are helpful since urea may be low in SIADH and increased in CSW. Central venous pressure is normal in SIADH but low in CSW. If the diagnosis is not clear, careful administration of NaCl 0.9% is useful. No change or even a decrease in serum sodium will be noticed in SIADH, while an increase in serum sodium levels will be achieved in CSW [36,47,48]. According to the recently proposed algorithm by Maesaka et al., patients with CSW exhibit increased FEUA (>11%) after the restoration of hyponatremia. On the contrary, patients with SIADH usually present with FEUA <11% when normonatremia has been achieved [36].

9. Failure to recognize other causes of hyponatremia not usually considered in the evaluation of hyponatremic patients

The reset osmostat syndrome should be considered in the differential diagnosis of hyponatremia. Patients with this condition present with repeatedly moderately low serum sodium levels due to resetting of the osmostat to lower serum osmolality levels. This condition should be suspected in hyponatremic patients with quadriplegia, tuberculosis, chronic malnutrition and psychosis [49–52]. Interestingly, this phenomenon is also found in pregnant women leading to a reduction of serum sodium levels by approximately 4–5 mEq/l [53]. The diagnosis can be confirmed by a water load test (administration of a water load 20 ml/kg). In contrast to SIADH, these patients are able to normally excrete >80% of the water load within 4 h and accordingly reduce Uosm [54]. Moreover, a normal FEUA (4–11%) in a nonedematous hyponatremic patient with Uosm >100 mOsm/kg is highly suggestive of reset osmostat syndrome [36].

Another rare cause of hyponatremia is the nephrogenic syndrome of inappropriate antidiuresis due to functional mutations of the V2 receptors of ADH leading to water retention and decreased sodium levels [55,56].

Prolonged strenuous exercise (as in marathon runners or in those hot-heated hiking, etc) is occasionally associated with acute symptomatic hyponatremia due to non-osmotically stimulated ADH secretion but also due to excessive water intake. Losses of salt and chloride may also play a role in the development of hyponatremia in such patients [57–59].

10. Failure to realize the supreme role of a growing list of medications associated with decreased sodium levels

In many cases, medications are the underlying cause or contribute to the development of hyponatremia [43]. Special emphasis should be given to thiazides, which impair the ability of the kidneys to excrete water [60,61]. These drugs, as well as the selective serotonin reuptake inhibitors (SSRIs), the norepinephrine reuptake inhibitors (SNRIs), carbamazepine and oxcarbamazepine, are rather common causes of hyponatremia through various implicated mechanisms [43]. Finally, “ecstasy” is also a cause of acute life-threatening hyponatremia due to SIADH and it should always be considered in young patients with severe hyponatremia [62].

Conflict of interest statement

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References

[1] Upadhyay A, Jaber BL, Madias NE. Incidence and prevalence of hyponatremia. Am J Med 2006;119:S30–5.
[2] Beukhof CM, Hoorn EJ, Lindemans J, Zietse R. Novel risk factors for hospital-acquired hyponatraemia: a matched case–control study. Clin Endocrinol (Oxf) 2007;66:367–72.
[3] Upadhyay A, Jaber BL, Madias NE. Epidemiology of hyponatremia. Semin Nephrol 2009;29:227–38.
[4] Spasovski G, Vanholder R, Allolio B, Annane D, Ball S, Bichet D, et al. Clinical practice guideline on diagnosis and treatment of hyponatraemia. Eur J Endocrinol 2014;170:G1–G47.
[5] Verbalis JG, Goldsmith SR, Greenberg A, Korzelius C, Schrier RW, Sterns RH, et al. Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. Am J Med 2013;126:S1–S42.
[6] Henry DA. Hyponatremia. Ann Intern Med 2015;163:ITC1.
[7] Weisberg LS. Pseudohyponatremia: a reappraisal. Am J Med 1989;86:315–8.
[8] Steinberger BA, Ford SM, Coleman TA. Intravenous immunoglobulin therapy results in post-infusional hyperproteinemia, increased serum viscosity, and pseudohyponatremia. Am J Hematol 2003;73:97–100.
[9] Liamis G, Liberopoulos E, Barkas F, Elisaf M. Spurious electrolyte disorders: a diagnostic challenge for clinicians. Am J Nephrol 2013;38:50–7.
[10] Hussain I, Ahmad Z, Garg A. Extreme hypercholesterolemia presenting with pseudohyponatremia—a case report and review of the literature. J Clin Lipidol 2015;9:260–4.
[11] Fortgens P, Pillay TS. Pseudohyponatremia revisited: a modern-day pitfall. Arch Pathol Lab Med 2011;135:516–9.
[12] Lippi G, Aloe R. Hyponatremia and pseudohyponatremia: first, do no harm. Am J Med 2010;123, e17.
[13] Liamis G, Tsimihodimos V, Elisaf M. Hyponatremia in diabetes mellitus: clues to diagnosis and treatment. J Diabetes Metab 2015;6:560.
[14] Hillier TA, Abbott RD, Barrett EJ. Hyponatremia: evaluating the correction factor for hyperglycemia. Am J Med 1999;106:399–403.
[15] Palmer BF, Clegg DJ. Electrolyte and acid–base disturbances in patients with diabetes mellitus. N Engl J Med 2015;373:548–59.
[16] Liamis G, Liberopoulos E, Barkas F, Elisaf M. Diabetes mellitus and electrolyte disorders. World J Clin Cases 2014;2:488–96.
[17] Aviram A, Pfau A, Czaczkes JW, Ullmann TD. Hyperosmolality with hyponatremia, caused by inappropriate administration of mannitol. Am J Med 1967;42:648–50.
[18] Margetic B, Aukst Margetic B. Neglected issues in follow-up of psychiatric patients with hyponatremia. Psychiatry Res 2015;225:221–2.
[19] Thaler SM, Teitelbaum I, Berl T. "Beer potomania" in non-beer drinkers: effect of low dietary solute intake. Am J Kidney Dis 1998;31:1028–31.
[20] Pallavi R. An unsuspected cause of hyponatremia: beer potomania. J Am Geriatr Soc 2015;63:1714–5.
[21] Srisung W, Mankongpaisarnrung C, Anaele C, Dumrongmongcolgul N, Ahmed V. A rare case of low-solute hyponatremia in a nonalcoholic person. Case Rep Nephrol Dial 2015;5:49–53.
[22] Sanghvi SR, Kellerman PS, Nanovic L. Beer potomania: an unusual cause of hyponatremia at high risk of complications from rapid correction. Am J Kidney Dis 2007;50:673–80.
[23] Goldman MB, Luchins DJ, Robertson GL. Mechanisms of altered water metabolism in psychotic patients with polydipsia and hyponatremia. N Engl J Med 1988;318:397–403.
[24] Adrogue HJ, Madias NE. The challenge of hyponatremia. J Am Soc Nephrol 2012;23:1140–8.
[25] Kovesdy CP, Lott EH, Lu JL, Malakauskas SM, Ma JZ, Molnar MZ, et al. Hyponatremia, hypernatremia, and mortality in patients with chronic kidney disease with and without congestive heart failure. Circulation 2012;125:677–84.
[26] O'Donoghue D, Trehan A. SIADH and hyponatraemia: foreword. NDT Plus 2009;2:iii1–4.
[27] Chung HM, Kluge R, Schrier RW, Anderson RJ. Clinical assessment of extracellular fluid volume in hyponatremia. Am J Med 1987;83:905–8.
[28] Filippatos TD, Elisaf MS. Hyponatremia in patients with heart failure. World J Cardiol 2013;5:317–28.
[29] Decaux G, Musch W. Clinical laboratory evaluation of the syndrome of inappropriate secretion of antidiuretic hormone. Clin J Am Soc Nephrol 2008;3:1175–84.
[30] Milionis HJ, Liamis GL, Elisaf MS. The hyponatremic patient: a systematic approach to laboratory diagnosis. CMAJ 2002;166:1056–62.
[31] Sherman RA, Eisinger RP. The use (and misuse) of urinary sodium and chloride measurements. JAMA 1982;247:3121–4.
[32] Musch W, Decaux G. Utility and limitations of biochemical parameters in the evaluation of hyponatremia in the elderly. Int Urol Nephrol 2001;32:475–93.
[33] Liamis G, Christidis D, Alexandridis G, Bairaktari E, Madias NE, Elisaf M. Uric acid homeostasis in the evaluation of diuretic-induced hyponatremia. J Investig Med 2007;55:36–44.
[34] Liamis G, Mitrogianni Z, Liberopoulos EN, Tsimihodimos V, Elisaf M. Electrolyte disturbances in patients with hyponatremia. Intern Med 2007;46:685–90.
[35] Fenske W, Stork S, Koschker AC, Blechschmidt A, Lorenz D, Wortmann S, et al. Value of fractional uric acid excretion in differential diagnosis of hyponatremic patients on diuretics. J Clin Endocrinol Metab 2008;93:2991–7.
[36] Maesaka JK, Imbriano L, Mattana J, Gallagher D, Bade N, Sharif S. Differentiating SIADH from cerebral/renal salt wasting: failure of the volume approach and need for a new approach to hyponatremia. J Clin Med 2014;3:1373–85.
[37] Musch W, Thimpont J, Vandervelde D, Verhaeverbeke I, Berghmans T, Decaux G. Combined fractional excretion of sodium and urea better predicts response to saline in hyponatremia than do usual clinical and biochemical parameters. Am J Med 1995;99:348–55.
[38] Bartter FC, Schwartz WB. The syndrome of inappropriate secretion of antidiuretic hormone. Am J Med 1967;42:790–806.
[39] Liamis G, Elisaf M. Treatment of hyponatremia: what the clinician needs to know. J Nephrology Res 2015;1:19–21.
[40] Liamis G, Milionis HJ, Elisaf M. Endocrine disorders: causes of hyponatremia not to neglect. Ann Med 2011;43:179–87.
[41] Liamis G, Milionis HJ, Elisaf M. Hyponatremia in patients with infectious diseases. J Infect 2011;63:327–35.
[42] Janicic N, Verbalis JG. Evaluation and management of hypo-osmolality in hospitalized patients. Endocrinol Metab Clin North Am 2003;32:459–81 (vii).
[43] Liamis G, Milionis H, Elisaf M. A review of drug-induced hyponatremia. Am J Kidney Dis 2008;52:144–53.
[44] Momi J, Tang CM, Abcar AC, Kujubu DA, Sim JJ. Hyponatremia—what is cerebral salt wasting? Perm J 2010;14:62–5.
[45] Zomp A, Alexander E. Syndrome of inappropriate antidiuretic hormone and cerebral salt wasting in critically ill patients. AACN Adv Crit Care 2012;23:233–9 (quiz 40–1).
[46] Cerda-Esteve M, Cuadrado-Godia E, Chillaron JJ, Pont-Sunyer C, Cucurella G, Fernandez M, et al. Cerebral salt wasting syndrome: review. Eur J Intern Med 2008;19:249–54.
[47] Oh JY, Shin JI. Syndrome of inappropriate antidiuretic hormone secretion and cerebral/renal salt wasting syndrome: similarities and differences. Front Pediatr 2014;2:146.
[48] Verbalis JG. Hyponatremia with intracranial disease: not often cerebral salt wasting. J Clin Endocrinol Metab 2014;99:59–62.
[49] Vale BM, Morais S, Mesquita J, Mimoso G. Reset osmostat: a rare cause of hyponatraemia. BMJ Case Rep 2015;2015.
[50] Elisaf MS, Konstantinides A, Siamopoulos KC. Chronic hyponatremia due to reset osmostat in a patient with colon cancer. Am J Nephrol 1996;16:349–51.
[51] Liamis GL, Milionis HJ, Rizos EC, Siamopoulos KC, Elisaf MS. Mechanisms of hyponatraemia in alcohol patients. Alcohol Alcohol 2000;35:612–6.
[52] Hoorn EJ, Swart RM, Westerink M, van den Dorpel MA, Berghout A, Bakker JJ. Hyponatremia due to reset osmostat in dementia with lewy bodies. J Am Geriatr Soc 2008;56:567–9.
[53] Harris K, Shankar R, Black K, Rochelson B. Reset osmostat in pregnancy: a case report. J Matern Fetal Neonatal Med 2014;27:530–3.
[54] Saghafi D. Water loading test in the reset osmostat variant of SIADH. Am J Med 1993;95:343.
[55] Feldman BJ, Rosenthal SM, Vargas GA, Fenwick RG, Huang EA, Matsuda-Abedini M, et al. Nephrogenic syndrome of inappropriate antidiuresis. N Engl J Med 2005;352:1884–90.
[56] Erdelyi LS, Mann WA, Morris-Rosendahl DJ, Gross U, Nagel M, Varnai P, et al. Mutation in the V2 vasopressin receptor gene, AVPR2, causes nephrogenic syndrome of inappropriate diuresis. Kidney Int 2015;88:1070–8.
[57] Almond CS, Shin AY, Fortescue EB, Mannix RC, Wypij D, Binstadt BA, et al. Hyponatremia among runners in the Boston Marathon. N Engl J Med 2005;352:1550–6.
[58] Cairns RS, Hew-Butler T. Incidence of exercise-associated hyponatremia and its association with nonosmotic stimuli of arginine vasopressin in the GNW100s ultra-endurance marathon. Clin J Sport Med 2015;25:347–54.
[59] Khodaee M, Luyten D, Hew-Butler T. Exercise-associated hyponatremia in an ultra-endurance mountain biker: a case report. Sports Health 2013;5:334–6.
[60] Sardar GK, Eilbert WP. Severe hyponatremia associated with thiazide diuretic use. J Emerg Med 2015;48:305–9.
[61] Barber J, McKeever TM, McDowell SE, Clayton JA, Ferner RE, Gordon RD, et al. A systematic review and meta-analysis of thiazide-induced hyponatraemia: time to reconsider electrolyte monitoring regimens after thiazide initiation? Br J Clin Pharmacol 2015;79:566–77.
[62] van Dijken GD, Blom RE, Hené RJ, Boer WH. High incidence of mild hyponatraemia in females using ecstasy at a rave party. Nephrol Dial Transplant 2013;28:2277–83.