Reviewer’s report

Title: Efficacy and tolerability of PEG-only laxative on faecal impaction and chronic constipation in children: a randomized controlled study vs a standard PEG-electrolyte laxative.

Version: 3 Date: 7 August 2012

Reviewer: Hannah Ladenhauf

Reviewer’s report:

Major Compulsory Revisions
(4), (5), (6), (7), (8)

Minor Essential Revisions
(1), (2), (3)

Discretionary Revisions
None.

Dear Authors,

Thank you for submitting your research on this interesting topic. This is a randomized, single-blinded, parallel group study that compared the effectiveness and tolerability of two polyethylene glycol solution laxatives, one with electrolytes, and the other one without. I did read this article with interest; however some question did come up during reading your article.

Conflict of Interest, Funding:
You state, that the experimental products you used were supplied free of charge by PROMEFARM. From my understanding, the results of your study do support the merchandise of the new PEG-electrolyte laxative, distributed by PROMEFARM. Consider clarifying your industrial relationship with PROMEFARM. Also this should be mentioned in your conflict of interest statement.

Enrollment of Patients:
1) Age:
In your methods section you mention, that children aged between 2 and 16 were included in your study. Your patient demographics (see table 1) divide all children according to their age into three subgroups, with subgroup nr. 1 counting a total of 30 vs. 26 children. The mean age of children is 5.5 years. However, in your discussion, you state, that “we evaluated the use of PEG products in children aged 4 years and older”. Does that mean you did not include any children aged 2 or 3 years old? Please clarify by supplying an age range for all subgroups.
Study Program:
2) Faecal Impaction:
Visit 1 did occur at day -7/-10. If a child with faecal impaction was enrolled, you started treatment immediately. GCP rules, state that you have to consent parents 24 hours before enrolling into the study. How did you resolve this issue for the ethical committee? Also treatment for faecal impaction lasted 7 days, does this mean at visit 2 you stopped treatment? Did you do a follow-up on these patients?

3) Follow-Up:
Did you follow-up patients with chronic constipation after visit 3? Please clarify.

Analysis:
4) You state that two different study groups were set up: one including children with faecal impaction, one with children that were treated for chronic constipation. In your results section you state that you can not comment on the patients with faecal impaction, since only 14 children could be enrolled. Therefore, you should be consistent in not commenting on these patients – unlike in the discussion part, where you still do so – please see comment Nr. 8. Moreover, from my point of view, you should not include these children into your analysis because of the substantially different etiology and timing of administration. Thus, these 14 children ought to be excluded from your analysis.

5) In your flow-chart (see figure 1) you show us, that 96 children were randomized. Of those 49 were consented for the PEG only group, 42 for the PEG-EL group.

In the PEG only group 1 dropped out for bad taste, in 1 the treatment was interrupted. Also 2 patients used stimulant laxatives (see table 2). In your exclusion criteria (methods section) you state, that “children receiving medication influencing gastrointestinal motility” were excluded. Still you analyzed 48 instead of 45 (this number including all patients with chronic constipation and faecal impaction).

In the PEG-EL group 42 received treatments, 2 dropped out due to bad taste, one for adverse effect. 3 children used an additional stimulant laxative. Therefore, only 36 children should have been analyzed.

I don’t understand why you introduce exclusion criteria if you do not implement them and nevertheless include all patients into your analysis. This represents a major flaw in the study setup and makes the reader doubt the appropriate care in observing your own rules. Either exclude these children or further clarify your inclusion/exclusion criteria.

6) Power analysis:
In your statistical analysis you tell us you conducted a power analysis. You state, that “with a type I error of 5% and type II error of 20%, 44 patients per group were needed to test the null hypothesis”. You included 48 and 39 children (which
is too little to begin with), including either faecal impaction or chronic constipation. If you exclude the children according to your exclusion criteria, and also those with faecal impaction, only 38 versus 29 children remain.

While it is certainly preferable to conduct sensitivity analysis beforehand, one should generally subsequently stick to its results. I don't know why you did not – please explain.

Discussion:
7) You conclude that “both agents were effective, safe and well tolerated”. Since you did not evaluate safety you can not comment on it. Only because you did not encounter side effects in more than 2 patients you can not comment on safety since this was not the aim of your study. I would suggest leaving this out.

8) You write, that “this study confirms that PEG-based agents are also effective for faecal impaction.” In light of your previous statements, your statistical analysis does not allow you to conclude this, since your number of participants is too small.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.