MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2016; 22: 4978-4985
DOI: 10.12659/MSM.898538

Received: 2016.03.16
Accepted: 2016.05.11
Published: 2016.12.18

Hyponatremia, Cognitive Function, and Mobility in an Outpatient Heart Failure Population

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1 Monirah Albabtain
BCDEF 2 Michael J. Brenner
ABDEF 3 John M. Nicklas
BDEF 3 Scott L. Hummel
BCDEF 4 Michael P. McCormick
BCDEF 4 Jeffrey L. Pawlowski
ABCDEF 5 Tami L. Remington
ADEF 6 Tanya R. Gure
ACDEF 5 Michael P. Dorsch
ABCDEF 7 Barry E. Bleske

1 Department of Pharmacy, Prince Sultan Military Medical City, Riyadh, Saudi Arabia
2 VA Ann Arbor Healthcare System, Ann Arbor, MI, U.S.A.
3 Division of Cardiology, University of Michigan Health Systems, Ann Arbor, MI, U.S.A.
4 College of Pharmacy, University of Michigan, Ann Arbor, MI, U.S.A.
5 College of Pharmacy and Health System, University of Michigan, Ann Arbor, MI, U.S.A.
6 Division of General Internal Medicine & Geriatrics, College of Medicine, The Ohio State University, Columbus, OH, U.S.A.
7 College of Pharmacy, University of New Mexico, Albuquerque, NM, U.S.A.

Corresponding Author: Barry E. Bleske, e-mail: bbleske@salud.unm.edu
Source of support: Departmental sources

Background: The association of hyponatremia with cognitive impairment and mobility in heart failure (HF) patients is unknown. The purpose of this study was to determine if hyponatremia is associated with cognitive and mobility impairment as measured by simple, validated, and time-sensitive tests.

Material/Methods: This was a prospective study in patients with reduced and preserved ejection fraction (HFrEF, HFpEF) seen in outpatient HF clinics. Hyponatremia was defined as sodium level ≤136 mEq/L. Cognitive function was measured using the Montreal Cognitive Assessment (MoCA) tool, and mobility was measured with the Timed Up and Go test (TUG-t).

Results: A total of 121 patients were evaluated; 30% were hyponatremic (134±1.9 mEq/l, range 128–136 mEq/l). Overall, 92% of hyponatremic patients had cognitive impairment (MoCA <26) compared to 76% of the non-hyponatremic patients [relative risk 1.2 (confidence interval: 1.02–1.4, p=0.02)]. In regard to mobility, 72% of hyponatremic patients and 62% of non-hyponatremic patients (p=0.4) had TUG-t times that were considered to be worse than average. A total of 84% (N=76) of HFrEF and 71% (N=22) of HFpEF patients had cognitive impairment (p=0.86). HFrEF patients had significantly lower overall MoCA scores (21.2±3.7 *vs.* 23.3±3.6, p=0.006) and similar TUG-t times compared to HFpEF patients.

Conclusions: Most heart failure patients (HFrEF and HFpEF) seen in an ambulatory setting had impairment of cognitive function and mobility, with a higher prevalence among those with hyponatremia. Screening can be done using tests that can be administered in a clinical setting.

MeSH Keywords: Heart Failure • Hyponatremia • Mild Cognitive Impairment

Full-text PDF: http://www.medscimonit.com/abstract/index/idArt/898538

3245 3 — 40

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Background

Heart failure (HF) is a major health problem that affects over 5 million Americans. HF is also associated with significant mortality, which can range from 5% to 50% on an annual basis. However, patient-centered goals such as quality of life, as well as ability to live and function independently, are of equal importance to patients, caregivers, and health care providers [1].

Cognitive impairment is considered to be common and directly related to poor outcomes in HF patients. Cognitive impairment affects 25–85% of patients with HF and develops earlier in these patients with HF as opposed to people without HF at a similar age [1–4]. Patients with HF have up to a 2-fold increased risk of impaired cognitive function compared with age-matched controls in the domains of memory, psychomotor speed, attention, and executive function [4–6].

Hyponatremia is also a frequent finding in patients with HF, with prevalence rates ranging from 8% to 28%, depending on HF severity, and is a marker for poor outcomes [7–10]. Most commonly, hyponatremia observed in HF patients is chronic in nature and mild-to-moderate in severity. Often, hyponatremia is considered by the clinician to be associated with minimal or no symptoms. However, limited data suggest that hyponatremia, due to any cause, may be associated with cognitive impairment and gait abnormalities [11]. The specific role of hyponatremia in cognitive and functional outcomes in HF patients is largely unknown. The purpose of this study was to determine the association of hyponatremia with cognitive function and mobility in HF patients. We used standard cognitive and mobility tests that are relatively time sensitive and can be administered in a clinical setting by any trained personnel, including students and medical assistants. The findings from this investigation may help to determine when a HF patient is manifesting symptoms of hyponatremia that may be amenable to intervention.

Material and Methods

A prospective study was conducted in HF clinics based at 2 medical centers (a university academic center and a Veterans Affairs medical center) over an approximate 9-month time period (October 2013 to June 2014). Patients were recruited at the time of their clinic visit on a consecutive basis. The study protocol was approved by each center's Institutional Review Board and all participants provided written informed consent.

Patients

Patients >18 years of age with a documented diagnosis of either HFrEF (heart failure with reduced ejection fraction) or HFpEF (heart failure with preserved ejection fraction) receiving beta blocker and loop diuretic therapy were eligible for the study. Patients with HFrEF and HFpEF were identified through physician diagnosis by heart failure specialists (chart review) and confirmed by ejection fraction (HFrEF ≤40%, HFpEF >40%). Patients were excluded if they had documented conditions known to cause cognitive impairment: stroke, dementia, Alzheimer disease, or any other neurological disorder. Patients with a history of significant psychological problems or with long-term use of narcotics, benzodiazepines, antipsychotics, or anti-depressants were also excluded from the study. Patients requiring a wheelchair or any assistance with walking were waived from testing of mobility.

Evaluation of cognitive function

Trained personnel administered the Montreal Cognitive Assessment (MoCA) version 7.1 to eligible patients (permission to use the MoCA tool for the study was obtained) [12]. The MoCA assesses short-term recall, visuospatial abilities, executive function, attention, concentration, working memory, language, and orientation [13]. One advantage of utilizing the MoCA tool is that it can be administered to patients in approximately 10 minutes, which makes the use of this tool potentially feasible in a clinical setting. MoCA scores range from 0 to 30 points, with lower scores reflecting worse cognitive function. The MoCA has been validated in non-HF patients; a score <26 suggests cognitive impairment [14–16]. We further classified our sample into 3 cognitive categories using established MoCA cut-points of severity: mild cognitive impairment (22–25 points), moderate impairment (17–21 points), and severe impairment (0–16 points) [18].

Mobility assessment

Mobility was assessed with the Timed Up and Go test (TUG-t), a simple and observed measure of gait speed that can predict fall risk in older adults. Multiple studies have confirmed the content validity, concurrent validity, and predictive validity of TUG-t [19–21]. Subjects were required to stand up from a chair on the word "Go" and walk on the floor to a line (3 meters away from the chair), turn around, and walk back to the chair and sit down. Subjects were instructed to walk at their normal pace. Timing (in seconds) started from the word "Go" until they were seated again correctly in the chair. TUG-t times were considered worse than average if they exceed 9.0 seconds for 60–69-year-olds, 10.2 seconds for 70–79-year-olds, and 12.7 seconds for individuals 80–99-year-olds [20].

Sodium levels and lab measurements

We defined hyponatremia as a serum sodium level ≤136 mEq/L [22,23]. Sodium levels were measured within 1 week of the

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

study participant's clinic visit. In addition to the sodium measurement obtained at the time of the study visit, an additional sodium value was obtained nearest to the study visit date by chart review. Investigators were blind to the serum sodium measurement at the time of recruitment. Additional lab values recorded were brain natriuretic peptide (BNP) levels, serum creatinine, blood urea nitrogen, albumin, hemoglobin, and ejection fraction (EF).

Data analysis

Statistical analysis was performed using SPSS for IBM version 21. Data are presented as mean± standard deviation (SD) with differences reported as significant if p< 0.05. Comparisons between hyponatremic patients and non-hyponatremic subjects were made using simple *t* test for continuous variables and using the chi-square or Fisher's exact tests for nominal and categorical variables, respectively. Univariate analysis was used to test the correlation between serum sodium level, MoCA, and TUG-t.

Results

A total of 121 patients were evaluated; most were males (91%) and the mean age was 66±10 years. Patient baseline characteristics are shown in Table 1. No significant differences were seen between hyponatremic and non-hyponatremic patients with respect to age, sex, education level, systolic blood pressure, ejection fraction, serum creatinine, hemoglobin, or other co-morbidities. There was no difference in the use of HF-specific medications between the 2 groups except for the greater use of aldosterone antagonists and thiazide diuretics in the hyponatremic group (Table 1).

Overall, 30% (n=36) of the patients enrolled had study-defined hyponatremia with a mean serum sodium of 134± 1.9 mEq/l (range 128–136 mEq/l). A total of 31 patients (86%) had chronic hyponatremia, suggested by 2 consecutive sodium measurements ≤136 mEq/l. Pre-study sodium levels (134.3±2.5 mEq/L) were measured at 84.5±63.6 days prior to the start of the study. HF patients with chronic hyponatremia had a mean sodium level of 133.8±2.0 mEq/L on the study day. Only 5 HF patients had hyponatremia only on the study day (mean, 135.0±0.7 mEq/l; p=0.2).

The overall MoCA score for hyponatremic and non-hyponatremic HF patients was consistent with mild cognitive impairment. The mean MoCA scores were not significantly different between the 2 groups (21.7±2.9 and 21.7±4.1, p=0.92). The prevalence of cognitive impairment was 92% among the HF hyponatremic patients and 76% among non-hyponatremic HF patient [relative risk 1.2 (confidence interval: 1.02–1.4, p=0.02)]. Among those classified as cognitively impaired, there were no differences in baseline characteristics between patients who had HF with hyponatremia and those without hyponatremia except for the use of aldosterone antagonists (67% *vs.* 39%, respectively) and thiazide diuretics (8% *vs.* 1%, respectively). In addition, there was no difference in the MoCA scores between the 2 groups when evaluating only those patients that were deemed to have cognitive impairment (21.2±2.43 *vs.* 20.1±3.1, p=0.063). There were also no differences seen in the severity of the cognitive impairment between the hyponatremic and non-hyponatremic groups (Table 2). No significant correlation was found between sodium levels and MoCA score (r2=0.0004, p=0.8).

When examining the specific cognitive domains of the MoCA, we found significantly lower scores in all domains with the exception of lower orientation scores in HF patients with cognitive impairment, irrespective of sodium level. There were no differences in the subscores between patients with hyponatremia versus patients without hyponatremia who were cognitively impaired. (Table 3)

The TUG-t times did not differ between the hyponatremic and non-hyponatremic HF patients (13.5±4.5 seconds *vs.* 12.6±4.1 seconds, p=0.3, respectively). The mean times for both groups were considered to be worse than average for most age groups. In fact, 72% of hyponatremic patients and 62% of non-hyponatremic patients (p=0.4) had TUG-t times worse than average. No significant correlation was found between sodium levels and TUG-t performance (r2=0.21, p=0.2)

In regard to overall MoCA score and age, approximately 34% of patients were <65 years of age (58±6 years). Patients ≥65 years (72±7 years) had significantly lower MoCA scores (19.8±2.9 *vs.* 21.8±2.4 p=0.0005). There were no differences in TUG-t times between the 2 groups when analyzed by age group. No baseline characteristics were significantly different between the 2 groups.

Evaluating the data according to the type of HF, there was a significant difference in overall MoCA scores (21.2±3.7 *vs.* 23.3±3.6, p=0.006) between patients with HFrEF (EF=25±8%) and HFpEF (EF=55±6%) patients. There was no significant difference in the percent of patients with cognitive impairment between the HFrEF and HFpEF groups (84.4% *vs.* 71%, p=0.086). When evaluating patients with cognitive impairment, HFrEF patients had significantly lower MoCA scores compared to HFpEF patients (20.1±3 *vs.* 21.5±2.6, p=0.036). When evaluating the individual MoCA cognitive domain scores, there were no differences between the 2 groups, and no significant difference was seen in TUG-t times between HFrEF and HFpEF patients (12.7±4 seconds *vs.* 13.3±4.8 seconds, p=0.592). Baseline variables, other than ejection fraction and diagnosis, were similar between the 2 groups.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Table 1. Baseline characteristics (mean and standard deviation).

Characteristics [mean and standard deviation or N (%)]	No hyponatremia N=85 (70%)	Hyponatremia N=36 (30%)	P
Age	66.6±11.1	65.1±7.9	0.45
Sex			0.105
Male	75 (88)	35 (97)	
Female	10 (11.8)	1 (2.8)	
Serum Sodium (mEq/L)	139.5±1.8	134±1.9	<0.0001
Systolic Blood Pressure (mmHg)	114.2±21.45	117.5±20.1	0.42
Ejection Fraction%	36.3±15.3	32.4±15.5	0.4
BMI	31.7±7.2	32.41±8.3	0.66
BNP (pg/mL)	435.8±740.3	498.9±615.8	0.66
Serum creatinine (mg/dL)	1.4±0.55	1.5±0.7	0.28
Blood urea nitrogen (mg/dL)	25.9±14.4	26.9±16.7	0.79
Albumin (g/dL)	3.8±0.6	3.7±0.6	0.58
Hemoglobin (g/dL)	13.6±1.8	13.4±1.7	0.53
Education level			0.2
None	4 (4.7)	5 (13.9)	
High School	37 (43.5)	18 (50)	
Some College	33 (38.8)	11 (30.6)	
Higher	11 (12.9)	2 (5.6)	
HF characteristics			
Diagnosis	**N=85**	**N=36**	**0.14**
HFrEF	60 (70.6)	30 (83.3)	
HFpEF	25 (29.4)	6 (20)	
Etiology	**N=70**	**N=32**	**0.4**
Ischemic HF	40 (57.14)	20 (62.5)	
Non- Ischemic	30 (42.9)	12 (37.5)	
NYHA	**N=62**	**N=25**	**0.76**
Class I	8 (13.3)	2 (8)	
Class II	35 (56.5)	15 (60)	
Class III	18 (29.03)	8 (32)	
Class IV	1 (1.6)	0	
Other comorbidities			
Diabetes Mellitus	38 (44.7)	21 (58.3)	0.23
Hypertension	49 (57.6)	23 (63.88)	0.55
Hyperlipidemia	48 (56.5)	20 (55.6)	1.000
Arthritis	22 (25.9)	5 (13.8)	0.23

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Table 1 continued. Baseline characteristics (mean and standard deviation).

Characteristics [mean and standard deviation or N (%)]	No hyponatremia N=85 (70%)		Hyponatremia N=36 (30%)		P
Medication use					
B blocker	85	(100)	36	(100)	
Loop diuretic	85	(100)	36	(100)	
Ace Inhibitors	51	(60)	15	(41.7)	0.06
Angiotensin blockers	17	(20)	11	(30.6)	0.21
Aldosterone Antagonist	33	(38.82)	24	(66.7)	0.005
Thiazide diuretics	1	(1.2)	3	(8.33)	0.04

HFrEF – Heart failure with reduced ejection fraction; HFpEF – heart failure with preserved ejection fraction; NYHA – New York Heart Association.

Table 2. Categories of the degree of cognitive impairment (CI).

Cognitive impairment category*	Non-hyponatremia N=85 % (N)		Hyponatremia N=36 % (N)	
Mild cognitive impairment	18.8	(16)	33.3	(12)
Moderate cognitive impairment	44.7	(38)	52.8	(19)
Severe cognitive impairment	12.9	(11)	5.6	(2)

* Mild: <26 and >22; Moderate: ≤22 and ≥17; Severe: <17.

Table 3. MoCA cognitive domain median scores.

Cognitive Domain	MoCA Item	Total possible score	MoCA ≥26 (n=23)	MoCA <26 hyponatremia (n=33)	MoCA <26 Non-hyponatremia (n=65)	p Value*
Sort-term memory	Delayed recall	5	4.0	2.0	2.0	<0.0001
Visuospatial function	Draw Clock; Copy Cube	4	3.0	2.0	2.0	<0.0001
Executive function	Trail Making; Fluency; Abstraction	4	3.0	2.0	2.0	<0.0001
Attention, concentration, working, memory	Tapping; Serial Subtraction; Numbers	6	6.0	5.0	5.0	<0.0001
Language	Naming; Sentence Repetition; Fluency	5	6.0	4.0	4.0	<0.0001
Orientation	Date; Month; Year; Day; Place; Time	6	6.0	6.0	6.0	0.14

* Comparison of patients with a MoCA score ≥26 and MoCA <26. No significant difference was seen between hyponatremic and non-hyponatremic patients with MoCA scores <26.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Discussion

Our study showed that in a sampling of ambulatory patients with HF, approximately 30% of patients had hyponatremia. We found a 92% prevalence of cognitive impairment in the hyponatremic group and 76% in HF patients without hyponatremia. Both groups demonstrated similar declines in cognitive function as measured by overall MoCA score, but the difference was not statistically significant. Sixty-five percent of HF patients in our sample had mobility impairment based on the TUG-t times. TUGt times were similar between hyponatremic and non-hyponatremic groups. We also found that patients with HFrEF had lower MoCA scores as compared to HFpEF patients. In regard to the primary objective of the study, the results showed that HF patients with hyponatremia had a higher prevalence of cognitive impairment. However, our findings also showed that, in general, a significant number of HF patients even without hyponatremia have measurable cognitive impairment and are likely to be at greater than average risk of falling, irrespective of serum sodium level.

The number of patients observed with hyponatremia is consistent with other reports in the literature. For example, results of the ESCAPE (Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness) trial reported community-associated hyponatremia in 23.8% of hospitalized patients with HF [7]. Hyponatremia was an independent predictor of mortality and rehospitalization even when adjusted for clinical and hemodynamic improvements. Hyponatremia seen in HF is often due to excess fluid accumulation (hypervolemic or dilutional hyponatremia). Driving factors include increased sympathetic activity, stimulation of renin-angiotensin-aldosterone system, and the nonosmotic release of arginine vasopressin leading to sodium and water retention [24]. Hypervolemic hyponatremia seen in HF patients tends to be chronic and is not often associated with critical sodium levels (e.g., <120 mEq/L). Patients with chronic hyponatremia and associated decrease in plasma osmolality will adapt over time, especially in regard to the central nervous system (CNS). To maintain cerebral osmolality, organic osmolytes play a critical role in cellular adaptation to chronic hyponatremia and decreased osmolality. Acute hyponatremia involves rapid shifts of electrolytes between brain cells and plasma and cerebrospinal fluid. Sodium, potassium, and chloride leave the cell and water enters, leading to cerebral edema. Over time, the CNS adapts to lower osmolality by increasing brain osmolality by shifting organic osmolytes (e.g., glutamate, glutamine, taurine, and phosphocreatine/creatine) from brain cells into the extracellular fluid [25,26]. It can be postulated that these shifts and resultant decrease in cellular organic osmolyte concentrations may decrease cognitive function and mobility in chronic hyponatremia. Another mechanism leading to altered CNS function may be decreased nerve conduction [27].

Most patients defined as having hyponatremia in our study appeared to have consistent hyponatremia as measured by 2 consecutive sodium levels (86% of patients with hyponatremia). It can be postulated that the CNS has likely adapted to a hyponatremic state in most of our hyponatremic patients. This suggestion is supported by our findings that 92% of our hyponatremic patients had cognitive impairment. In addition to cognitive impairment, the proportion of patients with above average TUGt times was also higher in the hyponatremic group (72% *vs.* 62%, p>0.05) which is not an unexpected finding. Our findings are consistent with other studies. A case-control study by Renneboog et al. showed that 21% of patients with hyponatremia (126±5 mEq/L) were admitted for falls as compared to 5.3% of control patients (p <0.001) [11]. In the same study, 16 patients were evaluated for gait and underwent 8 attention tests. These patients had chronic hyponatremia (128±3 mEq/L) and acted as their own control following correction of their hyponatremia (138 ± 2 mEq/L). When patients were hyponatremic, gait and attentions tests were significantly worse as compared to following correction of the hyponatremia. In another retrospective study, 44 patients with chronic hyponatremia (124.8±4.9 mEq/L) underwent a battery of neuropsychological tests [28]; significant differences were seen in a number of tests, including finger-tapping test, simple reaction time, and in continuous performance tests.

What appears to be clear from this study is that most patients evaluated have some form of cognitive impairment. It should be noted that the high percentage of patients observed to have cognitive impairment is related in part to the use of the MoCA instrument, which is more sensitive in detecting mild cognitive impairment as compared to the Mini-Mental State Examination (MMSE). The MMSE was developed as a screening tool for dementia and may not adequately assess mild cognitive impairment. Recent studies in HF patients have indeed shown that the MoCA identified a higher percentage of patients with cognitive impairment as compared to the patients assessed with the MMSE [3,13,18,29]. These studies also showed, similar to our findings, that many HF patients have some form of cognitive impairment (22–70%). The reasons for the high percentage of cognitive impairment in heart failure patients is not known and is likely related to a multitude of factors, including changes in cardiac output, cerebral perfusion pressure, and perhaps hyponatremia [2,30–32].

In our study, approximately 25% of the patients evaluated had HFpEF. There are very limited data on evaluation of cognitive function in patients with preserved ejection fraction [33–35]. The study that most directly addresses cognitive impairment in HFpEF patients also used the MoCA instrument [33]. In that study, a secondary analysis of a cross-sectional study in 90 patients demonstrated that patients with systolic dysfunction had significantly lower MoCA scores compared to patients

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

with diastolic heart failure. In addition, 61% (42 of 69) of systolic heart failure patients had a score below 26 on the MoCA compared with 52% (11 of 21) of participants with diastolic failure. These findings are similar to the results of the present study. The reason for the differences in scores between HFrEF or HFpEF patients is unknown but may be related to a number of factors, including differences in cerebral perfusion, as well as neurohormonal and cytokine activation. However, patients with HFpEF have cognitive impairment and, in general, the cognitive impairment is somewhat less severe than in HFrEF patients.

Our data also show that approximately 34% of patients with cognitive impairment were less than 65 years of age. In this group of patients, cognitive impairment was less severe than in older patients, which would be anticipated. However, younger HF patients are at risk for cognitive impairment. Cognitive impairment has been associated with poor outcomes in HF patients [6,10,36]. In addition, cognitive impairment in HF patients may limit a patient's ability to actively manage their heart failure (i.e., self-care) [37,38]. Cognitive impairment, especially in the domains we and others have identified, can make it more difficult for patients to follow medication plans (medication adherence), self-monitor, and maintain dietary patterns. Based on our results and those of others, it is important for clinicians to be cognizant of the high incidence of cognitive impairment in HF patients (young, old, HFrEF, and HFpEF) and to screen for cognitive impairment when appropriate. One risk factor to take into consideration is hyponatremia. In patients with cognitive impairment, specific interventions such as family engagement, along with appropriate patient education and follow-up need, to be specifically designed to accommodate these patients. It is unknown if correcting a patient's hyponatremia improves cognitive function or balance. Future research focusing on whether cognitive performance can be improved by correcting the underlying hyponatremia in HF patients could be an important next direction. At this time, correcting hyponatremia (>136 mEq/L) through better fluid management, medication optimization, and perhaps other non-drug therapies such as cardiac resynchronization therapy may need to be considered [39].

There are a number of limitations in the present study, including the small sample size of hyponatremic patients. Since the overall MoCA scores between the 2 groups were nearly identical, it is unlikely that recruitment of additional patients would have demonstrated any significant differences in actual MoCA score. However, when evaluating the MoCA score for patients with cognitive impairment, there was trend for patients without hyponatremia to have lower score. The study lacks power (<80%) to show statistical significance between the groups. Although, the clinical significance in the difference between the two scores (21.2±2.43 *vs.* 20.1±3.1) is probably minimal since both scores are within what is considered moderate cognitive impairment. Another consideration is whether other confounding variables or disease severity may have contributed to our findings. We attempted to evaluate a number of potential variables that may influence cognitive function, including age, social factors (education level), and physiological markers. As shown in Table 1, other than aldosterone antagonists and thiazide diuretic use, both groups were very similar in regards to potential confounding factors. Another concern, as previously discussed, is ability of the standardized tests utilized in the study to detect differences in cognitive function and balance. It is possible that the use of different instruments may have found differences in severity of cognitive impairment between the 2 groups. For the most part, the hyponatremia observed in the study would be considered "mild". It is likely that patients with more severe hyponatremia (e.g., 125 mEq/L) may have more cognitive dysfunction due to delirium and/or cognitive impairment. However, as seen in this study, patients in the ambulatory setting tend to have less severe hyponatremia, which suggests that the results of this study are generalizable to the outpatient population with heart failure. Finally, we did not capture data on diuretic dose or timing of diuretic administration in relation to hyponatremia or measurement of serum sodium.

Conclusions

Our study shows that a high percentage of HF patients have cognitive and gait impairment. We also found that cognitive impairment occurs in younger HF patients and may be more severe in HFrEF patients as measured by 2 easily administered and validated instruments. The results also showed that hyponatremia is often associated with cognitive impairment. Our findings further support the approach of routinely evaluating cognition and mobility as part of a comprehensive care plan for HF patients [40].

Acknowledgement

Thanks to Syeda Maahin Mahmood, Pharm. D. candidate, University of Michigan College of Pharmacy for finishing data collection and helping with data analysis.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

References:

1. Sila CA: Cognitive impairment in chronic heart failure. Cleve Clin J Med, 2007; 74(Suppl.1): S132–37
2. Vogels RL, Oosterman JM, van Harten B et al: Profile of cognitive impairment in chronic heart failure. J Am Geriatr Soc, 2007; 55: 1764–70
3. Harkness K, Demers C, Heckman GA, McKelvie RS: Screening for cognitive deficits using the Montreal Cognitive Assessment tool in outpatients ≥65 years of age with heart failure. Am J Cardiol, 2011; 107: 1203–7
4. Athilingam P, King KB: Heart and brain matters in heart failure: A literature review. J NY State Nurses Assoc, 2007; 38: 13–19
5. Cacciatore F, Abete P, Ferrara N et al: Congestive heart failure and cognitive impairment in an older population. Osservatorio Geriatrico Campano Study Group. Am Geriatr Soc, 1998; 46: 1343–48
6. Pressler SJ, Subramanian U, Kareken D et al: Cognitive deficits in chronic heart failure. Nurs Res, 2010; 59: 127–39
7. Gheorghiade M, Rossi JS, Cotts W et al: Characterization and prognostic value of persistent hyponatremia in patients with severe heart failure in the ESCAPE Trial. Arch Intern Med, 2007; 167: 1998–2005
8. Hauptman PJ, Burnett J, Gheorghiade M et al: Clinical course of patients with hyponatremia and decompensated systolic heart failure and the effect of vasopressin receptor antagonism with tolvaptan. J Card Fail, 2013; 19: 390–97
9. Gheorghiade M, Gattis WA, O'Connor CM et al: Acute and chronic therapeutic impact of a vasopressin antagonist in congestive heart failure (ACTIV in CHF) Investigators. Effects of tolvaptan, a vasopressin antagonist, in patients hospitalized with worsening heart failure: A randomized controlled trial. JAMA, 2004; 291: 1963–71
10. Gelow JM, Mudd JO, Chien CV, Lee CS: Usefulness of cognitive dysfunction in heart failure to predict cardiovascular risk at 180 days. Am J Cardiol, 2015; 115(6): 778–82
11. Renneboog B, Musch W, Vandemergel X et al: Mild chronic hyponatremia is associated with falls, unsteadiness, and attention deficits. Am J Med, 2006; 119(1): 71.e1–8
12. *http://www.mocatest.org/* Last accessed on August, 2015
13. Hawkins MA, Gathright EC, Gunstad J et al: The MoCA and MMSE as screeners for cognitive impairment in a heart failure population: A study with comprehensive neuropsychological testing. Heart Lung, 2014; 43: 462–68
14. Smith T, Gildeh N, Holmes C: The Montreal Cognitive Assessment: Validity and utility in a memory clinic setting. Can J Psychiatry, 2007; 52(5): 329–32
15. Luis CA, Keegan AP, Mullan M: Cross validation of the Montreal Cognitive Assessment in community dwelling older adults residing in the Southeastern US. Int J Geriatr Psychiatry, 2009; 24(2): 197–201
16. Rossetti HC, Lacritz LH, Cullum CM, Weiner MF: Normative data for the Montreal Cognitive Assessment (MoCA) in a population-based sample. Neurology, 2011; 77(13): 1272–75
17. Davis KK, Dennison Himmelfarb CR, Szanton SL et al: Predictors of heart failure self-care in patients who screened positive for mild cognitive impairment. J Cardiovasc Nurs, 2015; 30: 152–60
18. Athilingam P, King KB, Burgin SW et al: Montreal Cognitive Assessment and Mini-Mental Status Examination compared as cognitive screening tools in heart failure. Heart Lung, 2011; 40: 521–29
19. Shumway-Cook A, Brauer S, Woollacott M: Predicting the probability for falls in community-dwelling older adults using the Timed Up &Go Test. Phys Ther, 2000; 80: 896–903
20. Bohannon RW: Reference values for the Timed Up and Go Test: A Descriptive Meta-Analysis. J Geriatr Phys Ther, 2006; 29: 64–68
21. Kristensen MT, Foss NB, Kehlet H: Timed "Up and Go" Test as a predictor of falls within 6 months after hip fracture surgery. Phys Ther, 2007; 87(1): 24–30
22. Wald R, Jaber BL, Price LL et al: Impact of hospital-associated hyponatremia on selected outcomes. Arch Intern Med, 2010; 170: 294–302
23. Verbalis JG, Goldsmith SR, Greenberg A et al: Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. Am J Med, 2013; 126(10 Suppl.1): S1–42
24. Schrier RW: Body fluid regulation in health and disease: A unifying hypothesis. Ann Int Med, 1990; 113: 155–59
25. Lien YH, Shapiro JI, Chan L: Study of brain electrolytes and organic osmolytes during correction of chronic hyponatremia. Implications for the pathogenesis of central pontine myelinolysis. J Clin Invest, 1991; 88: 303–9
26. Verbalis JG, Gullans SR: Hyponatremia causes large sustained reductions in brain content of multiple organic osmolytes in rats. Brain Res, 1991; 567: 274–82
27. Aranyi Z, Kovacs T, Szirmai I, Vastagh I: Reversible nerve conduction slowing in hyponatremia. J Neurol, 2004; 251: 1532–33
28. Josiassen RC, Filmyer DM, Geboy AG et al: Psychomotor deficits associated with hyponatremia: a retrospective analysis. Clin Neuropsychol, 2012; 26: 74–87
29. Gallagher R, Sullivan A, Burke R et al: Mild cognitive impairment, screening, and patient perceptions in heart failure patients. J Card Fail, 2013; 19: 641–46
30. O'Brien JT: Vascular cognitive impairment. Am J Geriatr Psychiatry, 2006; 14: 724–33
31. Ogren JA, Fonarow GC, Woo MA: Cerebral impairment in heart failure. Curr Heart Fail Rep, 2014; 11: 321–29
32. Gure TR, Blaum CS, Giordani B et al: Prevalence of cognitive impairment in older adults with heart failure. J Am Geriatr Soc, 2012; 60: 1724–29
33. Athilingam P, D'Aoust RF, Miller L, Chen L: Cognitive profile in persons with systolic and diastolic heart failure. Congest Heart Fail, 2013; 19: 44–50
34. Arangalage D, Ederhy S, Dufour L et al: Relationship between cognitive impairment and echocardiographic parameters: A review. J Am Soc Echocardiogr, 2015; 28: 264–74
35. Suwa M, Ito T: Correlation between cognitive impairment and left ventricular diastolic dysfunction in patients with cardiovascular diseases. Int J Cardiol, 2009; 136: 351–54
36. Zuccalà G, Pedone C, Cesari M et al: The effects of cognitive impairment on mortality among hospitalized patients with heart failure. Am J Med, 2003; 115: 97–103
37. Lee CS, Gelow JM, Bidwell JT et al: Blunted responses to heart failure symptoms in adults with mild cognitive dysfunction. J Cardiovasc Nurs, 2013; 28: 534–40
38. Currie K, Rideout A, Lindsay G, Harkness K: The association between mild cognitive impairment and self-care in adults with chronic heart failure: A systematic review and narrative synthesis. J Cardiovasc Nurs, 2015; 30(5): 382–93
39. Proietti R, Manzoni GM, Cravello L et al: Can cardiac resynchronization therapy improve cognitive function? A systematic review. Pacing Clin Electrophysiol, 2014; 37: 520–30
40. Cameron J, Ski CF, Thompson DR: Cognitive impairment in chronic heart failure and the need for screening. Am J Cardiol, 2011; 107: 1547–48

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]