Reviewer’s report

Title: Cluster randomised comparison of the effectiveness of 100% oxygen versus titrated oxygen in patients with a sustained return of spontaneous circulation following out of hospital cardiac arrest: a feasibility study. PROXY: Post ROSC OXYgenation Study

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Reviewer: Markus B Skrifvars

Reviewer's report:

REgarding the manuscript " Cluster randomised comparison of the effectiveness of 100% oxygen versus titrated oxygen in patients with a sustained return of spontaneous circulation following out of hospital cardiac arrest: a feasibility study. PROXY: Post ROSC OXYgenation Study" submitted to BMC Emergency Medicine.

This manuscript presents a feasibility study for conducting a large RCT on the use of oxygen in cardiac arrest. Given challenges in conducting pre-hospital cardiac arrest research a pilot such as this is warranted.

I have the following comments:

- The authors state in the Conclusions "We have shown that it is feasible to complete a randomised trial of titrated versus unrestricted oxygen in the first hour after ROSC following OHCA in the UK". If the authors state this as the main conclusion then they need to make a case for how big this RCT would be, and given the Results of this pilot, how long would that future RCT take to complete? This should also take into account the quite high rate of patients who were randomized but who did not receive the intervention. This would be a major challenge for such a trial.

- The fact that we do not really know how the intervention succeeded (oxygen saturation, used FiO2) in the lower group is a big problem. Was there any separation between groups?

- In the previous pilot from New Zealand (Hot or Not) hypoxia was a problem in the lower oxygen group, this is a worry. Where there cases of hypoxia in the titrated arm? How about cases where the patient has aspirated and requires 100% FiO2, where there such cases included?

- Is 100% FiO2 during transport to hospital current practice in the UK? If not, one may ask whether the 100% FiO2 group receives current standard care or something else. Or are the authors suggesting that indeed patients should receive 100% FiO2?
- In both groups 15-25% of the patients did not receive the intervention. Again this is a big concern and should be discussed.

- Given the small sample size I am not convinced that Table 2 is needed.

- The authors cite the smaller study in AMI patients suggesting that oxygen administration may be harmful. There is however a larger study from Sweden that showed no difference in outcome between those who received oxygen and those who did not. There was no benefit but no harm either.

- What the optimal oxygen level is in OHCA patients is currently unclear. Some studies suggest harm and some do not. I miss a more nuanced discussion of this in the paper.

- The authors cite the paper by Kuisma. This is an important paper but it needs to be stated that in that paper there was a difference in NSE favoring the lower FiO2 group in one subgroup only (those who did not receive TTM).

All in all the authors have studied a new approach to perform an RCT in the prehospital setting.

They have some valuable data but I think the presentation and analysis can be improved.

**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.

Yes

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

No

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