Reviewer’s report

Title: In-patient Tolvaptan use in SIADH: Care Audit, Therapy Observations and Outcomes Analysis

Version: 0 Date: 06 Nov 2016

Reviewer: Mark Hannon

Reviewer’s report:

This is an interesting paper and worthy of publication. However, some revisions are required.

Major Corrections:

The abstract is poorly written and the Aims section does not actually delineate any aims. THis needs revision.

Page 3 paragraph 2: This paragraph is clunky and needs revision. The point here is that relatively mild hyponatraemia is also increasingly thought to be clinically significant in terms of falls, bone turnover etc (Verbalis 2010, Renneboog 2006, etc). Author should cite some of the many papers showing the adverse consequences of "mild" hyponatraemia in various patients (Stelfox, Gankam Kengne, etc).

Page 3 line 77: fluid restriction remains the mainstay of treatment despite the poor data behind it - this should be discussed in more detail, with references.

Page 4 line 82: the US and European guidelines on the management of hyponatraemia should be cited and briefly discussed as they offer very different viewpoints on the use of tolvaptan.

Page 8 line 193: the lowest starting sodium in the study was 108, which is very low for tolvaptan use. In the SALT1 and 2 studies, tolvaptan was only used in those with Na > 120. How can the authors be sure that none of the patients with starting sodiums as low as 108 did not have acute severe hyponatraemia requiring hypertonic saline? Tolvaptan is not licensed for this severity of hyponatraemia.

Page 8 line 198: How was 12 mmol/L selected as the cut off used to define an excessive rise in plasma sodium? This blanket cut off would not be endorsed by the recent US or European guidelines. The cut off used to define an excessive rise should be guideline endorsed.

Results section: this is very wordy and should be tabulated. A table of the results (in particular the aetiology of SIADH in study participants - type of malignancy etc) would be more useful than some of the graphics which are included.
Page 11 line 273: Again, these cut offs used to define excessively fast Na rise aren't guideline supported and no citations are given.

Page 12 line 302: I don't disagree with this statement but a reference needs to be given.

Page 14 line 347: the US guidelines recommendation should be given as a comparison the European guidelines, which are very anti V2R antagonists.

Page 15 line 371: This statement is hard to support as the main malignancy to cause SIADH is small cell lung ca which in itself has a very poor prognosis. Again, a table listing the types of malignancies involved needs to be provided.

Table 1: This hospital guideline is not evidence based. Why is a figure of < 750 ml chosen as the fluid restriction cut off? Fluid restriction needs to be 500 ml less than urinary output to be successful. Also, monitoring Na at 6 and 12 hours would not be frequent enough for those with Na < 115 (as some people in the study did), as per the US and European guidelines.

Minor Corrections:

Page 4 line 100: needs revision - I presume the author means "inpatient specialty"?

Page 5 line 109: change "euvolaemic hyponatraemia" to "SIADH" as SIADH is the only indication for tolvaptan use.

Page 5 line 112: is there a reference to support this?

Page 13 line 320: I presume the "poor outcomes" referred to relate to CPM rather than tolvaptan use??

Page 15 line 356: Change "unnecessary" to "unnecessarily"

Page 15 line 362: this line needs grammatical revision.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
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Yes

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