

## Detecting and Preventing Dehydration in Alzheimer's Patients: Multidisciplinary Approaches to Dementia Care

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### Abstract

Abnormalities of water homeostasis can be early expressions of neuronal dysfunction, brain atrophy, chronic cerebrovasculopathy and neurodegenerative disease. The aim of this study was to analyze the serum osmolality of subjects with cognitive impairment. The hydromolecular hypothesis intends to explain the relationship between dehydration and cognitive impairment in older patients as the result of protein misfolding and aggregation, in the presence of a low interstitial fluid volume, which is a defect of the microcirculation. Defective proteins were shown to impair the amount of information in brain biomolecular mechanisms, with consequent neuronal and synaptic damage.

**Keywords** hydromolecular hypothesis; dehydration; dementia

### Introduction

The regulation of water balance is governed by a feedback mechanism involving the function and interaction of different regions of the central nervous system and the kidneys. Plasma osmolality indicates the level of body hydration and hypothalamus osmoreceptors detect and are sensitive to its variations. High plasma osmolality, increased to levels above a physiologic threshold (290 to 295 mOsm per kilogram of water), leads to secretion of the peptide hormone, vasopressin, from the vasopressinergic nerve endings in the neurohypophysis. Vasopressin binds receptors in the kidney that decrease the excretion of water, and subsequently, a greater fraction of filtered water is returned to the blood. This process lowers the plasma osmolality, reduces the stimulus for vasopressin secretion and thirst and completes the feedback loop. Failure of this mechanism, which is commonly observed in hospitalized patients, results in a variety of water balance disorders. More recent evidence has clarified that the aging process is commonly related to multiple abnormalities in water homeostasis, highlighting its effects on morbidity, cognition, osteoporosis, fractures, gait instability, and mortality. In older patients, water homeostasis regulation can be altered because of multifactorial mechanisms, such as renal function alterations, body composition and hypothalamic-pituitary regulation of thirst and vasopressin secretion changes.

### Materials and Methods

The present study was conducted according to the Declaration of Helsinki, the Guidelines for Good Clinical Practice and the Guidelines for Strengthening the Reporting of Observational Studies in Epidemiology, and it was approved by the local ethics committee for human experimentation (Prot. No. 3877/DS). The study was an observational study, in which the assignment of an intervention to the participants, its effect assessment and health-related biomedical or behavioural outcomes are not considered. In the present study, healthy participants were recruited as control subjects.

### Study Sample

Inclusion criteria were as follows: (1) age  $\geq 65$  years; (2) diagnosis of a subjective cognitive impairment (SCI) according to the Subjective Cognitive Decline Initiative (SCD-I) Working Group ; (3) diagnosis of late-life depression (LLD) according to the (Diagnostic and Statistical Manual of Mental Disorders Fifth Edition) DSM 5 criteria; (4) diagnosis of mild cognitive impairment (MCI) according to the National Institute on Aging—Alzheimer's Association (NIAAA) criteria; (5) diagnosis of Alzheimer's disease (AD) according to the NIAAA criteria; (6) diagnosis of Lewy body disease (LBD) according to the (Dementia with Lewy bodies) DLB consortium criteria; (7) diagnosis of vascular dementia (VaD) according to the criteria of the National Institute of Neurological Disorders and Stroke—Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN) [work group; (8) the ability to provide informed consent or the availability of a relative or legal guardian in the case of severe demented patients. The exclusion criteria were as follows: (1) diagnosis of mixed dementia (MxD); (2) presence of a serious comorbidity, tumors, other diseases or physiological status (ascertained blood infections, vitamin B12 deficiency, anemia, disorders of the thyroid, kidneys, or liver), that could be causally related to cognitive impairment; (3) history of alcohol or drug abuse, head trauma, and other causes that could cause memory impairment.

### Statistical Analyses

For dichotomous variables, hypotheses regarding differences between groups were tested using the Fisher's exact test. This analysis was made using the 2-Way Contingency Table Analysis.

### Results

During the enrolment period, 1135 older patients were screened for inclusion in the study. Of these, nine patients were excluded because they were younger than 65 years, 12 patients had an incomplete examination and 23 patients had MxD. Thus, the final population included 1091 patients, 542 men (49.70%) and 549 women (50.3%), with a mean age of  $78.80 \pm 6.72$  years and an age range from 65 to 97 years.



Therefore, 520 patients (Male: 326, Female: 194; mean age of  $77.64 \pm 6.60$  years, range 65–95 years) were included in the control group, and 571 patients (Male: 216, Female: 355; mean age of  $79.94 \pm 6.67$  years, range 65–97 years) had cognitive decline and/or depression mood (CD-DM). The demographic and clinical characteristics of the control group and patients with CD-DM are summarized in Table 1.

**Table 1**

Demographic and clinical characteristics of control group and patients with cognitive decline and/or depression mood (CD-DM).

	Control Group <i>n</i> = 520	CD-DM <i>n</i> = 571	<i>p</i> Value	Whole Population <i>n</i> = 1091
Male sex *	326 (62.7%)	216 (37.8%)	<0.001	542 (49.7%)
Age (years) **	77.64 ± 6.60 (65–95)	79.94 ± 6.67 (65–97)	<0.001	78.80 ± 6.72 (65–97)
MMSE **	29.00 ± 0.61 (29–30)	18.00 ± 6.72 (0–30)	<0.001	23.28 ± 7.32 (0–30)
HRS-D-21 **	2.48 ± 1.61 (1–6)	10.96 ± 6.93 (0–31)	<0.001	6.57 ± 6.66 (0–31)
ADL **	6.00 ± 0.00 (6–6)	4.14 ± 1.88 (0–6)	<0.001	4.98 ± 1.65 (0–6)
IADL **	8.00 ± 0.00 (8–8)	3.31 ± 3.18 (0–8)	<0.001	5.39 ± 3.38 (0–8)
MNA **	24.26 ± 3.42 (9–29)	23.02 ± 4.45 (0–29)	<0.001	23.61 ± 4.00 (0–29)
ESS **	19.32 ± 0.78 (18–20)	17.32 ± 2.35 (9–20)	<0.001	18.27 ± 2.05 (9–20)
CIRS **	2.23 ± 1.39 (0–7)	2.33 ± 1.50 (0–9)	0.241	2.28 ± 1.45 (0–9)
Glucose (mmol/L) **	5.53 ± 1.96 (2.24–17.22)	5.54 ± 1.51 (3.64–14.42)	0.903	5.54 ± 1.76 (2.23–17.22)
Urea (mmol/L) **	7.44 ± 2.61 (2.34–19.00)	7.55 ± 3.12 (2.82–34.53)	0.571	7.43 ± 2.82 (2.31–34.53)
Scr (μmol/L) **	83.82 ± 27.95 (35.42–221)	81 ± 27.22 (36.21–212.20)	0.107	82.40 ± 27.63 (35.42–221)

## Discussion

Dehydration has been reported to be the most common fluid and electrolyte imbalance in older adults [1]. Recent clinical studies have shown that the hydration state affects cognitive performance, particularly visual attention and mood. The changes in extracellular osmolality inevitably affect the intracellular environment determining important alterations in the volume and function of cellular mechanisms causing irreversible morphological and functional damage. Thus, these changes could be major contributing factors to age-related neurovascular vulnerabilities and are currently under intense investigation as potential therapeutic targets. It has been hypothesized that chronic hypovolemia, due to hypohydration, is perhaps one of the principal mechanisms behind the development of obesity, diabetes, hypertension, and even Alzheimer's disease. Hospitalized older adults suffering from dehydration have been reported to have mortality rates as high as 45–46%, but only a few studies exist regarding water intake and excretion in older patients.

## Conclusion

Thus, dehydration among patients with Alzheimer's disease is an issue that nursing staff must recognize. Nursing staff should receive the appropriate education in order to address the issue of dehydration with this population. Having a plan of care for hydration for each patient may identify the barriers of hydration and lead to interventions that are needed to decrease the risk of dehydration. Interventions to overcome these hydration barriers must be developed, implemented, and evaluated not only by the nursing staff but by the family members. This collaborative effort may decrease the chances of a patient from becoming dehydrated and having to be treated for dehydration.

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