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

Version: 0 Date: 19 Jul 2018

Reviewer: Glenn M Eastwood

Reviewer's report:

Dear Authors,

The reviewed manuscript reports your study undertaken to evaluate the feasibility of titrating oxygen therapy to OHCA patients by EMS service officers. The endeavour to understand the feasibility of this intervention is of interest and has been explored, as described, by other investigators located outside of the United Kingdom.

As presented I did not find it easy to understand what the 'cluster' referred to. Initially I thought it was going to related to the titration of patients to the '100% oxygen' arm and then switch cluster to the 'titrated oxygen' approach. Yet it appears to read that you have recruited paramedics, provided training and then they were notified of the treatment allocation. Figure 1 only identifies the 'Algorithm for titration of oxygen + the consort diagram is the patient flow diagram. I do not see a cluster figure. Furthermore, as side from the treatment algorithm were there any other study tools or oxygen therapy allocation reminders provided for use at scene?

Background - The shortness of the background together with a clear objective is appreciated. However, as your trial was evaluating the pre-hospital delivery of oxygen to OHCA patients please provide a comment on the rationale/literature to this area. It may also help that, apart from your 'objective', which I'd recommend calling an 'Aim' is to then comment on the 'objectives of the trial'. By this I mean explaining what you go on to record in relation to feasibility, delivery, recruitment, treatment allocation and separation and patient outcomes. Note, the reference made at the end of the third paragraph doesn't meet the journal requirements.

No quality of life data at 90 days was presented, only survival status. Please amend.

The Discussion section was shorter than expected.

In the Summary of Findings - please identified 3-4 key findings based on the feasibility or not of your trial. There is the paramedic arm (recruitment, education, delivery), the ability to randomised, the ability to remain in the allocated treatment, and the patient outcomes (delivery of therapy, ability to obtain a useable trace) and arrival to hospital + hospital outcomes. Further,
there is only mention of the NZ study and not discuss of this study and its findings in relation to your trial. I would expect a paragraph or more comparing the two studies.

Limitations

While I agree that no separation via ABG findings were identified this was not an aim of your study. The feasiblity aspect looked at the ability to recruit paramedics, the ability of the paramedics to enrol patients, the ability to delivery the treatment, the reasons why treatment was both delivered or abandoned, the ability to record data, the ability to maintain a safe saturation and the ability or not for the hospital to continue treatment allocation. You haven't shown the oxygen saturation data at this stage.

For pragmatic and safety reasons it wouldn't be expected that blinding of treatment allocation in this study at this stage of development (feasibility + safety) would be a limitation. Also, the cluster component still confuses me as I don't understand clearly where the cluster is. The reference to the EXACT study could be address and expanded on in the Future trials section.

Your conclusion that it is feasible to enrol paramedics and delivery titrated oxygen therapy in the pre-hospital setting for OHCA patients isn't strongly supported by the data. It would be advisable that, following the known limitations and aspects identified during the PROXY trial that additional feasibility trials be conducted.

Comments related to the Manuscript, Tables and Figures

Manuscript -

It was submitted in tracked changed format. Please avoid this.

Figures -

Figure 1 has a 'comment' visible as this too is in tracked-change mode.

Figure 2 is unclear and wording is omitted from several boxes (e.g. allocation box and follow-up box).

Table

Table 1 - I found the working 'Arm A' and 'Arm B' lacked necessary information, please identify the group they represent. Further more this Table will need the abbreviations explained and would benefit from greater description of the cardiac arrest characteristics. Such characteristics would include greater baseline detail particular in the initial cardiac rhythm (shockable, non-shockable, undetermined), cause of cardiac arrest (medical, traumatic, drowning, drug overdose,
electrocution, asphyxia, not identified or missing), witness of cardiac arrest (none, paramedic, bystander, not identified, missing), CPR performed (by bystander, by paramedic, not identified, missing).

Table 2. Treatment group allocation should be identified here too please. If discharge means 'hospital' please state 'hospital discharge'

consider a table reporting the characteristics of paramedics is suboptimal. Please consider adding years of service, familiar with equipment, any estimate of the number of CA attended, any educational sessions attended in relation to the study protocol.

**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.

No

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

No

**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.

Not relevant to this manuscript

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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