Format for ANSWERING REVIEWERS

June 15, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 19420-review.doc).

Title: Current Role of Non-Anesthesiologist Administered Propofol (NAAP) Sedation in Advanced Interventional Endoscopy

Author: Daniela Elena Burtea, Anca Dimitriu, Anca Elena Maloş, Adrian Săftoiu

Name of Journal: *World Journal of Gastrointestinal Endoscopy*

ESPS Manuscript NO: 19420

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

Reviewer 1 (02455208)

Comment: A very well-written review, concise and comprehensive review. The only drawback is that this subject has been published extensively, both as reviews and as clinical trials It would be interesting if the authors would present their own strategy.

Response: We have addressed our own strategy in the revised manuscript (Page 10, Last Paragraph).

"Our own approach for the patients with advanced interventional endoscopic procedures (EUS and/or ERCP) consists of exclusive use of propofol sedation in the presence of an anesthesiologist, as required by the current national and local legislation practices. Based on a total number of 192 patients examined during one year in the Research Center of Gastroenterology and Hepatology Craiova, Romania, we have encountered no severe adverse events, with drowsiness, nausea, vomiting, dizziness, headache, coughing or shivers being the most frequent, while less than 2% of patients had mild braycardia."

Reviewer 2 (00031150)

Comment: This is a good overview on EDP (endoscopist directed propofol sedation). However there is are a few points to be clarified: 1) P6, cahpter 2: There exists one study which states the combination of propofol and midazolam to be better than a mono-medication. Sieg a, bng-study group, Beck S et al. J Gastroenterol Hepatol. 2014 Mar;29(3):517-23. Safety analysis of endoscopist-directed propofol sedation: a prospective, national multicenter study of 24?441 patients in German outpatient practices. 2) The effect of sedation on pulmonary syndrome is not described: There exists one study describing exactly the risk of pulmonary syndrome in sedated patients: Respiratory Complications in Outpatient Endoscopy with Endoscopist-Directed Sedation Kilian Friedrich, Sabine G. Scholl, Sebastian Beck et al.J Gastrointestin Liver Dis. 2014 Sep;23(3):255-9.

Response: We briefly discussed and added both references according to the reviewer's sugestions (Page 9, Last paragraph, Ref. 38, Page 10, First paragraph, Ref. 43).

Reviewer 3 (02455208)

Comments: Title and short title (running head): appropriate to define the content of the article. **Key words: are missing.** Abstract: not structured, 157 words, informative. Core tip: 89 words, appropriate. Introduction: 489 words, the reader is acquainted with the known facts about sedation in endoscopy. The article is divided into

meaningful chapters addressing the topic. Methods of sedation: 712 words, explained are different, most commonly used sedation drugs: benzodiazepins (midazolam, alprazolam, bromazepam, diazepam), opioids (fentanyl and meperidine/pethidine) and propofol. **Advanced endoscopy: advanced therapeutic procedures such as EUS or ERCP (but also difficult polypectomy/mucosectomy, PEG insertion and others ??) are often longer and complicated, thus requiring higher doses of sedatives.** Non-anesthesiologist administered (NAAP) propofol sedation: 568 words, the chapter presents guidelines of associations (such as European Society of Gastrointestinal Endoscopy (ESGE), European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA), European Society of Anesthesiology (ESA)), and the advantages/disadvantages of this procedure sedation. Trained registered nurses or endoscopists can safely administer propofol during ongoing endoscopy, with a very low rate of respiratory events requiring endotracheal intubation. **However, it will be necessary to clarify the legal issues that may arise if the complications of sedation occur when administered by endoscopist/trained nurse.** Conclusion: short, 96 words, with a clear final message: expectations of the authors that this form of sedation will in the future prevail in hospitals and private practice. References: 44, contemporary, from 2000 (Acad Emerg Med) to 2015 (World J Gastrointest Endosc), with the guidelines of the most influential associations (including Japanese - 2015, Spanish - 2014, American Association for the Study of Liver Diseases; American College of Gastroenterology; American Gastroenterological Association Institute; American Society for Gastrointestinal Endoscopy; Society for Gastroenterology Nurses and Associates - 2012, European Society of Gastrointestinal Endoscopy, European Society of Gastroenterology and Endoscopy Nurses and Associates, and the European Society of Anaesthesiology Guideline - 2010, “Sektion Endoskopie im Auftrag der Deutschen Gesellschaft für Verdauungs - und Stoffwechselerkrankungen” e.V. (DGVS) 2008...) Conflict of interest: no conflict declared. Source of funding: the article was financed by the Partnership program in priority areas – PN II, implemented with support from National Authority of Scientific Research (ANCS), CNDI – UEFISCDI, ROMANIA, project nr. 2011-3.1-0252 (NANO-ABLATION).

Response:

The following key words were added at the suggestion of the reviewer: Non-Anesthesiologist Administered Propofol (NAAP) Sedation, Advanced Interventional Endoscopy, Endoscopic Ultrasound (EUS), Endoscopic Retrograde Cholangiopancreatography (ERCP) (Page 2, Last paragraph)

As the article was directed to distinct subtypes of advanced interventional procedures (EUS and/or ERCP), we have not included other types of endoscopic procedures which might require less sedation (such as EMR, ESD, PEG, etc.).

According to the reviewer comment a phrase has added to highlight the legal implications of NAAP procedures (Page 10, First paragraph): “In order to generalize this approach there are important legal issues that may arise if sedation complications occur during NAAP procedures, while these legal implications usually have country or even hospital specificities and particularities.”

Thank you again for publishing our manuscript in the *World Journal of Gastrointestinal Endoscopy*

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Kind regards,

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