Reviewer’s report

Title: Gender differences in acute recreational drug toxicity: a case series from Oslo, Norway

Version: 0 Date: 14 Feb 2019

Reviewer: David Robinson

Reviewer's report:

The objective of this case series study of female recreational drug users was to report gender differences in clinical state and toxic agents. The author cite various references that female drug abusers (as defined by heroin dependence, overdoses, psychiatric disease, and substance use disorders) have higher mortality and worse morbidity than their male counterparts. Comparative gender studies associated with recreational drug use, as opposed to abuse, was not cited. Therefore, the background comments that the health of female drug users are generally poorer than males may not be substantiated when studying recreational users. Patients receiving methadone or are part of a drug rehabilitation program might have been used as controls.

The criteria excluded those who used drugs for suicide or self harm, and for cases involving harm to others. GHB is specifically used in some social communities as a disinhibiting medication given often to females intentionally as a 'date rape' drug. This study reports a significantly higher rate of ingestion/coingestion of GHB in female from both the outpatient and Hospital ED group. The trial also reports that it excluded those who were given it unbeknownst to them. How did the study group control for the potential for accidental but intentional inflicted ingestion? Would this have been less significant if the subjects were able to verify that they voluntarily took GHB as part of their substance usage during their visit?

The reported findings citing a lack of clinical difference between gender is more consistent with recreational drug users, as is the study group. The background citations describe a more chronic abusers with much more health issues. To enhance this study, a differentiation must be made between patients with preexisting health issues related to chronic drug abuse and those who actually used drugs recreationally.

Confidence intervals would have yielded more precision for the mean Peak CK and Cr data, and would could have yielded more information to the reader if the mean SBP was reported (as opposed to 'SBP≤ 90'). Also, comparatively worse hypotension in the outpatient group of females coingesting drugs with opioids is an interesting clinical finding worth mentioning, though not reported in the conclusions.

In summary, the outcomes of the trial reported that only about ¼ of recreational drug users presenting to a Norway health care system were female. Reports from the European Monitoring Centre (http://www.emcdda.europa.eu) support this study's findings, adding that Norway has the
10th highest lifetime prevalence for illicit drugs. In it, the ratio of females to males with illicit drug problems is comparable to this trial.

**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.

No

**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