Clinical Presentation of Hypernatremia in Elderly Patients: A Case Control Study

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OBJECTIVES: To assess early clinical signs and their prognostic value in elderly patients with hypernatremia.

DESIGN: Prospective, case control study of 150 patients with hypernatremia matched to 300 controls.

SETTING: Multicenter study including seven short- and long-term geriatric care facilities.

MEASUREMENTS: Clinical assessment of hydration status at bedside, such as abnormal skin turgor or dry oral mucosa. Secondary outcome measures: 30-day mortality rate and clinical indicators (assessed at the peak of natremia) associated with mortality.

RESULTS: Patients and controls were comparable in terms of drugs and underlying diseases, except for history of dementia, which was more frequent in patients than in controls. Patients were significantly more likely than controls to have low blood pressure, tachycardia, dry oral mucosa, abnormal skin turgor, and recent change of consciousness. Only three clinical findings were found in at least 60% of patients with hypernatremia: orthostatic blood pressure and abnormal subclavicular and forearm skin turgor. The latter two signs were significantly more frequent in patients with hypernatremia. Four other signs (tachycardia, abnormal subclavicular skin turgor, dry oral mucosa, and recent change of consciousness) had a specificity of greater than 79%. Using logistic regression, four signs were significantly and independently associated with hypernatremia: abnormal subclavicular and thigh skin turgor, dry oral mucosa, and recent change of consciousness. The mortality rate was 41.5% and was significantly higher in patients with hypernatremia. The status of consciousness when hypernatremia was diagnosed was the single prognostic indicator associated with mortality (odds ratio = 2.3, 95% confidence interval = 1.01–5.2).

CONCLUSION: Most of the classical signs of dehydration are irregularly present in patients with hypernatremia. Caregivers should carefully screen any variations in consciousness, because they may reveal severe hypernatremia.

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Key words: elderly; hypernatremia; mortality

Hypernatremia is a common biological disorder that particularly occurs in frail elderly patients. Hypernatremia is primarily dehydration that results from insufficient water intake but that certain physiological conditions may enhance.[1,2] Of these, thirst impairment, a change associated with aging, has been well documented.[3,4] Thirst may be absent in two-thirds of elderly patients with hypernatremia. Moreover, thirst is difficult to assess in cognitively impaired elderly patients.[3] In one study,[5] patient thirst was even independent of the severity of dehydration, and in another, hypodipsia was observed in patients with a previous history of stroke, even in the presence of hyperosmolality.[4]

The groups at high risk of hypernatremia are very elderly disabled people with altered cognitive function such as dementia.[6–9] In institutions, women aged 85 and older with more than four chronic medical conditions taking more than four medications per day and with severe mobility impairment (confined to bed) should be considered high-risk patients.[6]

In these elderly patients, mortality from hypernatremia ranges from 42% to 60%.[7,10,11] This mortality rate may be worse because of delays in diagnosis or inappropriate treatment.[1,10]

Because of poor prognosis and because hypernatremia is directly correlated to access to water (rather than sudden loss of water), many authors consider this condition to be an indicator of quality of care in geriatric units.[11,12] When hypernatremia occurs during hospitalization, it can be considered to be a failure in primary prevention.[11,13]

Because of the high frequency and mortality of hypernatremia in older people, the disease should be diagnosed quickly to provide early well-adapted treatment. Unfortunately, the clinical description and presentation of hyper-

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natremia in older people is still lacking and has been shown to be unique.[1,5,14,15]

The aim of this prospective study was to assess the sensitivity and specificity of the main clinical characteristics of elderly people with hypernatremia. The relationship between these clinical signs and mortality from hypernatremia was also investigated.

METHODS

Study Design

From July 2003 to September 2004, 150 inpatients aged 65 and older with hypernatremia (serum sodium concentration >150 mmol/L) were identified. The study was conducted in seven geriatric departments, including long-term (579 beds) and short-term (109 beds) care facilities.

The physicians in charge of patients requested blood tests based on their own usual clinical examination without any specific routine procedure. In each center, one of the investigators screened the results of all electrolyte blood samples three times a week to detect patients with hypernatremia as defined in this study.

The Ethics Committee for Biomedical Research of the University of Rouen approved the study.

Patients

All patients with hypernatremia identified during the study period underwent a second blood test to confirm hypernatremia within 4 hours after the first abnormal laboratory result receipt. The attending physician also performed a standardized questionnaire and a specific clinical examination when hypernatremia was confirmed within 4 hours.

The following data were collected for each patient: age, sex, body temperature, medical history, functional ability (assessed using the Barthel Index), and daily intake of drugs prescribed for at least 1 month.

Specific data related to hydration status were obtained when hypernatremia had been confirmed: heart rate (at rest), body weight, blood pressure (BP), orthostatic BP (systolic BP decline of $\geq$20 mmHg or diastolic BP decline of $\geq$10 mmHg at 1 minute or 3 minutes from supine to sitting position).

Patient consciousness status was assessed when hypernatremia was confirmed according to laboratory tests. Patients were classified into three categories (normal, mildly impaired, coma). This status was compared with baseline status (on the previous day) found in nurses' charts to determine any change in consciousness that may have occurred. Two groups were defined: patients with acquired consciousness impairment (worse than their usual status) and patients with no change in their consciousness status. Symptoms such as difficulty focusing attention or lack of attention or who were hypoalert or had reduced sensitivity to environmental stimuli characterized change of consciousness.

Dry oral mucosa was assessed by placing the finger inside the cheek and feeling whether it was wet or dry; abnormal skin turgor was positive when it lasted at least 3 seconds after 3 seconds of skin pinching. Abnormal skin turgor was simultaneously assessed at four sites: subclavicular, anterior forearm, anterior thigh, and sternum.

Blood urea nitrogen (BUN)/creatinine ratios were calculated and considered to be a significant marker of dehydration when values were 25 or greater.[5]

The mean duration of hypernatremia was calculated, and mortality rate was defined as the percentage of patients who died within 30 days after diagnosis. There was no available information about water intake before hypernatremia, because this information is not routinely investigated in selected units, particularly for nondisabled residents who are expected to manage their beverage intake alone. Details on the conditions associated with hypernatremia were collected when it was possible, especially in patients admitted to acute geriatric units.

In this noninterventional study, the patient's primary service unit determined the treatment of patients with hypernatremia without intervention from the investigative group.

For each case, two control subjects without hypernatremia (blood tests were selected from routine laboratory examinations performed on residents living in institutions participating in the study) or significantly elevated BUN/creatinine ratio were selected. Controls were matched as closely as possible to cases for age, sex, type of facility, and level of dependency (assessed using the Barthel Index). The main aim was to assess the clinical symptoms of hypernatremia at the onset of the disease and not to investigate risk factors of hypernatremia, such as severely impaired mobility, which are well known. Therefore, it was decided to perform a cross-match study between patients and controls based on their age, sex, and level of dependency. The same physician who had examined the patient collected information from controls. Controls were compared with cases in a "one case-versus-two controls" analysis.

Statistical Analysis

Comparisons for significant differences between patients and controls were performed using the chi-square test (or Yates) for qualitative variables and Fisher test or Student *t* test for quantitative data, as appropriate. For all statistical tests, two-sided *P*-values $<.05$ were considered to be significant.

To calculate the sensitivity and the specificity of signs, a sign was considered to be a true positive when it was present in a hypernatremic patient and a false positive when a control had one of the signs.

Sensitivity was determined as the ratio of true positives to all patients with hypernatremia and specificity as the ratio of true negatives to all controls. Analysis (sensitivity or specificity calculations) was not performed according to individual value of hypernatremia.

Multivariate analysis was performed on the parameters that were significant after univariate analysis to determine which signs were significantly and independently associated with hypernatremia. Multivariate analysis was repeated to investigate which signs were significantly associated with mortality considering only patients with hypernatremia with a normal BUN/creatinine ratio.

BMDP (Release 7, BMDP Statistical Software Inc., Los Angeles, CA) and StatXact-3 (version 3.01, Cytel Corporation, Cambridge, MA) software were used.

RESULTS

Two hundred ninety-three (65.1%) of the 450 included subjects were selected from short-term medical units and 157 (34.9%) from long-term care facilities. For patients from acute geriatrics units, hypernatremia was associated with infectious process (mainly pulmonary infections) in 56% of cases (mainly pulmonary and urinary tract infections), with delirium in 13% of cases, with stroke in 7% of cases, and with miscellaneous causes (e.g., falls and arrhythmia) in 25% of cases.

The control group was comparable (Table 1) in terms of drug intake (especially antihypertensive agents, diuretics, and psychotropic agents) and for underlying diseases except dementia. Dementia was significantly ($P<.02$) more frequent in patients with hypernatremia. Fifty-six patients (from the acute geriatric wards) were hypernatremic upon hospital admission.

A significant increase in creatinine level or a decline of more than 25% in creatinine clearance from baseline was significantly associated with hypernatremia independent of any previous medical history of chronic renal insufficiency (Table 1). A significant increase in BUN/creatinine ratio was observed in 12% of patients. Patients with hypernatremia had significantly lower systolic BP and body weight (Table 2). They were also significantly more likely to have tachycardia. Consciousness status associated with hypernatremia was different from that in controls: 69 patients had mildly impaired consciousness, and 40 had more-severe impairment close to coma. Dry oral mucosa and abnormal skin turgor (whatever the location) were found more often in patients with hypernatremia.

In patients with hypernatremia (Table 3), three signs had a sensitivity above 0.60 (more than 60% of the patients with hypernatremia had the sign): orthostatic BP and abnormal subclavicular and forearm skin turgor. The latter two signs were significantly more frequent in the group with hypernatremia. Tachycardia, abnormal skin turgor (measured at the subclavicular level, the sternum, or the thigh), dry oral mucosa, and a significant change in consciousness were specific for hypernatremic dehydration. When signs related to hypernatremia (associated with extracellular dehydration, which is defined as a significant increase in BUN/creatinine ratio) were combined by computing the odds ratio (OR), four signs (abnormal subclavicular skin turgor (OR = 5.22, 95% confidence interval (CI) = 3.04–8.96), abnormal thigh skin turgor (OR = 4.48, 95% CI = 2.45–8.19), dry oral mucosa (OR = 6.84, 95% CI = 3.59–13.03), and a change in consciousness (OR = 2.28, 95% CI = 1.33–3.91)) were significantly and independently associated with hypernatremia.

When multivariate analysis was repeated in patients with isolated hypernatremia (excluding patients with extracellular dehydration), dry oral mucosa (OR = 10.46, 95% CI = 6.04–18.09) and change in consciousness (OR = 2.55, 95% CI = 1.59–4.12) were significantly associated with the disease.

Table 1. Characteristics and Underlying Diseases in the Studied Groups

Characteristic	Patients (n = 150)	Controls (n = 300)	*P*-value
Demography			
Age, mean ± SD (range)	87.1 ± 6.94 (70–107)	86.4 ± 6.8 (70–106)	
Female, %	57.1	57	
Barthel Index (/100), mean ± SD	20.8 ± 26.9	23.2 ± 27.7	
Underlying diseases, n (%)			
Dementia	88 (56.4)	136 (44.1)	.02
Hypertension	69 (44.2)	144 (46.6)	.59
Stroke	40 (28.1)	90 (29.1)	.87
Cardiac failure	37 (23.7)	90 (29.1)	.21
Chronic renal failure	7 (4.5)	19 (6.1)	.35
Cancer	7 (4.5)	16 (5.2)	.65
Depression	25/16	65/21	.15
Diabetes mellitus	13/17	20/13	.36
Number of drugs			
Mean ± SD (/day)	4.4 ± 2.3	4.6 ± 2.7	.40
Antihypertensive agents, n (%)*	80 (53.3)	172 (57.3)	.62
Diuretics, n (%)	52 (33.3)	105 (34.1)	.87
Psychotropic agents, n (%)†	54 (34.6)	123 (39.9)	.26
Natremia, mmol/L, mean ± SD (range)	155.1 ± 5.81 (150–181)	138.4 ± 4.1 (135–145)	
Creatinine, μmol/L, mean ± SD (range)	144 ± 79.5 (44–457)	96.3 ± 48.1 (43–370)	<.001
Creatinine clearance, mL/min, mean ± SD‡	27.62 ± 13.27	44.89 ± 34.82	.001
Blood urea nitrogen/creatinine, mean ± SD	17.95 ± 6.97	12.93 ± 9.50	<.001
Osmolality, mmol/L, mean ± SD	347.1 ± 19.3	301.4 ± 11	

* Diuretics, beta-blockers, calcium channel blockers, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, direct-acting vasodilators, centrally acting agents.
† Antipsychotic agents, sedative/hypnotic agents, benzodiazepines, antidepressants.
‡ According to Cockcroft-Gault formula.
SD = standard deviation.

Table 2. Baseline Hydration Clinical Status

Characteristic	Patients (n = 150)	Controls (n = 300)	*P*-value
Systolic BP, mmHg, mean ± SD	126.8 ± 25.5	133.1 ± 20.9	.005
Diastolic BP, mmHg, mean ± SD	72.3 ± 14.4	73.3 ± 12.8	.43
Body weight, kg, mean ± SD	52.8 ± 10.6	58.9 ± 13.6	<.001
Pulse, bpm, mean ± SD	83.4 ± 17.5	77.3 ± 13.1	.001
Tachycardia (>100 bpm), n (%)	27 (17.9)	18 (6)	<.001
Body temperature, °C, mean ± SD	37.3 ± 0.8	37.1 ± 0.5	<.001
Consciousness status, n (%)*			
Normal	41 (27.3)	178 (59.3)	<.001
Mild impaired	69 (46.0)	104 (34.7)	
Coma	40 (26.7)	18 (6.0)	
Change in consciousness, n (%)†			
Yes	76 (49)	3 (1)	<.001
No	74 (51)	297 (99)	
Orthostatic blood pressure, n (%)‡	32 (61.5)	82 (49.3)	.12
Oral mucosa dry, n (%)	70 (49)	23 (7.8)	.001
Abnormal skin turgor, n (%)			
Subclavicular	110 (73.3)	63 (20.7)	.001
Sternum	74 (50.3)	60 (19.7)	.001
Forearm	99 (68.3)	98 (32.2)	.001
Thigh	76 (51.7)	36 (11.8)	.001

* Clinical assessment of consciousness associated with hypernatremia disclosure.
† Change in consciousness compared with baseline status.
‡ Systolic blood pressure (BP) decline of ≥20 mmHg or a diastolic BP decline of ≥10 mmHg at 1 minute or 3 minutes from supine to sitting.
SD = standard deviation; bpm = beats per minute.

The mortality rate within 30 days after a diagnosis of hypernatremia was 41.5%, versus 12.9% in the control group ($P<.001$). Logistic regression analysis showed that initial consciousness status (OR = 2.3, 95% CI = 1.005–5.2; $P<.02$) was the only indicator of mortality that remained significant even when a history of dementia was included in the model.

DISCUSSION

In older people, hypernatremia is a common and severe metabolic condition. Its prevalence in a cohort of 15,187 hospitalized patients aged 65 and older has been calculated as approximately 1.1%.[7]

This study found that in dehydrated patients with hypernatremia, four signs were significantly and independently associated with hypernatremia: abnormal subclavicular or thigh skin turgor, dry oral mucosa, and a recent change of consciousness (compared with mental status before hypernatremia). The sensitivity of the studied signs of hypernatremia remains poor. Only three signs (orthostatic BP and abnormal subclavicular and forearm skin turgor) were present in more than 60% of patients. The clinical interpretation of a basic sign such as abnormal skin turgor, mucosal dryness, or recent change in consciousness is much more difficult in older people. For example, although poor abnormal skin turgor may reflect interstitial space dehydration, it is also directly correlated with skin protein elastin levels, which decrease significantly with aging.[15] Assessment of abnormal skin turgor may also be unreliable between clinicians.[16] The findings of the current study suggest that abnormal skin turgor should be evaluated in the

Table 3. Sensitivity and Specificity of Signs in Subjects with Hypernatremia

Characteristic	Sensitivity %	Specificity %	Odds Ratio	95% Confidence Interval
Tachycardia (heart rate >100 beats per minute)	17.8	94.0	3.45	(1.83–6.49)
Orthostatic blood pressure	61.5	50.6	1.64	(0.87–3.10)
Abnormal skin turgor				
Subclavicular	73.3	79.0	10.52	(6.67–16.6)
Sternum	50.3	19.0	3.93	(2.56–6.01)
Forearm	68.3	67.8	4.52	(2.96–6.92)
Thigh	51.7	88.2	7.97	(4.96–12.81)
Change in consciousness	49.0	99.0	98.13	(30.15–319.32)
Oral mucosa dry	49.0	87.8	6.07	(3.76–9.82)

same location, especially at the subclavicular site, which is the most sensitive and specific area. Mucosal dryness seems to be even more complicated than skin turgor assessment. In one study,[17] axillary sweating in elderly dehydrated patients was measured using standardized preweighted tissue paper. This method had poor sensitivity (0.50) but good specificity (0.82) and was associated with a negative predictive value of approximately 0.84 to detect dehydration. In the current study, performed in seven centers, only oral mucosa (wet or dry) were investigated, because the investigators decided that this location for mucosal dryness would be more reliable than others. As found in other studies,[5] it was confirmed that sudden change in consciousness was strongly associated with hypernatremia. This association should be analyzed with caution in relation to baseline cognitive status or intake of sedative drugs. Although consumption of psychotropic agents was comparable in the two groups, significantly more patients than controls had dementia. In practice and particularly in institutions, daily mental status or cognitive assessment by caregivers is crucial to detect any new medical illnesses, including metabolic disorders such as dehydration.

In the logistic model, only recent change in consciousness was significantly and independently associated with the disease. These results confirm data reported previously,[7] which suggested that dementia represents a major risk factor for hypernatremia in older people but may also prevent early detection of hypernatremia, because subtle variations of consciousness associated with severe dehydration cannot be detected in these patients.[18,19]

Because the description of subjective signs such as abnormal skin turgor or variations in consciousness may be difficult to assess in frail elderly people, reliable and standardized clinical parameters must be found. Unfortunately, most of these objective and reliable signs (such as tachycardia or orthostatic BP) suggest volume depletion rather than intracellular dehydration.

In patients with both hydration conditions (hypernatremia and volume depletion), the sensitivity of orthostatic BP was 0.61 (OR = 1.64). Tachycardia was less frequent (sensitivity = 0.17) but much more specific (specificity = 0.94). These results appear to be independent of the clinical characteristics of studied patients whose histories of hypertension, cardiac failure, and diuretic drug intake were comparable between patients and controls.

In the literature, the mortality rate of hypernatremia ranges from approximately 46% to 70%[11] and may be seven times greater than in age-matched inpatients without hypernatremia.[7] In the current study, mortality rate within 30 days was 41.5%, similar to other published data.[10] Of all the studied signs, the only indicator of a poor prognosis upon diagnosis of hypernatremia was the status of consciousness (OR = 2.3).

In this study, as previously described,[7,10] the severity of hypernatremia or osmolality was independent of mortality.

Caregivers should be particularly careful to note the onset of any changes in consciousness, as suggested in a study on predictive models to identify confusion in high-risk patient groups, including those with dementia.[20] The nonspecific sign may be associated with hypernatremia and is associated with a poor prognosis.

This study has several limitations. First, all the signs of dehydration described in medical textbooks were listed, even if some of them, such as abnormal skin turgor, are only associated with extracellular dehydration. The aim was to consider the basic clinical indicators of dehydration that clinicians use when hypernatremia is diagnosed. It was attempted to identify the parameters that were most suggestive of severe dehydration—defined by hypernatremia—in frail elderly subjects. It was decided to focus on patients with hypernatremia rather than dehydrated patients. This choice was based on epidemiological data that have demonstrated the severity of the former and its high frequency in old patients, such as those living in institutions.

Second, it was demonstrated that changes in consciousness were probably the best indicators of dehydration and that these signs should prompt clinicians to perform electrolyte measurements quickly. Assessment of consciousness remains difficult in elderly residents, who had dementia in 50% of the cases of the cohort. Daily comparison of cognitive function with prior status is a daily practice in geriatric units, and these reports are of great interest for identifying the development of acute medical conditions such as dehydration.

Third, the main clinical signs of dehydration, such as dry oral mucosa and abnormal skin turgor, remain highly subjective and are based more on individual experience than on precise guidelines. Although it was attempted to apply precise criteria to define studied signs, the clinical unblinded assessments (which could be particularly important in control subjects) from the investigators could be unreliable. Interobserver reliability was not calculated between investigators.

Fourth, information about medical conditions associated with hypernatremia for patients living in institutions (which could partly modified interpretations of signs) were not systematically checked, nor were clinical signs reassessed after the rehydration procedure. For instance, when dry oral mucosa was noticed in a patient hospitalized for pneumonia, the sign may have been incorrectly attributed to hypernatremia rather than to the infection.

In conclusion, in elderly patients with hypernatremia, the most common signs or symptoms are irregular and do not appear to be pathognomonic, considering their specificity. Nevertheless, particular attention should be given to the detection of any new variations in the status of consciousness in these patients.

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REFERENCES

1. Adrogue HJ, Madias NE. Hypernatremia. N Engl J Med 2000;342:1493–1499.

2. Silver AJ. Aging and risks for dehydration. Cleve Clin J Med 1990;57: 341–344.
3. Fitsimmons JT. The physiological basis of thirst. Kidney Int 1976;10:3–11.
4. Miller PD, Krebs RA, Neal BJ et al. Hypodipsia in geriatric patients. Am J Med 1982;73:354–356.
5. Gross CR, Lindquist RD, Wooley AC et al. Clinical indicators of dehydration severity in elderly patients. J Emerg Med 1992;10:267–274.
6. Lavizzo-Mourey R, Johnson J, Stolley P. Risk factors for dehydration among elderly nursing home residents. J Am Geriatr Soc 1988;36:213–218.
7. Snyder NA, Feigal DW, Arieff AI. Hypernatremia in elderly patients. Ann Intern Med 1987;107:309–318.
8. Solomon LR, Lye M. Hypernatraemia in the elderly patient. Gerontology 1990;36:171–179.
9. McDonald NJ, McConell KN, Stephen MR et al. Hypernatraemic dehydration in patients in a large hospital for the mentally handicapped. BMJ 1989;299: 1426–1429.
10. Mandal AK, Saklayen MG, Hillman NM et al. Predictive factors for high mortality in hypernatremic patients. Am J Emerg Med 1997;15:130–132.
11. Himmelstein DU, Jones AA, Woolhandler S. Hypernatremic dehydration in nursing home patients. An indicator of neglect. J Am Geriatr Soc 1983;31: 466–471.
12. Simmons SF, Alessi C, Schnelle JF. An intervention to increase fluid intake in nursing home residents: Prompting and preference compliance. J Am Geriatr Soc 2001;49:926–933.
13. Palevsky PM, Bhagrath R, Greenberg A. Hypernatremia in hospitalized patients. Ann Intern Med 1996;124:197–203.
14. Kahn T. Hypernatremia with edema. Arch Intern Med 1999;159:93–98.
15. McGee S, Abernathy WB III, Simel DL. Is this patient hypovolemic? JAMA 1999;281:1022–1029.
16. Pals JK, Weinberg AD, Beaf LF et al. Clinical triggers for detection of fever and dehydration: Implications for long-term care nursing. J Gerontol Nurs 1995; 21:13–19.
17. Eaton D, Bannister P, Mulley GP et al. Axillary sweating in clinical assessment of dehydration in ill elderly patients. BMJ 1994;308:1271.
18. Weinberg AD, Minaker KL. Dehydration: Evaluation and management in older adults. JAMA 1995;274:1552–1556.
19. Weinberg AD, Pals JK, McGlinchey-Berroth R et al. Indices of dehydration among frail nursing home patients: Highly variable but stable over time. J Am Geriatr Soc 1994;42:1070–1073.
20. Inouye SK, Bogardus ST, Charpentier PA. A multicomponent intervention to prevent delirium in hospitalized older patients. N Engl J Med 1999;340: 669–676.