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Is Asymptomatic Hyponatremia Really Asymptomatic?

Guy Decaux, MD, PhD

Department of General Internal Medicine, Erasme University Hospital, Brussels, Belgium

ABSTRACT

Consequences of hyponatremia are generally mild and remain unnoticed by both physician and patient. When water restriction, usually prescribed to avoid water intoxication, fails to normalize serum sodium values, clinicians will tolerate mild stable hyponatremia (especially when serum sodium is >125 mEq/L [1 mEq/L = 1 mmol/L]). In a recent study, we observed that mild chronic hyponatremia contributes to an increased rate of falls, probably due to impairment of attention, posture, and gait mechanisms. Eight attention tests were used to assess 16 patients with asymptomatic hyponatremia (mean serum sodium, 128 ± 3 mEq/L) due to syndrome of inappropriate antidiuretic hormone secretion. On attention tests for visual and auditory stimuli, there was an increase in mean response latency of 58 msec ($P < 0.001$) and an increase in total error number of 20% ($P < 0.001$). The results of 3 stereotyped steps on a platform "in tandem" with eyes open, expressed as total traveled way of center of pressure, was also different in patients with hyponatremia (mean serum sodium, 128 ± 3 mEq/L) when compared with normonatremic patients (1.3 vs 1 m; $P < 0.003$). Noteworthy, in volunteers of similar age, after mild alcohol intake (0.55 g/kg body weight), attention and gait tests were less affected. In another series of 122 consecutive patients hospitalized from the emergency room with mild hyponatremia, approximately 21% were admitted for falls. After controlling for age, sex, and other known risk factors for falls, the adjusted odds ratio for falls in patients with hyponatremia was 67, compared with a control group. These data show that the concept of asymptomatic hyponatremia does not withstand a detailed epidemiologic analysis of falls or of sensitive posture, gait, and attention tests.

KEYWORDS: Attention deficit; Falls; Gait; Hyponatremia; Seizure; Sodium level

Symptoms related to hyponatremia can be very subtle and difficult to detect clinically, partly because they can be attributed to those of the associated diseases. In most cases the symptoms of hyponatremia are mild and remain unnoticed by patient and physician.[1] Symptoms depend chiefly on the magnitude and the rapidity of onset of hyponatremia. Acute, severe hyponatremia, which occurs in <48 hours, induces a dramatic condition due to intracranial hypertension[2]; stable, mild chronic hyponatremia (≥48 hours) is generally considered asymptomatic when using typical clinical criteria.[3] Nevertheless, water restriction is usually prescribed to avoid worsened water intoxication.[4] When water restriction does not normalize the serum sodium concentration, clinicians usually tolerate mild stable hyponatremia (particularly when serum sodium is >125 mEq/L [1 mEq/L = 1 mmol/L]). For example, in many patients with hyponatremia secondary to medications (e.g., carbamazepine, oxcarbazepine,[5] selective serotonin reuptake inhibitors), cardiac failure, cirrhosis, or idiopathic syndrome of inappropriate antidiuretic hormone secretion[5] (SIADH), which is particularly frequent in the elderly, physicians generally tolerate the presence of mild hyponatremia.[6]

A recent study reported that mild chronic hyponatremia could contribute to falls, especially in elderly people, probably as a result of attention, posture, and gait impairments.[7] In this study, the authors selected 16 patients with mild chronic hyponatremia (mean serum sodium, 128 ± 3 mEq/L) who were considered to be clinically asymptomatic. The patients had no complaints and a normal neurologic examination. Consequently, neither the patients nor the physician could clinically determine whether the patients had hyponatremia. All patients' Mini-Mental State Examination scores were 29 of 30 or 30 of 30.

Hyponatremia was stable for ≥3 days (in most patients, the condition was present for weeks or months). All patients were

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Requests for reprints should be addressed to Guy Decaux, MD, PhD, Department of General Internal Medicine, Erasme University Hospital, 808 Route de Lennik, 1070 Brussels, Belgium.

E-mail address: guy.decaux@skynet.be.

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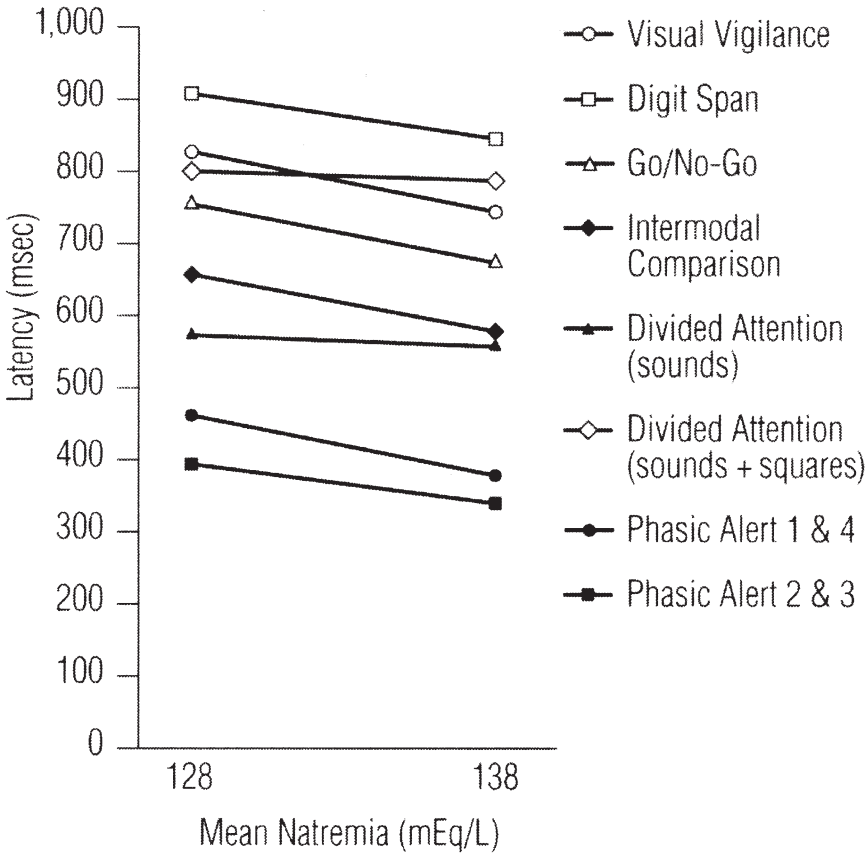

Figure 1 Evolution of median response latencies in 8 attention tests performed in 16 patients with mild chronic hyponatremia (mean serum sodium, 128 ± 3 mEq/L [1 mEq/L = 1 mmol/L]) before and after correction of the serum sodium. Median response time during hyponatremia, 672 ± 182 msec; median response time with normal serum sodium, 615 ± 184 msec; difference = 58 msec ($P < 0.001$). (Adapted from *Am J Med.*[7]).

in stable general medical condition, and all had hyponatremia due to SIADH from various causes (idiopathic in 5 patients, oat-cell carcinoma in 2 patients, carbamazepine in 2 patients, fluoxetine in 3 patients, and citalopram in 4 patients). Three sets of tests (attention, posture assessment, and gait tests) were performed when the patients were in a hyponatremic state and after they were corrected to a normal serum sodium concentration. Each patient served as his or her own control, and the serum sodium concentration was the only plausible factor that could affect the results of the study. The salient points of this recent study, i.e., attention test, evaluation of posture and gait, and falls, will be briefly discussed and are detailed elsewhere.[7]

ATTENTION TESTS

Among a battery of potential attentional tests, several very simple but well-validated tests were selected. The tasks consisted of easily distinguishable stimuli to which the patients reacted with a simple motor response.

A total of 8 different visual and auditory tests were performed using computerized attentional tasks. Patients were seated in an isolated and quiet room in front of a 14-inch computer screen at a viewing distance of 40 to 50 cm. Patients had as much training as necessary to perform the task correctly. The 4 most sensitive tests were as follows:

- The Go/No-Go test (25 trials): the patient has to react quickly and selectively to 1 class of stimuli appearing successively on the screen (e.g., squares with different textures, only 2 of which are targets)[8]
- The intermodal comparison test (20 trials): the patient must press a key as soon as there is a match between a pitch (high or low) and the direction of the arrow (up or down) appearing on the screen[9]
- The phasic alert test (20 trials not preceded by an acoustic warning, series 1 and 4): the patient must react quickly to the appearance of a cross on the screen (without benefit of a warning beep)[9,10]
- The phasic alert test (20 trials preceded by an acoustic warning, series 2 and 3): the patient must press a key as soon as a cross appears on the screen (the appearance of the cross is preceded by a beep)[9,10]

These 4 most sensitive tests take about 10 to 15 minutes to complete, whereas all 8 tests require about 75 minutes.[7] For each test, reaction times and error numbers were recorded during hyponatremia and after a normal serum sodium level had been achieved for ≥3 days. The mean response time and the sum of errors of all the tests were taken together as an indicator of the general attentional performance of the group. All the tests tended to greater latencies during hyponatremic