Hyponatraemia in heart failure: a call for redefinition

Jalal K. Ghali

Wayne State University, University Health Center, 2E, Detroit, MI 48201, USA

Online publish-ahead-of-print 12 April 2007

This editorial refers to ‘Relationship between admission serum sodium concentration and clinical outcomes in patients hospitalized for heart failure: an analysis from the OPTIMIZE-HF Registry’ by M. Gheorghiade et al., on page 980.

Hyponatraemia, defined as a serum sodium concentration of <136 mol/L (1 mmol/L = 1 meq/L), is the most common electrolyte abnormality in hospitalized patients with a prevalence of 1–45% depending on the clinical setting, patient population, and the serum value used to define it.1

In heart failure, this has been associated with increased risk of haemodynamic deterioration, longer hospital stay, and higher rehospitalization and higher mortality.2–5 Hyponatraemia in patients with heart failure is also a marker of activation of the renin–angiotensin–aldosterone system with higher levels of renin, angiotensin II, aldosterone, catecholamines, and vasopressin as well as more severe impairment in hepatic and renal blood flow and glomerular filtration rate when compared with patients with heart failure and normal serum [Na+] level.6,7

Despite our increasing knowledge of the link between heart failure and hyponatraemia, there are major gaps in our understanding of this relationship including whether it is a cause-and-effect and if so would correction of hyponatraemia improve outcome, and the specific cut-off level of serum [Na+] that should define hyponatraemia.

Gheorghiade et al.8 report on the relationship between serum [Na+] concentration and clinical outcomes in 47,647 patients hospitalized for heart failure and enrolled in the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patient with Heart Failure (OPTIMIZE-HF), a registry and quality of care interventional programme, that included 60–90 days of follow-up in 10% of the patients.

The mean age was 73 years, 52% were women and 49% were classified as having left ventricular systolic dysfunction and clinical outcomes. Median admission serum [Na+] was 138 ± 5 mmol/L. Nineteen per cent of the patients had hyponatraemia, defined as serum [Na+] <135 mmol/L. Patients with hyponatraemia were more likely to have lower systolic blood pressure and higher heart rate, to be placed on inotropes and vasodilators, and to receive mechanical ventilation or left ventricular assist device. They were also more likely to receive aldosterone antagonists and thiazides or loop diuretics.

When compared with patients with higher serum [Na+], those with hyponatraemia had higher in-hospital mortality rate (3.2 vs. 6.0%, respectively), longer median hospital length of stay (5.5 vs. 6.4 days, respectively), and higher post-discharge mortality. The association between serum [Na+] and length of stay or in-hospital mortality was independent of left ventricular systolic function.

Do these new data help us better understand the role of hyponatraemia in heart failure?

Gheorghiade et al. have certainly provided valuable information, based on prospectively collected very large data.

They confirmed the relatively high prevalence of hyponatraemia in hospitalized patients with heart failure as well as its independent prognostic value in predicting in-hospital mortality regardless of left ventricular systolic function.

The author’s analysis also suggested that the association of hyponatraemia with worse post-discharge mortality was restricted to patients with heart failure and left ventricular systolic dysfunction, and a trend for an association with rehospitalization rate was confined to patients without left ventricular systolic dysfunction. As the author’s note, however, the lack of available data on pre-discharge [Na+] limits the interpretation of these data.

It is noteworthy to mention that a single-centre retrospective study of 160 patients with systolic heart failure receiving contemporary management who died over 3-year period showed that hyponatraemia was worse in the months preceding death than at the time of death.9 Therefore, further exploration and a closer observation of changes in serum [Na+] preceding death are required for better understanding of the correlation of serum [Na+] with post-discharge mortality.

Perhaps, the greatest contribution Gheorghiade et al.8 have made is their finding of a significantly increased risk of in-hospital mortality at [Na+] levels between 135 and 138 mmol/L. Hyponatraemia defined as serum [Na+] below 136 or 135 mmol/L has been found to be a strong predictor of outcome. However, by appropriately analysing the serum [Na+] as a continuous variable, the authors demonstrated a clear association of [Na+] levels between 135 and 138 mmol/L with in-hospital mortality. Therefore, a strong argument can be made that hyponatraemia in heart failure should be defined as a serum level of <138 mmol/L. It is of interest to note that in the first study that correlated
hyponatraemia with poor outcome in patients with heart failure,\(^2\) \(<137\) mmol/L was the cut-off used to define hyponatraemia, and in the study by Kearney et al. on predictors of death in patients with mild-to-moderate heart failure,\(^4\) the mean serum \([\text{Na}^+]\) was 138 mmol/L in non-survivors.

Adoption of this definition may not drastically change current management of heart failure patients with this level of hyponatraemia; however, with the increasing interest in exploring the potential role of vasopressin receptor antagonists in the treatment of heart failure,\(^10\) it may soon markedly expand the number of patients who would potentially benefit from such an approach.

In planning future trials designed to study the effects of correcting hyponatraemia in heart failure, serious consideration should be given to define hyponatraemia as a serum level of \(<138\) mmol/L.

This report from OPTIMIZE-HF is an inspiring reminder of the valuable and unique contribution that registries provide.

Conflict of interest: J.K.G. has received research grants from Otsuka Maryland Medicinal Laboratories, Inc. and Astella Pharma USA, Inc.

References


