Essential Hypernatremia: Is There such a Thing?

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Louis Welt [1], in an editorial related to the case of a hypematremic child with a thirst defect, first reported by Avioli et al. [2], proposed the term essential hypernatremia. He defined the term as: upward resetting of the osmostat for ADH release, maintenance of the ability to dilute the urine at higher than normal serum sodium concentration, and the absence of volume depletion. Welt reasoned that the only actual abnormality in this condition was regulation of ADH release at higher than usual extracellular osmolality, and that all other functions, especially renal function, were normal. He predicted that effective vascular volume in essential hypernatremia must be normal. A number of investigators doubt the existence of upward resetting of the osmostat, preferring the interpretation that what appears to be the upward resetting of the osmoreceptor actually represents destruction of osmoreceptor cells [3,4].

The purpose of this communication is not to argue whether upward resetting does occur but to propose that even if upward resetting did occur, the absence of volume depletion would not be an expected finding. The argument hinges on the role of serum sodium concentration as a determinant of renal sodium excretion [5, 6], a factor ignored in Welt’s formulation. This discussion will explain why serum sodium concentration is a predictor of effective vascular volume in chronic hyper- and hyponatremia.

Most observers believe that a patient with diabetes insipidus who develops hypernatremia because of inadequate treatment would be dehydrated, and that the degree of dehydration would be positively correlated to the degree of hypernatremia. Yet, in the case of hypematremic patients with upward resetting of the osmostat, these observers predict a normal effective vascular volume [7-11].

The following case illustration will make it clear that volume depletion must accompany any hypernatremia when the kidney is functioning normally. Let us suppose that a patient with combined central diabetes insipidus and defective thirst is being treated with pitressin, and that he maintains normal serum sodium and normal effective vascular volume. Let the patient then develop hypernatremia because of insufficient pitressin dosage, receive pitressin when serum sodium rises to a level above 170 mEq/l, and receive no more drug when serum sodium returns to 170 mEq/l. This situation would be a physiological duplicate of upward resetting of the osmostat, and hypernatremia in both situations would be due initially to water deficit. The patient would be volume depleted, and the kidneys would retain sodium in response to volume depletion. However, renal sodium retention would stop before volume was restored to normal because hypernatremia itself
enhances renal sodium excretion [5,6]. In the steady state, i.e. when sodium intake equals sodium output, effective vascular volume would remain diminished. The major factor determining the degree of volume depletion in hypernatremia of any cause is of course the severity of water deficit. When water deficit occurs rapidly without an opportunity for sodium to be retained, serum sodium mathematically reflects the degree of water loss. However, when water loss occurs chronically and sodium intake continues, volume depletion causes renal sodium retention, and hypernatremia is then the result of sodium retention as well as water loss. Sodium retention continues until the natriuretic effect of hypernatremia overcomes the salt-retaining effect of volume depletion. At equilibrium, the patient will remain volume depleted and hypernatremic. Since the natriuretic effect of hypernatremia is positively correlated to its magnitude, the degree of volume depletion is also a function of the degree of hypernatremia. Thus, the degree of volume depletion would be essentially the same for a given magnitude of hypernatremia whether hypernatremia was caused by primary hypodipsia with intact ADH mechanism, osmoreceptor dysfunction, or diabetes insipidus with insufficient water intake.

It goes without saying that the mere presence of hypernatremia implies some inability of the subject to maintain adequate intake of free water: unconsciousness, lack of thirst, lack of access to water, inability to drink water, etc. The same physiological principle would predict the development of volume depletion if hypernatremia resulted from primary salt excess, as in the case of infusion of hypertonic saline or ingestion of water from the ocean, as long as renal function is adequately maintained. In these situations the patient would be hypernatremic without volume depletion at the beginning. However, hypernatremia would cause sodium diuresis, which would continue until the salt-retaining effect of progressive volume depletion counterbalanced the natriuretic effect of hypernatremia. At equilibrium, the patient would be volume depleted. The effect of serum sodium concentration on renal salt excretion is also responsible for maintenance of increased effective arterial volume in patients with chronic hyponatremia due to SIADH. It is well known that patients with chronic hyponatremia due to SIADH are chronically hypervolemic, as shown by increased urea and uric acid clearance [12, 13]. If serum sodium did not affect renal sodium excretion, patients with hyponatremia due to SIADH would not remain volume expanded. If the kidney responded only to volume expansion caused by abnormal water retention in SIADH, renal sodium loss should continue until volume was normalized. Yet, hyponatremic patients with SIADH are hypervolemic in the steady state; renal sodium loss stops before volume is restored because of the antinatriuretic effect of hyponatremia. Again, as with hypernatremia, the degree of volume expansion is positively correlated to the degree of hyponatremia. The absence of clinically apparent dehydration in most patients with so-called ‘essential hypernatremia’ is probably due to the fact that the degree of hypernatremia is not severe in most cases. Furthermore, there are no sensitive clinical indices of mild to moderate dehydration. For example, we all know that diuretics, thiazides or loop diuretics, lead to decreased effective arterial volume. But we all know also that it is difficult to tell on the basis of clinical assessment of effective arterial volume alone that a patient is taking a diuretic. In fact, in one published report it was shown upon careful study that a ‘euvolemic’ patient with the clinical picture of ‘essential hypernatremia’ indeed had evidence of mild volume depletion [14]. In conclusion, if the term essential hypernatremia is used to describe an individual with normal effective vascular volume whose serum sodium is elevated because the osmostat is reset
upward, we conclude that the term is misapplied. Whether or not the osmostat can be upwardly reset, the laws of physiology would seem to require that chronic hypernatremia would be associated with reduced effective vascular volume.

References
