Reviewer’s report

Title: Small volume plasma exchange for Guillain-Barré syndrome in resource poor settings: a safety and feasibility study

Version: 0 Date: 31 Jul 2017

Reviewer: Sohail Mulla

Reviewer’s report:

Written by: Saadul Islam and Sohail Mulla

We have provided our review primarily on the methodological rigor of the submission. Neither of us is a clinician or a statistician, so we would defer to more experienced individuals on providing a comprehensive review of the submission as it related to these matters. Nevertheless, we have made a few clinical and statistical comments for the authors to consider.

Summary

The submission was a protocol for a clinical study that aims to determine the safety and feasibility of small volume plasma exchange (SVPE) for Guillain-Barré syndrome (GBS). The investigators aim to recruit 20 adult patients with GBS from a single centre (the National Institute of Neurosciences) in Bangladesh. The patients will undergo six daily sessions of SVPE for eight days. The primary safety outcomes are the number of patients developing severe sepsis due to central line-associated blood stream infection (CLABSI) and venous thrombosis in the limb. The primary feasibility outcome is the ability to remove at least eight litres of plasma over eight days. There are multiple secondary outcomes of safety and feasibility as well, including the relative risk of CLABSI due to SVPE compared to CLABSI in a control group of at least 20 patients whom the investigators will recruit during the study period. The investigators have recruited 15 patients with GBS and 18 control cases, since March 2016.

Strengths

* First study to evaluate the safety and feasibility of SVPE in a low-resource setting.

* Background incidence of CLABSI will be measured in a control group without GBS who will undergo CVC in the same ICU and HDU during the same period as the GBS patients.

* Strict inclusion and exclusion criteria, including pre-specified diagnostic criteria of the outcomes.

* Primary and secondary outcome measures of feasibility and safety are defined a priori.
* Strict aseptic measures will be taken to minimize contamination and infection.
* Stopping rule is in place.
* Quality control of fresh frozen plasma will be done.
* Baseline measurements of CBC and Hepatitis B, C and HIV to be done intermittently.
* Comprehensive list of parameters for SVPE, hemodynamic and autonomic status, infection, and sepsis will be documented to measure safety. A combination of clinical, imaging, biochemical and microbiological data will be collected and analyzed for safety parameters.
* Different neurological examinations will be done to assess clinical, functional and sensation status.
* Strong data management protocol, including having an independent DSMB.
* CONSORT diagram depicting protocol and operation of the trial provided.
* Illustration and description of the SVPE kit and procedure provided.
* SPIRIT 2013 checklist adhered to and provided.

Weaknesses (in no particular order)

* The title of the paper indicates "low-income countries," which seems inconsistent with the fact that the authors are conducting the study in a single country.
* The authors state, in the discussion section, that SVPE "may represent an effective treatment for GBS." They repeat this statement a few times throughout the paper. Is this assertion based on previous data or the results of the study? If it is the latter, that would not be appropriate, since the authors do not designate any effectiveness outcomes in their trial.
* The authors include a questionnaire (Appendix 1C) to measure healthcare personnel's acceptability and satisfaction. It is unclear if the authors have evidence of the psychometric properties (e.g. validity, reliability) of this questionnaire in previous settings. If not, would the authors consider generating some evidence within this study? If that is not feasible, that is a potential limitation that the authors need to acknowledge.
* The authors indicate that SVPE is available at a relatively low cost, i.e. 500 USD. We wondered if the authors are able to provide a breakdown of the cost, so that readers are able to fully appreciate the cost efficiency of this intervention.
* The authors should consider collecting recent history of antibiotics as part of their baseline data collection, since that would influence the risk of infections observed in the study.
Also, we are not sure if GBS is a recurrent condition; if so, would a previous history of GBS need to be documented? Further, any other condition that might influence the risk or symptoms of GBS would be worth collecting.

* While we appreciate the authors enrolling a control group of patients, we wondered if they would be able to leverage any existing data sources (e.g. national database) to obtain relevant information as well.

* The authors indicate having recruited 15 patients, but it is unclear if between the time of submitting the protocol and now, whether they have been able to recruit more participants. If so, they should update the manuscript. If not, should they be concerned about not recruiting a sufficient amount of patients? Should attainment of the recruitment goal not be a feasibility outcome?

* Do the authors expect any loss to follow-up? If so, they should indicate strategies to deal with this in the analyses.

* It was unclear if patients' data was encrypted. The authors should clarify.

* While we appreciate the study has received ethics approval, we wondered what would happen if the study is terminated prematurely for safety reasons, and participants receiving SVPE are unable to afford the standard treatment.

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