November 14, 2012

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name:\*\*\*).

**Title:** **EGD-assisted Bowel Preparation for Colonoscopy**

**Author:** Robert L. Barclay, MD, MSc, FRCP(C)

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO: 2345**

The manuscript has been improved according to the suggestions of reviewers:

1. Reviewer 00468097
2. Reviewer 00043115
3. Reviewer 3 (unknown number)

The following are itemized responses (in blue) to the reviewers’ comments:

**Reviewer 00468097**

1. Was any substantial nausea encountered?

Table 2. indicates the nausea profiles that were experienced by control and EGD-assisted prep groups. There was a statistically significant difference in the incidence of nausea between the groups, which favored EGD-assisted prep. This difference has been noted in the discussion, p. 15.

1. How many patients required anti-emetics to assist in prep ingestion?

Patients received a single dose of metoclopramide prior to either the EGD-assisted or oral dose of prep. No additional anti-emetics were used to assist in prep ingestion.

1. How many people did not complete the prep?

Table 2. indicates the numbers of subjects who were unable to complete either prep.

Six of 40 were unable to complete conventional prep and 3 of 42 subjects were unable to complete the EGD-assisted prep regimen. This difference was not statistically significant (P=0.2963)

1. How many electrolyte disturbances were encountered?

There were no clinically significant electrolyte disturbances encountered in either prep group.

Pre- and post-prep electrolyte values were not measured.

**Reviewer 00043115**

1. Authors should indicate the meaning of EGD stands even if it is known.

The full form of EGD – esophagogastroduodenoscopy – has been defined in the introduction paragraph.

1. I do not understand why there was only 5 minutes time between mean procedural EGD-assisted prep and EGD in PEG group subjects if the authors state that the time of instillation of the solution was 10 to 15 minutes. It would have been interesting to ask patients for the acceptance of EGD in both groups.

The difference in EGD procedure times between EGD-asssisted and conventional-PEG prep groups is more accurately appreciated by taking into account mean times and outliers. Mean times provide a more meaningful comparison between the groups than medians. Using means is also statistically appropriate as the EGD-procedure times fit a normal frequency distribution. Thus the analysis of the EGD times has been performed to address these aspects.

Six subjects in the EGD-assisted prep group had EGD procedural times of 10 minutes or less: Two who did not tolerate the endoscopic infusion of prep solution and 4 in whom the entire volume of prep solution was able to be instilled in less than 10 minutes. After eliminating these outliers from the analysis of EGD procedure times, the mean EGD-time in EGD-assisted prep subjects was 24 ± 10 minutes, compared to 15 ± 7 minutes in conventional-PEG prep subjects (P < 0.0001).

The above paragraph has been added to the Results section, p. 14.

1. It is not necessary that the authors indicate the DOI or PMID in the references when they come from published articles.

Changes will be made to the reference notations as needed.

**Reviewer # 3**

1. Page 5, first paragraph, last sentence. The suggestion that NG assisted bowel preparation carries the potential for ‘death’ is a little extreme. Overloading the foregut by infusing a large volume of polyethylene glycol in a sedated patient would, in my opinion, also carry the real potential for emesis and aspiration. As the author knows, emesis involves emptying of the foregut past the pylorus, and can include contents from the duodenum.

This comment is duly noted and important. Text has been modified on page 5, by deleting the risk of death associated with NG assisted preparation. I believe the existing sufficiently acknowledges the unknown but potential for serious risk of EGD-assisted preparation.

1. Methods, page 6, first paragraph, last sentence. Not sure what this means, please reword.

This sentence has been omitted.

Next paragraph: the author says ‘most common indication… was GI bleeding but other indications were permitted’ --- what other indications?

The non-bleeding indications included abdominal pain, positive fecal occult blood test with associated upper GI symptoms, and metastatic cancer of unclear origin. This sentence has been added to Methods section.

1. Methods, page 6. The author does not describe the patient population enrolled. The most compelling reason for performing a colonoscopy following an upper endoscopy would be patients with occult GI bleeding or iron deficiency anemia, with symptoms localizing the source to the foregut, where upper endoscopy was negative. In almost all clinical instances, the decision for bidirectional endoscopy can be made prior to upper endoscopy. In these instances, it is not good practice to split the procedures to separate sessions, as the patient then needs to undergo conscious sedation (with all its inherent risks) on two separate occasions.

The vast majority of procedures were performed for GI bleeding that was either suspected to be arising from an upper GI source; or to exclude an upper GI bleeding site in patients who presented with hematochezia.

1. Methods, page 7. Although there were 15 endoscopists in the author’s practice, he performed over half the procedures. There was no physician blinding. These are sources of bias.

As elaborated in Discussion, p. 18:

The fact that most of the EGD-assisted procedures were performed by a single endoscopist limits generalizability regarding safety of the procedure. In terms of study design, it was impractical for this study to be double-blinded, since the scheduling of hospital-based physicians precluded blinding endoscopists to patients’ prep assignments. However, the risk of physician bias in grading the prep was mitigated by adherence to a validated prep scoring system and by the fact that the majority of colonoscopies that followed EGD-assisted preparation were performed by endoscopists who had not conducted the prior EGD.

Further, when the analysis was confined to procedures in which the physician had been blinded to the prep assignment, the results mirrored those of the overall population of subjects.

1. Page 8. The author notes that PEG infusion was continued only if there was sufficient ‘bowel motility’ – how was this ascertained in the sedated patient? How was consistency established across the 16 endoscopists in the study?

Based on early experience with this method, endoscopists were given instruction to observe the presence of duodenal contractions and the effect that this had on the ability to instill more fluid. For example, if there was adequate motility to clear the lumen of fluid to such a degree as to appreciate an air-fluid interface, as opposed to a lumen completely full of fluid, then additional PEG solution could be instilled. This text has been added to Methods section, p. 9.

1. The fact that enemas were administered prior to colonoscopy confuses the results, as a tap water enema can by itself ensure adequate cleansing of the left half of the colon. This could have impacted the Ottawa scores used to assess outcome.

It is true that enemas may have impacted the cleansing scores. However, since both conventional and EGD-assisted subjects received this additional preparation, differences in the overall level of colon cleansing must be attributable to other factors.

1. Procedure durations are not quite consistent with the methods described. The range of times are described (page 13) as 3 min to 25 min for EGD assisted subjects. I would contend that one would be hard pressed to perform a diligent upper endoscopy without fluid infusion in 3 min! If the fluid infusion phase took 10-15 min, these numbers do not add up.

To correct the reviewer, as indicated in Results section, p. 14, EGD-times for EGD-assisted subjects ranged from 6 to 45 minutes; for conventional-PEG subjects, 3 to 25 minutes.

Regardless, I disagree that 3 minutes is an insufficient amount of time to perform a complete and thorough EGD. While there are no published data regarding what constitutes a sufficient time for an EGD, current ASGE guidelines recommend a minimum of 6 to 8 minutes during the withdrawal phase of a normal colonoscopy. I would submit that half this amount of time is sufficient to perform EGD, which is a much less time-consuming and tedious task which does not entail time-consuming maneuvers such as inspection behind haustral folds, washing and suctioning and segmental insufflation that are demanded of colonoscopy

The difference in EGD procedure times between EGD-asssisted and conventional-PEG prep groups is more readily appreciated by taking into account mean times and outliers. Mean times provide a more meaningful comparison between the groups than medians. Using means is also statistically appropriate as the EGD-procedure times fit a normal frequency distribution.

Six subjects in the EGD-assisted prep group had EGD procedural times of 10 minutes or less: Two who did not tolerate the endoscopic infusion of prep solution and 4 in whom the entire volume of prep solution was able to be instilled in less than 10 minutes. After eliminating these outliers from the analysis of EGD procedure times, the mean EGD-time in EGD-assisted prep subjects was 24 ± 10 minutes, compared to 15 ± 7 minutes in conventional-PEG prep subjects (P < 0.0001).

The above paragraph has been added to the Results section, p. 14.

1. Page 13, second paragraph, and page 8, second paragraph. The author mentions on page 8 that PEG infusion was ‘continued only if there was sufficient motility…’, and describes patients on page 13 where volume infused was decreased to accommodate for gastric emptying. Further, fluid refluxing back into the stomach was aspirated. Therefore, it does not sound that the volume of fluid infused was standardized. Please comment and explain further.

As indicated in Results section, p. 14, two subjects in the EGD-assisted prep group were administered a small volume of prep due to poor gastric emptying. In all other EGD-assisted prep subjects, only a small amount of prep solution was suctioned from the stomach, so that nearly all subjects received a standardized 2-liter infusion of prep solution. Text added to p. 15 for clarification.

Thank you again for publishing this manuscript in the *World Journal of Gastroenterology.*

Sincerely yours,

Robert L. Barclay, MD, MSc, FRCP