Author’s response to reviews

Title: Efficacy of Botulinum Toxin A in Modifying Spasticity to Improve Walking and Quality of Life in Post-Stroke Lower Limb Spasticity - a Randomized Double-blind Placebo Controlled Study.

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Itemized answers to the queries of the Editor, Reviewer 1 and Reviewer 2

1. Declarations completed
- Ethics approval and consent to participate
- Consent to publish
- Availability of data and materials
- Competing interests
- Funding
- Authors’ Contributions
- Acknowledgements

2. Author’s contribution
Dr Anupam Datta Gupta (ADG) has conceived, designed and produced the first draft of the study.
Dr Stuart Howell (SH) has helped with the statistical analysis and sample size calculation for the study.
Prof Renuka Visvanathan (RV), Prof Ian Cameron (IC), Prof Simon Koblar (SK) and Prof David Wilson (DW) – all have provided intellectual content in the preparation and editing of the manuscript.

3. Comments- Reviewer 1
   i) Reviewer 1 commented that the study is a well-designed RCT.
   ii) Passive range of motion is included in the outcome measures. In Australia total dose of
Botulinum toxin is limited to 400 units by Therapeutic Goods Administration (TGA).

iii) Note will made of first stroke or previous strokes and the duration of stroke. Passive ROM will be recorded as an outcome measure.

iv) Patients with significant aphasia (mostly receptive aphasia) will be excluded because patients with significant receptive aphasia will have difficulty in following and retaining instructions rephysiotherapy particularly the home program. The structured exercise program and home therapy is an important aspect of the RCT.

v) A sensory evaluation will be carried out in all the participants.

vi) As already mentioned, the investigators are restricted by regulatory authority (TGA) re maximum dose of Botulinum Toxin which is 400 units.

4. Comments Reviewer 2

i) Objective-clear, Design- appropriate approach, Execution- experiment and analysis- NA (This is a protocol paper, the RCT is underway).

ii) Statistics- Statistical design -such as sample size and the statistical methods for analysing the results are described in the manuscript.

iii) Interpretation- The RCT is underway, analysis will be done after completion of the trial.

iv) Overall manuscript potential- Current version is technically sound as per reviewer 2.

Other comments- re type of stroke

We will be looking at the imaging (CT/MRI) of the participants to determine the type of stroke either Ischaemic or Haemorrhagic. The Pharmacy team involved with randomization is stratifying the participants in two groups Ischaemic vs Haemorrhagic to improve the clarity of the protocol.