Reviewer’s report

Title: Polydrug abuse among opioid maintenance treatment patients is related to inadequate dose of maintenance treatment medicine

Version: 0 Date: 25 Apr 2017

Reviewer: Christian Tjagvad

Reviewer’s report:

General comments

This is an interesting paper examining polydrug abuse among OMT patients by using improved laboratory diagnostics. The main findings are that polydrug abuse was common among the examined group of OMT patients in Finland. This particularly applied to the group of patients who were treated with inadequate doses of OMT medication.

However, there are some concerns. All the medications detected by the LC-TOFMS method are stated as abuse. However, no information is collected on whether the medication was prescribed and how it was used. How do the authors know that (a considerable proportion of) the detected medication was not prescribed and used by the patient as part of a treatment.

Also, one of the main objectives is to assess whether polydrug abuse is related to the adequacy of the dose (adequate or inadequate) of the OMT medication as experienced by the patients. However, how this division is made is not clear. It is stated in the Method section that the rating for the dose adequacy can be too low, adequate, too high, or unsure, according to the patient's opinion. But it does not seem to be stated how this rating leads to the division; adequate or inadequate. Furthermore, if both a dose adequacy of too low and too high are defined as one group (inadequate), how is this definition clinically relevant? Patients who are treated with either too low or too high doses of OMT medication represent two entirely different set of challenges who require entirely different treatment regimes.

Background

1. Page 4, para 2, would stand out more clear and fluent if the narrative was more general than the present discussion between specific findings of listed papers. I recommend changing the narrative in this para.

Methods

2. All of the medications that were detected by the laboratory methods were specified as abused. However, the study does not include information on whether the medication detected by the laboratory methods was prescribed or non-prescribed. Instead, all the detected medications
were specified as abused. Could the difference in detection of BZDs between group IA and group I might be explained by other causes than abuse such as (inappropriate) prescription of BZDs by MDs?

3. The study included OMT-patients from a tertiary addiction clinic for OMT-patients with psychiatric/somatic co-morbidities in the capital of Finland (para 3, p 5). Further, the patients all had all failed withdrawal for opioids prior to admission at the clinic. Hence, the study population includes a subgroup of OMT-patients that have psychiatric/somatic co-morbidities and are more hard-to-treat. Could the results have been influenced by this more than just a higher proportion being treated with methadone (as mentioned in Limitations)? And do you have any considerations by comparing your results with the results of other studies including unselected OMT-patients?

4. Regarding ethical considerations, it is not mentioned, whether and where the study has been approved.

Results

5. One of the main results was that craving of opioids and withdrawal were found to be associated with inadequate doses of OMT medication (para 3, p 2). However, craving of opioids and withdrawal might also be regarded as measures or indicators of inadequate doses of OMT medication. Therefore, could this association be considered a validation of your system for rating adequate doses rather than an actual result?

6. In Table 4, the proportions in percentage seem to be missing in several places, eg. by methamphetamine, norbuprenorphine and fentanyl.

Discussion

7. Regarding the last sentence in page 13, para 1, it is strange that cocaine was not detected in any of the groups (para 1 p 13). But as you state this might be explained by more infrequent use of cocaine in Finland compared to many other countries.

8. Gabapentin is a quite commonly prescribed medication in the treatment of cannabis dependence. Could the finding of this medication in group IA might reflect a medical treatment of the higher proportion of cannabis users in this group rather than gabapentin abuse?

9. Consistency in use of key terms should be applied. The terms "abuse" (para 3, p 14 etc.) and "misuse" (para 3, p 13 etc.) are used interchangeably.

10. In para 1 p 16, it is stated that: "In addition, the 5 number of patients was relatively small, giving rise to possible statistical type I and II errors". How does a small number of patients give rise to a type 1 error?
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.

Yes

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

Yes

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

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?
If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal