

## Chronic hyponatremia: a new risk factor for fragility fractures in the elderly?

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To the Editor,

Multiple risk factors for osteoporotic fracture, including osteoporosis and falls, are widely known. It is also clear that osteoporotic fractures impose a significant morbidity and mortality in the elderly, with major monetary costs associated.

Recent studies suggest that chronic hyponatremia (serum [Na<sup>+</sup>] < 135mEq/L), albeit slight (serum [Na<sup>+</sup>] = 125-134 mEq/L), may be associated with falls, osteoporosis and fractures. PubMed search for “(“osteoporosis” OR “fracture” OR “falls”) AND “hyponatremia”” (March 1st 2014, last five years, english) retrieved three dozen results.

Several studies have shown associations between chronic hyponatremia and falls, fractures or osteoporosis:

- Falls incidence in elderly people with mild chronic hyponatremia is significant<sup>1</sup>
- Hyponatremia is not associated with lower bone mineral density<sup>1</sup> (despite the relation between hyponatremia and osteoporosis suggested by a previous cross-sectional survey<sup>2</sup>)
- Hyponatremia incidence in elderly patients admitted for fracture secondary to accidental fall is considerable<sup>3</sup>
- Hyponatremia is very prevalent in elderly patients with fragility fracture.<sup>4</sup>

But, can hyponatremia *per se* cause bone disease? Indeed, several studies have shown that chronic hyponatremia may be an independent risk factor for falls, fractures and osteoporosis due to increased probability of falls<sup>1</sup> [adjusted odds ratio (aOR) 1.35], osteoporosis<sup>2</sup> [aOR 2.85 for hip osteoporosis], fracture<sup>3</sup> [OR 4.16] and osteoporotic fracture<sup>5</sup> [OR 1.46], and the increased risk of incident nonvertebral fracture<sup>1</sup> [adjusted hazard ratio (aHR) 1.34 95% CI 1.08-1.68,

p=0.009] and vertebral fracture<sup>1</sup> (combined prevalent and incident) [aOR 1.61, 95% CI 1.00-2.59, p=0.049]. Furthermore, chronic hyponatremia is associated with increased likelihood of in-hospital death after hip fracture (OR 3.64)<sup>6</sup> and increased all-cause mortality risk (aHR 1.21, 95% CI 1.03-1.43, p=0.022)<sup>1</sup>.

Laboratory studies indicate that hyponatremia stimulates osteoclastogenesis<sup>7</sup> and animal model studies associate hyponatremia with decreased thickness of cortical bone and increased number of osteoclasts<sup>2</sup>. There are already proposals for the mechanism of bone disease induced by chronic hyponatremia in humans (Figure 1)<sup>8</sup>.

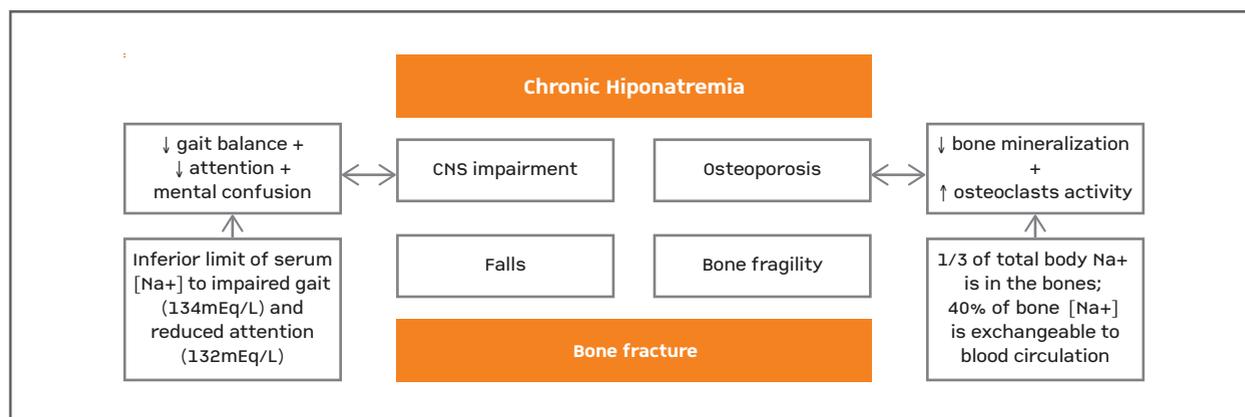
This question seems to be problematic considering that chronic hyponatremia is a common disorder in the elderly<sup>8</sup> and usually asymptomatic (75-80% of cases<sup>7</sup>): 7.2% of patients attending for the first time in primary care to 49.2% of those observed for the first time in the hospital<sup>9</sup>, 10% of patients admitted to the emergency room (ER), 10.7% of ambulatory elderly up to 53% of institutionalized elderly<sup>2</sup>.

Moreover, the elderly are subject to situations of greater propensity for chronic hyponatremia installation, as polypharmacy (e.g. diuretics, antidepressants, antiepileptics, proton pump inhibitors) and diseases (e.g. syndrome of inappropriate secretion of antidiuretic hormone ( $\pm$  50% of chronic hyponatremia cases), diabetes mellitus, hypothyroidism, hepatic cirrhosis, congestive heart failure, kidney disease)<sup>8</sup>.

Physicians who follow elderly patients should be aware for the association between bone disease and chronic hyponatremia. As the measurement of serum sodium is a simple, available and inexpensive procedure, it should be achieved in elderly patients with increased risk of hyponatremia, presenting clinical symptoms consistent with hyponatremia, or which are observed in the ER for bone injury<sup>8</sup>.

Upon the hyponatremia diagnosis it's necessary to establish the appropriate treatment. In the asymptomatic cases it's recommended, at least, the identification

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**FIGURE 1.** Mechanism of bone disease induced by chronic hyponatremia in humans

of reversible causes to prevent recurrence and fluid restriction of 0.5 to 1L/day. Selective vasopressin receptor V2 antagonists may be a treatment option in the future.

Benefits of prevention, diagnosis and effective treatment of chronic hyponatremia in falls, osteoporosis and fracture risk, as quality of life, are yet to prove<sup>8</sup>. For this, new prospective studies are needed.

Chronic hyponatremia may present itself as a new and important independent risk factor for falls, fractures and osteoporosis in the elderly. That said, medical community should be alert to this problem and invest in prevention, diagnosis and treatment!

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