Four years of tolvaptan: experience from two large teaching hospitals

Dr J Follows* Foundation Year 2, Dr A Iqbal* Speciality Registrar Diabetes and Endocrinology, Dr A Allahabadia - Consultant Endocrinologist
Department of Endocrinology, Northern General Hospital, Herries Road, Sheffield, S5 7AU
*Dr J Follows and Dr A Iqbal have contributed equally

Sheffield Teaching Hospitals NHS
NHS Foundation Trust

Introduction

- Hyponatraemia is a common cause of morbidity and mortality affecting 15-20% of inpatients (1,2).
- Chronic hyponatraemia needs to be corrected with caution; if corrected too rapidly it can result in osmotic demyelination (3).
- Tolvaptan is a competitive vasopressin receptor 2 antagonist; in the UK it is licenced for the treatment of hyponatraemia secondary to the syndrome of inappropriate anti-diuretic hormone secretion (SIADH).
- The BNF recommends sodium monitoring at least every 6 hours for the first 24-48hrs after initiating tolvaptan (4).
- The cost to Sheffield Teaching Hospitals (STH) is £89.60 per tablet (any dose).

Objectives

- To assess the indication for tolvaptan use at STH.
- To assess whether:
  1. tolvaptan was dosed appropriately.
  2. serum sodium was monitored appropriately .
- To assess whether changes in serum sodium were:
  1. within acceptable limits.
  2. managed appropriately where indicated.

Methods

- This was a retrospective audit between May 2010 and July 2014.
- Medical notes were used to identify patient demographics, indications for tolvaptan prescription, fluid restriction and use of demeclocycline prior to tolvaptan administration.
- Biochemical laboratory investigations. were obtained from the Sunquest ICE database.
- STH drug charts were used to assess the date, time and dose of tolvaptan administration.

Characteristics	No of patients (%)
Total number of patients:	17 (100 %)
Male	8 (47%)
Female	9 (53 %)
Minimum age: 59 yrs Maximum age: 92 yrs Mean age: 78 yrs Standard deviation: 8.49	
Diagnosis:	
SIADH	16 (94.1%)
Heart Failure	1 (5.9 %)

Fig. 1 Patient demographics

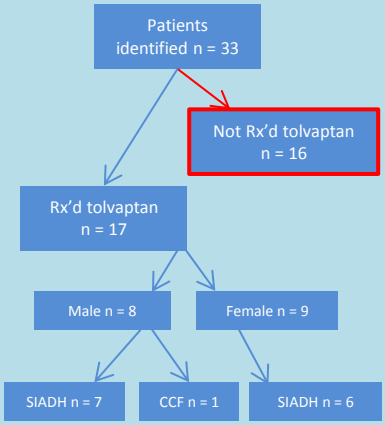


Fig. 2 Flow chart of patients audited

Criteria	Compliance
Appropriate indication for tolvaptan prescription	100% n = 17
Measurement of paired urine and serum sodium and osmolalities.	88% n = 15
Measurement of TSH and cortisol to exclude other causes of hyponatraemia	76% n = 13
Change in serum sodium within acceptable limits	82% n = 14
Change in serum sodium within acceptable limits after appropriate identification and intervention of limit exceedance	94% n = 16
Appropriate frequency of sodium monitoring in the first 24hrs	24% n = 4
Appropriate frequency of sodium monitoring in the second 24hrs	12% n = 2
Appropriate dosing of tolvaptan	100% n = 17
**All standards were expected to be met with 100% compliance*	

Fig. 3 Table of results; standards against which each patient was audited

Results

Fig. 5 Change in serum sodium

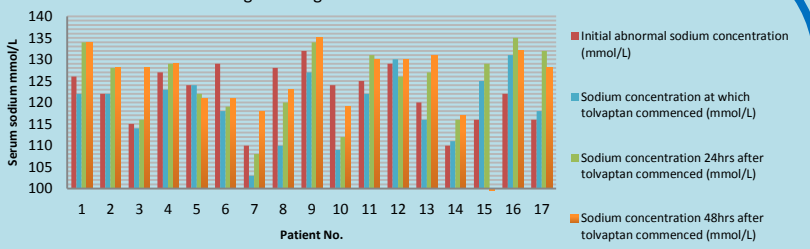
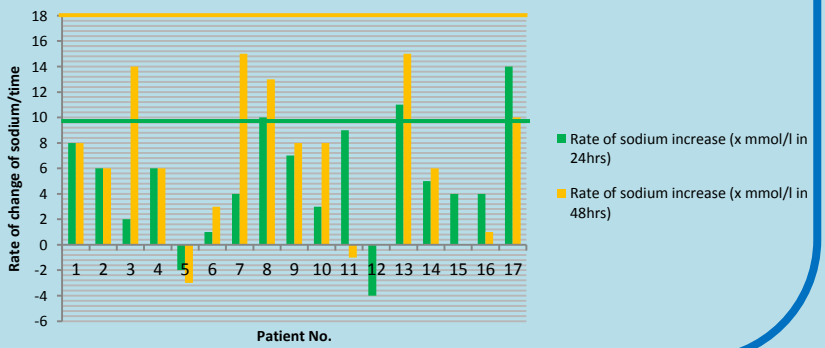


Fig 6. Rate of change in serum sodium following tolvaptan



Discussion

- Most patients are having necessary investigations to make the diagnosis of SIADH. SIADH is a diagnosis of exclusion; there is room for improvement in future practice.
- Patients 13 and 17 had a rise in serum sodium beyond acceptable parameters and were treated to arrest this rise.
- Patient 3 had a rise in serum sodium of 12mmol/L; between hours 24 and 48 after starting tolvaptan. This rise was not identified and no action was taken to arrest this rise.
- 76% of patients prescribed tolvaptan were not monitored at sufficiently regular intervals. Despite the fact that no patients audited came to harm, there is room for improvement with serum sodium monitoring.
- Patient 15 was discharged after 24hrs of sodium monitoring; they were not monitored for the full 48 hour period.

Limitations

- It is possible that the search of pharmacy records did not identify all patients prescribed tolvaptan .
- This audit was limited by a small sample size. However, use of tolvaptan is not common, and a comparable audit at a different trust yielded a similar sample size.
- Data collection in this audit was limited by poor or incomplete documentation in certain places.

Conclusions

- In the majority of cases, there was a clear documented indication for the use of tolvaptan
- There is scope for improving safety for patients who are prescribed tolvaptan

Recommendations

- Adjust electronic requesting to allow serial blood request forms to be printed simultaneously for four hourly intervals for serum sodium monitoring.
- Signposting in the medical notes (in the form of a sticker which comes from pharmacy with tolvptan or an eFlag for electronic notes triggered upon prescription of the drug) to ensure:
  1. Appropriate handover to out of hour nursing and medical teams has occurred.
  2. Instructions for monitoring of serum sodium, how to interpret data and what do to in circumstances where safe limits might be, or have been exceeded.
  3. Signposting for guidelines.
- Teaching for diabetes and endocrine junior doctors at the start of each four month rotation on safe monitoring of tolvaptan prescription.

References

1. Hawkins RC. Age and gender as risk factors for hyponatremia and hypernatremia. Clinica Chimica Acta.2003;337:169–172. doi: 10.1016/j.cccn.2003.08.001. [PubMed] [Cross Ref]
2. Upadhyay A, Jaber BL, Madias NE. Incidence and prevalence of hyponatremia. American Journal of Medicine. 2006;119:S30–S35. doi: 10.1016/j.amjmed.2006.05.005. [PubMed] [Cross Ref]
3. Verbalis, J.G, Adler, S, Schrier, R.W, Berl, T, Zhao, Q. Efficacy and safety of oral tolvaptan therapy in patients with the syndrome of inappropriate antidiuretic hormone secretion. Eur J Endocrinol. 2011;164(5): 725-32.
4. National Institute for Health and Clinical Excellence. *Tolvaptan. https://www.evidence.nhs.uk/formulary/bnf/current/6-endocrine-system/65-hypothalamic-and-pituitary-hormones-and-anti-oestrogens/652-posterior-pituitary-hormones-and-antagonists/tolvaptan/tolvaptan (accessed07/06/2015).*