Reviewer’s report

Title: Effects of thoracic epidural analgesia on plasma cAMP and cGMP levels in patients with heart failure

Version: 3 Date: 6 September 2013

Reviewer: Peter Alston

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This is an interesting study that examines the effects of using thoracic epidural anaesthesia (TEA) along with standard pharmacological treatment, to treat heart failure. It examines a number of symptomatic, biochemical and surrogate outcomes. The revisions has much improved the paper. However, it still has a number of important limitations.

Major compulsory revisions

1. It is surprising that ethical approval was given to put epidural catheter in the patients in the control group given the risks of epidural haematoma and abscess.
2. Information regarding where the patients were during the study and how they were managed should have been provided.
3. An explanation why the four week period was used should have been provided. Four weeks is a very long time to have an epidural catheter in place because of the risk of infection and epidural abscess.
4. No study population size estimate was provided to justify the sample size of the study. Alternatively, a retrospective power analysis would have been valuable to reassure the reader that any lack of significance was not due to Type II statistical error.
5. Multiple testing was applied inflating the risk of Type 1 statistical error. Correction for multiple testing should have applied or one outcome nominated as the primary outcome of interest and the rest as secondary outcomes.
6. Details of the reliability of the biochemical tests that were used should have been provided as well who performed the tests.
7. Details of who performed the ultrasonography should have been provided and with what kind of machine. Details of ultrasound equipment and how the measurements were performed should also have been provided.
8. Details of what statistical package and on what operating system should have been provided.
9. Information who gave the epidural top ups should have been provided and why the drug, dosing and timing of top-ups were chosen.
10. There is no evidence that the distribution of the data was was explored to determine if it was normal. It is likely that the biological data was of non-normal distribution and if so it should have been first transformed using something the
natural logarithm so that it was near-normal distribution.

11. It would have been valuable to have presented the distribution as 95% confidence intervals.

12. No details of the analysis of variance models were presented.

13. Complications should have been more completely reported as it is still not clear what bleeding and infectious complications are i.e. did they have epidural haematomas or abscesses. If either of these complication occurred then it outweighs any symptomatic benefits associated with TEA. It is essential that this point is clarified. Also, the outcome of these complications needed to be described for example paraplegia. In addition, the complications need to be addressed in the discussion. Also, was there problems with hypotension in the TEA group.

Minor essential revisions

1. There should have been more discussion regarding the limitations of the TEA.
2. Some of the English is pejorative and insufficiently scientifically objective e.g. abstract, results section: remarkably, introduction, paragraph 1: indispensible.

**Level of interest:** An article of importance in its field

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

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests