Reviewer's report

Title: Baclofen for maintenance treatment of opioid dependence: A randomized double-blind placebo-controlled clinical trial

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Reviewer: Richard P Mattick

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General

Baclofen for maintenance treatment of opioid dependence: a randomized double-blind placebo-controlled clinical trial.

This paper by Assadi and colleagues examines the effect of baclofen on retention in treatment and other outcomes, including use of opioids and alcohol, opioid craving, opioid withdrawal symptoms and depression. The study used a relatively small sample of individuals from Iran who were reportedly opioid-dependent using DSM-IV criteria. Sixty-eight percent were using opium and 33% heroin, with approximately half inhaling/ingesting and half injecting these substances. Participants were detoxified as part of the study. The sample was male, probably reflecting the fact that few women become opioid dependent and present for treatment in Iran.

The authors found that there was better retention for baclofen than placebo medication, as well as a greater decrease in the severity of opioid withdrawal on the Short Opiate Withdrawal Scale and lower depression ratings on the Hamilton Depression Scale. They reported no difference for baclofen and placebo, however, in opioid positive urine samples, cravings for opioids and self-reported opioid and alcohol use.

The authors appear to be correct that this is the first randomised double-blind placebo-controlled trial of baclofen in the treatment of opioid dependence. Presented as a pilot study, this paper seems to add something to the literature, in as much as it does advance the information about the role of baclofen in this important area of public health. There are a number of issues with this paper as identified below. To the credit of the authors, however, it is a well written, clearly laid out paper. Their final conclusion seems reasonable that there is some evidence that baclofen may have some value in the management of opioid dependence, but larger scale studies are required to be conclusive.

Discretionary Revisions (which the author can choose to ignore)

1. The small sample size limits the value of the paper, an issue of which the authors are cognizant. To their credit the authors have conducted power calculations, mentioned in the discussion section, and are aware of the limitations of the data they present.

2. The use of the term ‘maintenance’ may not be the best in this context. Maintenance therapies usually refer to opioid agonists such as methadone or buprenorphine. An alternative use of maintenance therapy is naltrexone. Baclofen would appear to be a medication to deal with withdrawal symptoms, rather than to maintain patients on an agonist or antagonist which is an opioid.

3. While the authors do point to the synaptic action of GABAergic substances and the effects on various neurotransmitter systems, they do not clearly discuss the function of baclofen and similar
substances on opioid-dependent people. Baclofen is a muscle relaxant and as such may be retaining individuals in treatment by virtue of reducing withdrawal symptoms. This is consistent with results obtained on the Short Opioid Withdrawal Scale. One of the common nervous system effects of baclofen is daytime sedation and drowsiness, and again this is probably an effect that is appealing to opioid-dependent people and helps to minimise withdrawal symptoms. One of the problems with the paper is a failure to discuss clearly the mechanism whereby baclofen may achieve its apparent superiority over placebo. The effects observed in terms of retention, severity of opiate withdrawal and depression may all be attributable to this action. The comments from the authors in the background section concerning the reinforcing properties of baclofen are interesting, but there may be a much simpler explanation as to why individuals are retained at a greater rate. Greater discussion of the mechanism of action may be helpful and is recommended.

4. The paper states that participants could withdraw their participation at any time and transfer to a ‘conventional treatment’. It would be helpful to know what the conventional treatment for opioid dependence is in Iran.

Minor Compulsory Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

5. Abstract, methods: capital not required in the word ‘Self-report’
6. Background, third paragraph: recommend ‘in our best knowledge’ be replaced with ‘to the best of our knowledge’
7. Methods, subjects and setting, second paragraph: replace ‘seeking opioid detoxification at addiction clinic…’ with ‘seeking opioid detoxification at the addiction clinic’; replace ‘the research steering committee at psychiatric department’ with ‘the research steering committee at the psychiatric department’, etc.
8. Methods, detoxification phase, first paragraph: replace ‘in the last half of detoxification period’ with ‘in the last half of the detoxification period’; replace ‘in the end of detoxification period’ with ‘at the end of the detoxification period’

Note, although English is probably not the first language of the authors this has not prevented them from expressing themselves very coherently in English. There are, however, numerous occasions throughout the manuscript where the words ‘the’ and ‘a’ have been omitted (see above examples). The paper should be proof-read thoroughly prior to publication to rectify these minor omissions.

9. Figure 3 has letters of words in both axis and the key missing.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

None.

Advice on publication: Accept after minor compulsory revisions

Level of interest: A paper whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Declaration of competing interests:

None.