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Peer Review File

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Reviewer A

Thank you for this opportunity to review the article by Popescu et al. I read the article with a lot interest. The authors present a very common healthcare issue in kids with neurological disability. Gastrointestinal intolerance is a frequent morbidity in this population. As authors discussed, refractory cases end up getting GJ tube which are difficult to maintain and leads to significant restriction on quality of life for both the care giver and the patients. Results of this study shows that, EndoFLIP guided assessment and botulinum injection can be a significant intervention for this pathology with encouraging results.

Reply: thank you

Reviewer B

The authors report on the rare experience of pyloric muscle measurements using EndoFLIP in children with neuromuscular disabilities. They also focus on the response to intrapyloric Botulinum toxin injection mentioning clinical symptoms and EndoFLIP measurements. This might have the potential to provide the essential base for pyloric measurements in pediatric populations. However, they are handling two big issues with so limited information that I am very unsure of exactly what was the point of this manuscript. Furthermore, this manuscript does not respect the elementary rules of scientific writing, i.e figure drawing. Therefore the authors are encouraged to rewrite it with more information, for example, normal EndoFLIP measurements and detailed clinical symptoms at pre/post BOTOX. Additionally, the manuscript would benefit tremendously from language and scientific editing by a professional editor.

Replay: thank you for taking the time to review our manuscript, we aim to share our limited experience with the wider pediatricians who are increasing faced with children with complex neurodisability and refractory foregut symptoms. We hope our data will provide further targeted therapeutic intervention and may set the foundation for future paediatric research in this subject. We did review the manuscript and extensively edited the language as detailed in reviewer C comments below.

Reviewer C

The authors provide a retrospective review of the use of the EndoFLIP device to measure pyloric diameter, distensibility, compliance and pressure in 12 children with

neuromuscular disabilities before and after pyloric botulinum toxin injections. This area is both interesting and novel since no studies have reported the use of FLIP in the pylorus in children and how it may be predictive of treatment response. However, this study would benefit from and in-depth comparison of FLIP findings with diagnostic tools, symptoms and response to treatment.

Line 56: Suggestion to begin sentence with word and not a number
Reply: done
Changes to text: number changed to word. Line 56

Line 65: correction of typo for “emptying”
Reply: done
Changes to text: correct spelling of emptying. Line 65

Line 71: Suggestion for this paragraph to be combine with paragraph above for continuity of thought from symptoms to treatment
Reply: done
Changes to text: reviewer suggestion was accepted.
Line 79: Suggest to consistently use the word “filled” rather than “inflated” to refer to filling of FLIP balloon
Reply: changed
Changes to text: inflated was changed to filled. Line 79

Line 82: Suggest adding pediatric references on the use of FLIP in pediatric studies (Menard-Katcher et al, Benitez et al).
Reply: added
Changes to text: suggested reference was added (reference number 19) line 84

Line 123: please clarify that this cutoff is in adults
Reply: clarified
Changes to text: the word adult was added at the end of the sentence line 123

Line 127: Suggest adding description of longitudinal FLIP procedure.
Reply: added
Changes to text: procedure description was included.

Line 129: Please clarify how the 335 measurements were obtained from the 12 patients. It is a little confusing to start with the 335 value. Suggest reporting number of patients and if needed to report the number of measurements to clarify what do

they refer to.
Reply: we recognize this can be confusion, thank you for noting this.
Changes to text, we have remove the confusing digit and started the sentence with the total number of children. We have also added an explanation on how the values were measured and recorded. Line 129-133

Line 132: Suggest creating a demographics table with clinical characteristics to better define the cohort studied.
Reply: created
Changes to text: table 1 was created.

Line 133: please clarify whether the two patients with “no unifying diagnosis” still qualify under the neuromuscular disorder group.
Reply: clarified.
Changes to text: one child had neuromuscular disorder and the other did not. Line 136

Line 135: please correct typo “but”
Reply: corrected. Thank you
Changes to text: typo was corrected. Line 143

Line 136: Please clarify type of symptoms, how they were assessed and whether there was significant improvement.
Reply: clarified
Changes to text: we have added an explanation on how the symptoms were assessed post Botox injection line 138-143

Line 137: reference to table 1 will need to be supported by additional information including assessment of significance between pre and post FLIP measurement as well as the follow up FLIP measurements.
Reply: added.
Changes to text: this data is now on table 2, extra columns were added to show the p values line 151-154

Line 142: please add reference to Table 1
Reply: added
Changes to text: reference to table 1 was added.

Line 142: please test for statistical significance or report increase or decrease in FLIP values.

Reply: added
Changes to text: p values were added. Line 151-155

Line 143: reference to Figure 1, please create a new graph for DI, compliance, diameter, and balloon pressure. Since the units are all different it would be helpful to see separate graphs for all FLIP measurements.
Reply: created
Changes to text: one figure contains all FLIP measurements.

Line 144: suggestion to start a new paragraph for the balloon pressure data and inform the reader why this is relevant to the study.
Reply: we accepted your suggestion. Thank you
Changes to text: new paragraph was started and an explanatory note was added. Line 158-165

Line 150: Suggest to expand the report of the symptoms data and the relationship with FLIP values. While it may be limited by the low sample number, it would be an interesting part of the data to explore further.
Reply: we thank the reviewer for this valid point. It has now been added.
Changes to text: we added an explanatory sentences to show the reported symptoms and their association with FLIP data. Line 169-174

Lines 155-163: unsure as how this section relates to the study and the data that is reported.
Reply: we wanted to show readers who may not be familiar with the paediatric guidance the available clinical recommendation for refractory foregut symptoms. We want clinicians to appreciate the value to EndoFLIP usage in avoiding an invasive form of enteral feeding ie jejunal tubes and the challenges associated with using jejunal feeding in children.

Lines 172-176: suggestion to include this information in the results and expand in the discussion.
Reply: this information is already present in the result section

Line 177-181: Information that should be included in the results.
Reply: already present in the result section

Lines 181-184: please elaborate on this area of “unplanned dilation”. Do the authors suggest there is stretching of the tissue that may lead to injury or just expansion of the

area due to balloon distension? How is the increasing pressure not affecting compliance and DI if pressure is part of the equation? Based on the results, all pressures were below the 60-mmHg safety pressure in the machine, should this be different in children? Please elaborate.
Reply: we agree with the reviewers observation about pressure values < 60mmHg, this statement is an observation we noticed during data collection and we wanted to share it with the wider audience. We do not think it can lead to tissue damage but it had certainly lead to pylorus stretch, is there a clinical value for this in older children it remains to be answered. We think it may have implications to small children where an unplanned pylorus dilatation can lead to inadvertent clinical intervention.
Changes to text: we have added an explanation to the text. Line 207-211

Line 192: Please report of procedure length and how the “easily performed” was assessed.
Reply added.
Changes to text we have added the duration of EndoFLIP (10min) line 219

Line 193: Please elaborate on how FLIP can guide the administration of pyloric botulinum toxin injection.
Reply: explained
Changes to text: explanation added. Line 224 - 226

Line 194: Please provide significance values for symptom data pre and post injection in results then ok to make this statement.
Reply added
Changes to text: p values were added.

Line 195: will need to be supported by data in results
Reply: added
Changes to text significant values were added and highlighted

Line 210: Suggest to include a paragraph on clinical implications
Reply we added a clinical implication paragraph at the end of the conclusion
Changes to text as above line 224 - 226

Line 301: Table 1- please provide significance values in table (pre vs post) as well as include longitudinal data. If data not evenly distributed please provide median values rather than means.
Reply added

Changes to text table 2 is modified.

Line 327: Figure 1- Please separate diameter from distensibility index and to include axis labels and statistical analysis results
Reply created
Changes to text a new figure was created to show all FLIP data separately

Line 331: Figure 2- Please separate pressure and compliance values and include axis labels and statistical analysis results
Reply created
Changes to text a new figure was created to show all FLIP data separately

Line 334: Figure 3- please provide correlation significance.
Reply added
Changes to text values added as suggested