Reviewer’s report

Title: Optimal treatment of opioid induced constipation in daily clinical practice - an observational study

Version: 0 Date: 19 Sep 2018

Reviewer: Judith A. Paice

Reviewer’s report:

This manuscript reports the results of two studies: a retrospective chart review of 39 patients along with a secondary analysis of a prospective observational study of methylnaltrexone. This is an important topic for readers of this journal. A few recommendations to strengthen the paper:

1. Was the methylnaltrexone administered orally or SQ? This should be included throughout the paper as well as in the abstract.

2. In the abstract and in the paper there is reference to 22 patients being admitted for OIC. Were they admitted to emergency department or inpatient and were these 22 discrete patients or 22 admissions?

3. On page 3 at the bottom of the page the paper states that methylnaltrexone has recently become available - it has been available for many years in US and other countries. Is this a mistake? Or has it just become available in the Netherlands?

4. In the retrospective chart review (Methods) did the investigators have access to actual intake of opioids rather than simply prescription information? Admissions to ED or hospital often occur for multiple reasons - is it possible admissions for OIC were missed as it was a secondary reason (e.g., pt with nausea/vomiting as reason for admit but underlying cause was OIC)?

5. Also in Methods in retrospective chart review, constipation was considered opioid induced if it was made explicit in the char or if there were no other major contributing factors - include your list of factors investigated.

6. Clarify if patients were on transdermal, IV or immediate release mucosal fentanyl.

7. In the Results section, please define "treatment intention", "intake failure" and "abdominal innervation" problems.

8. Also in Results, how were you able to identify dose of laxatives for comparison as there are many different products available?

9. On page 7, what equianalgesic ratio was used to convert/compare fentanyl with morphine? Also on page 7, what form of fentanyl was used for rescue?
10. On page 8 in describing the prospective trial, the numbers are small and imbalanced (8 oxycodone, 2 fentanyl and 1 morphine) - how was this handled statistically? It may be that due to these small numbers, this part of the manuscript should be deleted, reporting only on the retrospective data.

11. On page 10 there were mild side effects of methylnaltrexone reported - what were these?

12. Please define Macrogal for an international audience.

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

No

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

No

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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