Use of antidiuretic hormone antagonists results in lower hospital resource usage: a retrospective cohort study

Paul Grant[1], Clare Jamookeeah[2], Penny Dhanjal[3], Gethin Griffith[2]

[1]Oxford Centre for Diabetes, Endocrinology & Metabolism, Oxford, UK; [2]Otsuka Pharmaceutical Europe Ltd, Wexham, UK [3]Otsuka Pharmaceutical UK Ltd, Wexham, UK

Introduction

- Hyponatraemia is the electrolyte disturbance most commonly encountered in clinical practice (affecting 10–30% of hospitalised patients) and can be a marker of morbidity in many contexts, increasing mortality rates regardless of cause.[1]
- The syndrome of inappropriate antidiuretic hormone secretion (SIADH) is the most common cause of hypotonic hyponatraemia,[2] responsible for approximately 30% of all patients with hyponatraemia.
- Data from the US suggest that patients with hyponatraemia have a greater overall consumption of healthcare resources, and that hyponatraemia is associated with an increased length of hospital stay,[3-5] and increased direct medical costs.[6]
- The overall annual cost of hyponatraemia in the US alone has been estimated at $1.6–3.6 billion[7] – there are no comparable cost data for the UK.
- The UK Consensus Statement recommends pharmacological therapy (demeclocycline or tolvaptan) for patients with mild/moderate hyponatraemia secondary to SIADH without severe symptoms, after fluid restriction has been attempted or deemed inappropriate.[8]
- The aim of this study was to understand how hyponatraemia secondary to SIADH is currently treated in England, and to understand the associated resource use.

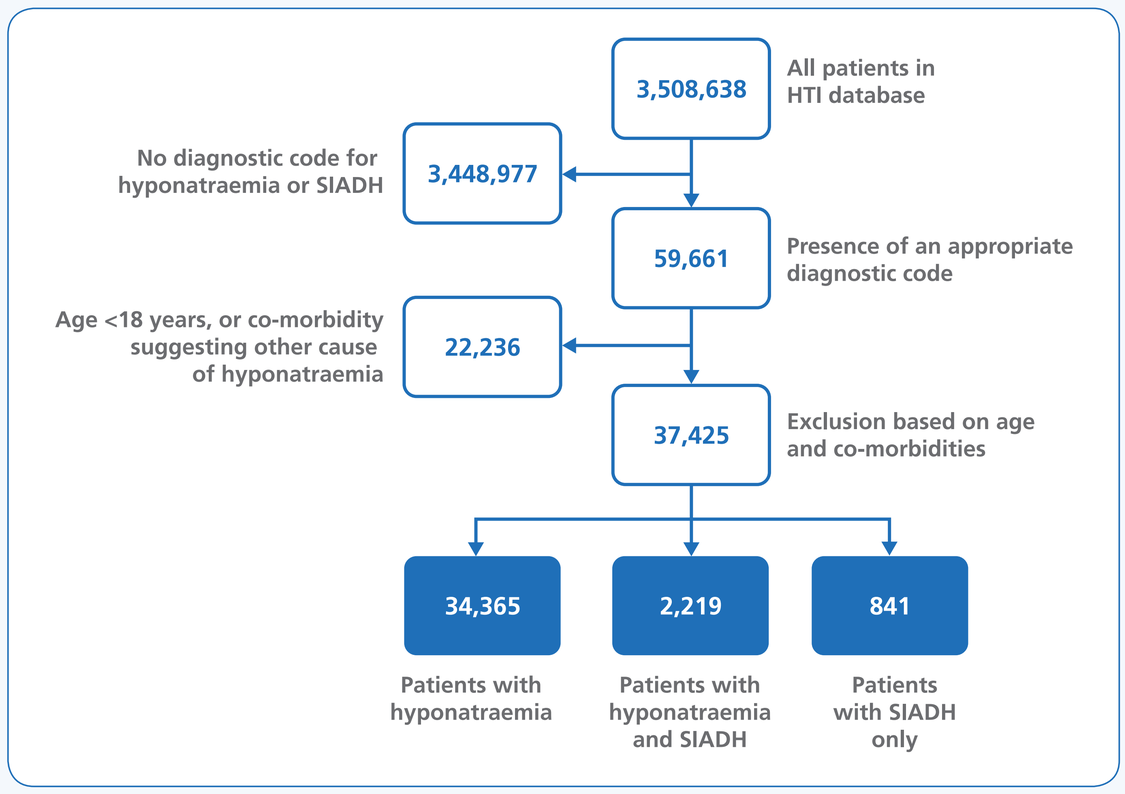
Methods

- A retrospective analysis of a patient cohort identified in IMS Hospital Treatment Insights (HTI) through hospital admission diagnosis codes from 1 January 2010 through to 31 October 2013 was conducted.
- The HTI database, comprising details of all admissions and outpatient appointments to NHS hospitals in England, contains records on 3.3 million English patients from a source population of 13 million.
- Adult patients were included if they had a new World Health Organization (WHO) ICD-10 diagnostic code for 'Hypo-osmolality and hyponatraemia' (E87.1) and/or a diagnostic code for SIADH (E22.2) during the study period.
- Exclusion criteria were patients <18 years of age or with no age recorded, or co-morbid conditions associated with hyponatraemia: liver cirrhosis; liver disease with ascites; heart failure; unspecified adrenocortical insufficiency; hypothyroidism; and type 1 diabetes.
- Study outcomes were captured through relevant WHO ICD-10 codes and comprised hospital admissions, outpatient visits, length of hospital stay, and in-hospital mortality.

Results

- In total, 37,425 patients were given a clinical code for SIADH or hyponatraemia (Figure 1); >60% of patients were ≥68 years of age.
- Of the patients with a diagnosis of hyponatraemia and/or SIADH, 1.8% were given demeclocycline, 0.3% were given tolvaptan, and 97.9% were not given any recorded pharmacological treatment. When pharmacological treatment was given, it was usually as monotherapy.
- Mean time from diagnosis to initiation of therapy was similar for both demeclocycline and tolvaptan (10.2 days).
  - Median time was 3 days longer with tolvaptan at 8 days.
- Patients receiving tolvaptan had a shorter mean (11.1 vs 19.3 days) and median (10 vs 14 days) length of hospital stay than those given demeclocycline.
- Time to readmission and readmission rates at 30 and 60 days appeared similar between the two treatment groups (Table 1).

Figure 1. Patient population



HTI, Hospital Treatment Insights; SIADH, syndrome of inappropriate antidiuretic hormone secretion

Table 1. Patient population

	Demeclocycline	Tolvaptan
Time to re-admission, days		
N (hospitalisations)	437	61
Mean	45.6	26.5
Median	5	14
Range	0–1041	0–176
Re-admission at 30 days, % (n)	74.6 (25.4)	72.1 (44)
Re-admission at 60 days, % (n)	82.8 (362)	85.2 (52)

SIADH, syndrome of inappropriate antidiuretic hormone secretion

- Tolvaptan treatment was associated with a 29% fewer accident and emergency (A&E) attendances per patient than demeclocycline (p=0.041).
  - Number of A&E attendances was significantly reduced across both treatments compared with patients not receiving any pharmacological treatment (p<0.00005)
- Receiving pharmacological treatment was associated with significant reductions in the number of outpatient appointments per patient
  - There were 0.788, 0.693 and 0.540 appointments/patient for demeclocycline, tolvaptan and no pharmacological treatment, respectively (p<0.05)

Conclusions

- Hyponatraemia and SIADH represent a substantial healthcare burden, and there are considerable variations in assessment and treatment.
- Under-reporting of hyponatraemia secondary to SIADH presents potentially serious implications for hospital remuneration.
- Pharmacological treatment results in considerably fewer A&E attendances than with no treatment; effective control of hyponatraemia may result in lower resource usage.
- Management of SIADH with tolvaptan may result in lower resource usage for hospitals and the wider health economy versus treatment with demeclocycline.

References:

1. Corona G, et al. *PLoS One* 2013;8:e80451; 2. Fenske W, et al. *Am J Med* 2010;123:652–657; 3. Sherlock M, et al. *Clin Endocrinol (Oxf)* 2006;64:250–254; 4. Sherlock M, et al. *Postgrad Med J* 2009;85:171–175; 5. Gill G, et al. *Clin Endocrinol (Oxf)* 2006;65:246–249; 6. Shea AM, et al. *J Am Soc Nephrol* 2008;19:764–770; 7. Boscoe A, et al. *Cost Eff Resour Alloc* 2006;4:10; 8. Grant P, et al. *Eur J Clin Invest* 2015; 45:888–894.