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Value of fractional excretion of urate in differential diagnosis of hyponatremia

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Hyponatremia, defined as serum sodium <135 mEq/L, is the most common electrolyte abnormality encountered in clinical practice worldwide (1-3).

Many clinical disorders can be associated with hyponatremia including syndrome of inappropriate ADH secretion (SIDH), renal salt eating (RSW), reset osmostat (RO), and endocrine dysfunction (4). The SIADH is the most common cause of hyponatremia in clinical practice, but current diagnosis and treatment recommendations in patients with SIADH are not well understood (5).

Differentiating SIADH from RSW and RO is crucial because of opposing therapeutic goals, which to provide water restriction to water-loaded patients with SIADH, salt and water to RSW and no treatment for patients with reset hyponatremia (1,2,5,6).

SIADH and RSW are diagnosed by presence of true hyponatremia, decreased plasma osmolality (<275 moms/kg), inappropriately concentrated urine (>100 moms/kg), and elevated urine sodium usually (>20 mEq/L), hypouricemia (<4 mg/dL), with normal renal, adrenal and thyroid function (2,5,6). A main difference between these two syndromes is the volume status, norovolemic in SIADH, despite water retention, and hypovolemic in RSW (2,5,6).

The water retention in SIADH is accompanied by hypouricemia and low blood urea nitrogen (BUN) (<5 mg/dL) due to increased urate excretion in the urine resulting from diminished proximal tubular reabsorption of uric acid (7-9). Stimulation of the vasopressor V_1 receptor also attributes to the increased urinary urate excretion (10).

Although hypouricemia is still considered as a hallmark of the SIADH, in routine clinical practice – contrary to what has been previously published – this difference is insufficient for hypouricemia to discriminate reliably between the SIADH and RSW (7-9,11,12).

RO can be found in a variety of clinical settings, including pulmonary and neurologic diseases, as well as in physiologic conditions such as pregnancy. RO diagnosis is made when normovolemic hyponatremia is associated with dilute urine (<100 moms/kg), normal serum uric acid, renal and endocrine function (13).

Despite the high prevalence of hyponatremia and published guidance on its diagnosis and treatment, differentiating SIADH from RSW and RO has been extremely difficult because of our inability to accurately estimate the volume status of patients by usual clinical criteria and significant laboratory overlapping between these syndromes (14).

Recently, Maesaka and colleagues constructed a practical algorithm, based on determinations of a unique relationship between fractional excretion of urate [FEurate], serum sodium, and distinctive responses to saline infusions to differentiate SIADH from other causes of hyponatremia without the need to consider the volume status of patients or determinations of urine sodium, plasma renin, uric acid, or aldosterone serum levels (14,15).

These authors recommend by applying the following two distinctive pathophysiologic characteristics we can readily differentiate SIADH from RSW and RO:

1. To demonstrate normalization of a previously enhanced FEurate in SIADH (from>11% to 4%-11%) with water restriction and persistent increase in FEurate as in RSW (>11%) after correction of hyponatremia by hypertonic saline.
2. To demonstrate whether isotonic saline infusion stimulates excretion of dilute urines (<100 most/kg) with a prompt increase in serum sodium as in RSW or continued excretion of concentrated urines >100 most/kg without amendment of hyponatremia as in SIADH (12,13).

The diagnosis of RO is readily made when a hyponatremic patient meets the criteria for SIADH and RSW but has normal FEurate (4%-11%) and is able to dilute urine <100 mosm/ kg after water-loading (10,11).

Implication for health policy/practice/research/medical education

Hyponatremia, defined as serum sodium <135 mEq/L, is the most common electrolyte abnormality encountered in clinical practice worldwide. Many clinical disorders can be associated with hyponatremia including SIDH, RSW and RO.

Keywords: Syndrome of inappropriate ADH secretion, Renal salt eating, Reset osmostat, Hyponatremia, Hypouricemia

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Summary

- Assessing the volume status of patients cannot make the diagnosis and treatment of hyponatremic patients.
- When dealing with hyponatremic individuals the initial treatment should be intravenous administration of normal saline, combined with measuring the FEurate.
- As serum sodium is corrected, individuals with SIADH will normalize the FEurate, while patients with RSW will have a persistently elevated FEurate.
- It seems that individuals with SIADH and RO will have a slow or no enhance in serum sodium with saline, while individuals with RSW will have a more rapid augment in serum sodium.

Author's contribution

FA is the single author of the manuscript.

Conflicts of interest

The author declared no competing interests.

Ethical considerations

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