EP-732 Efficacy and safety of tolvaptan in treatment of SIADH
A case series from 2 UK hospitals

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Introduction

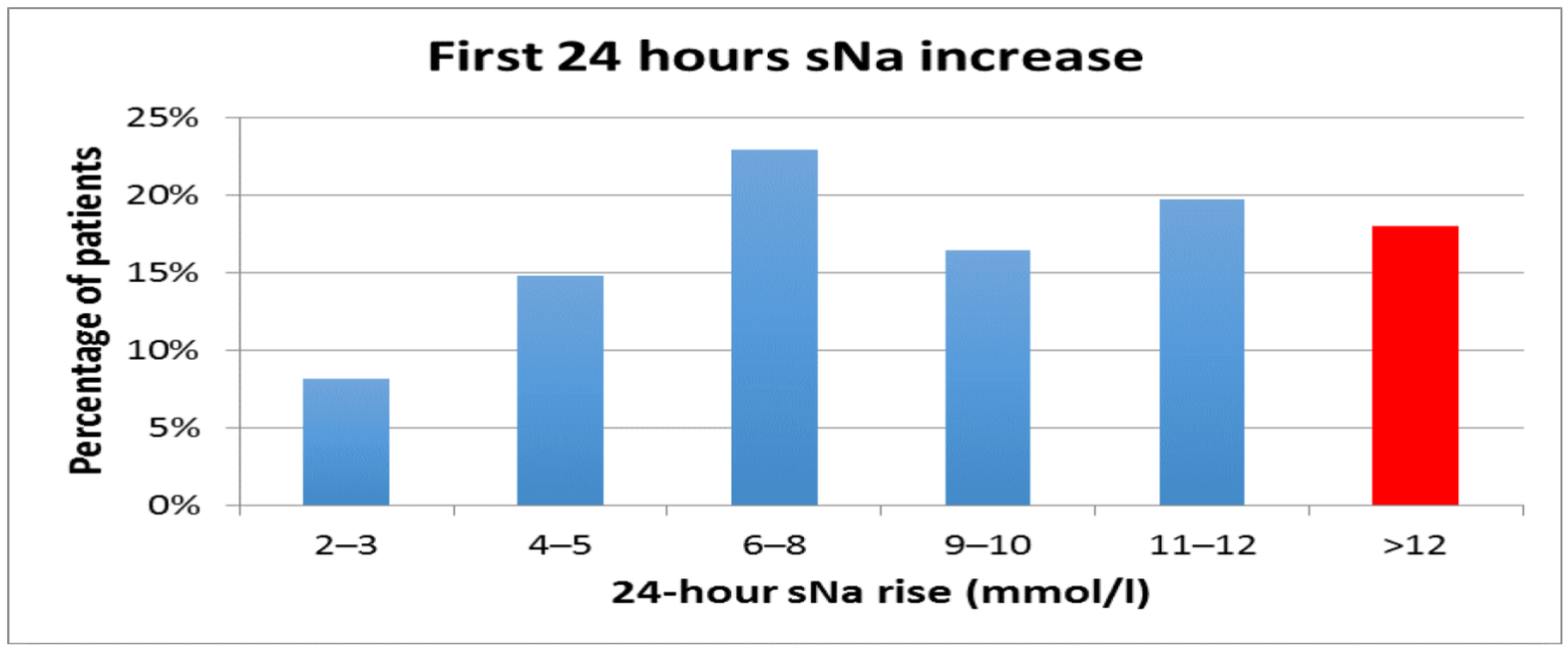
Tolvaptan, a vasopressin receptor antagonist, is the only agent licensed in Europe for treatment of syndrome of inappropriate antidiuretic hormone secretion (SIADH). However, European guidelines do not recommend tolvaptan use in view of concerns about risk of over rapid correction of hyponatraemia. This study evaluated the real-life effectiveness and safety of tolvaptan.

Methods

Retrospective case series of all inpatients treated with tolvaptan for SIADH in 2 UK hospitals between November 2010 and February 2014.

The main outcome measures were serum sodium (sNa) correction at different time points. All values were calculated as mean ± SD (standard deviation).

Results



Correction of sNa	
Baseline sNa (mmol/l)	119.9 ± 5.5
sNa change in first 24 hours (mmol/l)	9 ± 3.9
sNa change in first 48 hours (mmol/l)	11.4 ± 5.6

At the end of tolvaptan therapy	
Duration of therapy (days)	4.2 ± 4
sNa rise (mmol/l)	13.5 ± 5.9
sNa (mmol/l)	133.5 ± 4.5

Results

Tolvaptan was used in 61 patients (33 females, 28 males) aged 74.4 ± 15.3 years with sNa 119.9 ± 5.5 mmol/l. Initiation dose was 15 mg in all but 6 patients started on 7.5 mg. The cause of SIADH was malignancy (24.6%), unknown (24.6%), nervous system disorder (16.4%), pulmonary illness (14.7%), drug-induced (9.8%), post-operative (6.6%) and various (3.3%).

Excessive correction of hyponatraemia, defined as sNa increase > 12 mmol/l within 24 hours or > 18 mmol/l within 48 hours, was observed in 22.3% of patients with all these patients having baseline sNa < 125 mmol/l..

After tolvaptan treatment, 59/61 (96.7%) of patients had increase of sNa of ≥ 5 mmol/l with all patients having this rise within 48 hours.

Conclusions

- Tolvaptan is effective in correcting hyponatraemia, but carries a high risk of excessive correction when baseline sNa is < 125 mmol/l.
- No cases of osmotic demyelination were recorded.
- Rigorous electrolyte and fluid monitoring as well as local protocols to prevent / reverse over rapid correction are essential.
- Studies are needed to evaluate the safety and effectiveness of lower doses of tolvaptan.

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