Hyponatremia Now – A Goldmine or a Dead End?

Hiponatremia dziś – żyła złota czy ślepa uliczka?

Abstract

Hyponatremia is a clinically relevant disorder. Ten to twenty per cent of patients in hospitals are affected by it. Hyponatremia is found to occur in almost every clinical department. Recently, vasopressin antagonists have been licensed to treat hyponatremia of the syndrome of inappropriate antidiuretic hormone secretion (SIADH). They provide physicians with the first specific and effective therapy of this hyponatremia. This opens up new avenues for clinical research into the symptoms, findings and consequences of hyponatremia (Adv Clin Exp Med 2012, 21, 5, 559–561).

Key words: hyponatremia, vasopressin antagonist.

Streszczenie


Słowa kluczowe: hiponatremia, antagoniści wazopresyny.

The use of flame photometry to measure sodium concentration was introduced in the early 1950s. Over the years it has become obvious that hyponatremia is a very frequent electrolyte disorder. Reports have tended to peg its incidence at between 5% and 25% in hospitalized patients [1–3]. The literature is full of recommended therapies for hyponatremia: Fluid restriction, osmotic diuresis (urea), induction of nephrogenic diabetes insipidus by demeclocycline or lithium have been proposed, as well as other modalities [4–11]. It is surprising, then, that hyponatremia is such an unpopular disorder, and that physicians usually shrug their shoulders when confronted with a clinical case. What is the explanation for the apparent fact that physicians seem to do so little – and often in a misguided manner – about something that is as endemic as hyponatremia [12–14]?

Recent progress with vaptans – orally available, specific renal V-2 vasopressin receptor antagonists – has shed an entirely new light on these questions and opened up new avenues of research for the future [15–19]. The introduction of vaptans to the treatment of hyponatremia is a striking recent development [15–19], although to be precise in Europe vaptans are currently only approved for euvolemic hyponatremia associated with the syndrome of inappropriate antidiuretic hormone secretion (SIADH). These vaptans have turned out to be highly efficient and reliable. Vaptans should not be confused with diuretics [20]. Instead they function as “aquaretics”, i.e. agents enhancing the excretion of water by the kidneys only. They constitute the first clinical tool and therapy to regulate water excretion. This may be compared to installing a steering wheel in a car: It gives us a way to control the direction the car is heading. In other words, we can treat hyponatremia in a predictable, measurable and efficient manner for the first time. This has obvious advantages and will become a therapeutic breakthrough. However, the benefits of vaptans may go beyond the treatment of hyponatremia alone.
First, vaptans are proof of the principle that hyponatremia is a vasopressin disorder. Scientists have long asserted this [21–23], but this proposal did not seem to catch on with physicians. Many or most of them act as if they consider hyponatremia a state of total body NaCl depletion – as the somewhat misleading term “hyponatremia” appears to suggest – and they put their patients on NaCl (NaCl-capsules, salted crackers or isotonic saline infusions). They do not seem to notice that these “therapies” usually fail to correct euvoletic hyponatremia [14]. However, the effectiveness of vaptans in correcting euvoletic hyponatremia establishes that the nature of this particular electrolyte disorder is a problem of water retention, and not with salt depletion, beyond any reasonable doubt. In fact this water retention has been shown to be the result of too much anti-diuretic hormone (ADH) plus excessive fluid intake in these patients.

Second, vaptans will enable clinical scientists to delineate the symptoms of hyponatremia in a given patient in ways never possible before. In the past the nonspecific nature of these symptoms (poor memory, imbalance, apathy, depressed mood, lack of concentration, nausea, headache, general slowness, etc.) made it difficult or impossible to determine whether the cause was chronic hyponatremia or circumstances like cerebral arteriosclerosis in an elderly patient, alcoholism, the effects of a drug, depression, disturbed sleep, etc. Now, using vaptans it is possible to treat the hyponatremia within only a few days, and thus to ascertain whether the symptom(s) were due to hyponatremia (if they subside) or to something else (if they do not). This may seem trivial but in clinical practice it amounts to a seachange.

Despite hundreds of articles on hyponatremia the clinical relevance of this disorder has remained largely unexplored. The available literature does not include any randomized controlled trials (RCTs) of the effects of hyponatremia and its correction on the quality of life. There have been no prospective controlled studies on the extent to which nonspecific symptoms such as imbalance, falls, fractures, poor concentration, etc. could be improved or prevented by the correction of hyponatremia and what this would actually mean in terms of patients’ well-being [24, 25]. It has not been established what costs could be saved by treating hyponatremia [26, 27], e. g. in terms of earlier discharge from the hospital. It is unclear whether it is true that hyponatremia per se causes substantial loss of lives [28–31] that could potentially be saved by correcting hyponatremia. Finally, it is unclear whether or not chronic hyponatremia leads to significant osteoporosis [32, 33].

This amount of ignorance in so many fields may seem surprising. But it is due to a lack of appropriate tools – in the past – to correct hyponatremia specifically and in a controlled manner. As a consequence researchers have been unable to conduct reasonably sized studies of the clinical outcome of treating hyponatremia – until recently. The new perspective on hyponatremia is that vaptans put the therapist in a better position than before – and they also open up new avenues of research.

References


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