

## EDITORIAL

# Will societies of anesthesiologists partake in the take-off of non-anesthesiologist administration of propofol?

## INTRODUCTION

In this issue of the Revista Española de Enfermedades Digestivas, Álvarez et al. express their concern about non-anesthesiologist administration of propofol (NAAP) for gastrointestinal endoscopy (1). In Europe, the conflict between endoscopists and anesthesiologists was at a peak in 2010 when a Guideline about NAAP was endorsed by three European Societies, namely the European Society of Gastrointestinal Endoscopy (ESGE), the European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA) and the European Society of Anaesthesiology (ESA) (2). The ESA retracted its endorsement of this Guideline two years later, acknowledging that “Following evaluation of the scientific evidence by the ESA guidelines committee, the Board of Directors of the ESA decided unanimously to endorse the report. However, following their publication, a majority of the national societies of the ESA felt unable to support this guideline.” (3). We were astonished at the ESGE and ESGENA that the ESA endorsement of the Guideline was withdrawn for political reasons and not on the basis of new evidence that contradicted the Guideline. Indeed, the motives of the retraction of endorsement were not “highly dangerous for the safety and quality of endoscopic procedures”, as cited by Álvarez et al. within quotation marks although these words are absent from retraction letters (3,4).

Unfairness contributes to make people intransigent while the debate should have decreased in amplitude with time, good will, and the accumulation of evidence demonstrating the safety of NAAP.

## Morbidity and mortality related to sedation for endoscopy

With respect to the interpretation of Vargo’s study, I would allow Dr. González-Huix to defend himself about personal attacks but would nevertheless mention errors made by Álvarez et al. when they state “affirm that just one of ten patients died from sedation is a complete speculation; perhaps Vargo ignores the fact that most of the complications mentioned may be avoided with adequate sedation by an appropriately trained professional.” In reality, for EGD alone, Vargo et al. calculated the mortality rate based on 5, not 1, deaths (“Five deaths in the EGD group were potentially because of over-sedation (patients 5, 6, 8, 9, and 10), resulting in a rate of 5 of 508,053 (approximately 1/101,611)” (5). The arrogance of Álvarez et al. in insinuating that J.J. Vargo is an ignorant in terms of sedation is really surprising as J.J. Vargo alone has published more peer-reviewed articles about propofol sedation than the three authors who have signed this article.

Lower, Álvarez et al. again make incorrect citations, within quotation marks: Vargo et al. did not state “a prospective study in this setting would be unpractical given the low frequency of adverse events”, he stated “an appropriately powered randomized, prospective, controlled trial would be impractical because of the rarity of significant events” (5). This is completely different: Vargo et al. report that true, clinically relevant, adverse events occurred in 0.2%-0.4% of 1.38 million NAAP procedures. Such an incidence is too low to permit comparisons in a normal sized RCT with sufficient power to detect statistically significant differences.

This explains why the incidence of hypoxemia and of hypotension is reported in the scientific literature: these events are relatively frequent with propofol but hopefully not every hypoxemia or hypotension has clinical consequences. Thus, hypoxemia and hypotension serve as surrogate markers of true clinical complications. They permit statistical comparisons in relatively small samples of patients. Therefore, adverse events are not downgraded in the literature as suggested by Álvarez et al. but they are used as surrogate markers of clinical complications, allowing for comparisons in relatively small samples of patients.

Contrary to what is suggested by Álvarez et al., the incidence of such surrogate markers, written as a litany of abstract summaries in their article, are similar (or lower) when propofol is administered by an endoscopist as compared with an anesthesiologist. This can be observed by anyone who practices in the setting of both NAAP and anesthesiologist-administered propofol and it has been shown in all of the three RCTs that compared propofol sedation administered by an anesthesiologist *vs.* a non-anesthesiologist:

- In a first RCT (n = 90) (6), desaturation ( $\text{SaO}_2 < 95\%$  for more than 30 s) was more frequent if sedation was administered by an anesthesiologist than an endoscopist (36% *vs.* 7%, respectively;  $p < 0.008$ ). Of note, although sedation was deeper in the anesthesiologist group, the patient satisfaction and willingness to undergo further endoscopies was higher in the endoscopist-administered sedation group.

- In the second RCT (n = 277) (7), the incidence of adverse events was 39% in each group. There were no differences in cecal intubation and adenoma detection rates. Recovery times were longer in the anesthesiologist-administered sedation group (67 vs. 58 minutes; p = 0.03).
- In the third RCT (n = 208) (8), propofol-related cardiorespiratory adverse events were recorded in 2% vs. 3% of subjects sedated by an anesthesiologist vs. a gastroenterologist who used the SEDASYS System, respectively.

Also, a meta-analysis of 26 prospective non-randomized studies (> 5,000 advanced endoscopic procedures including EUS, ERCP, and deep small-intestinal enteroscopy) found similar patient safety when propofol sedation was administered by a non-anesthesia provider vs. an anesthesia provider (9).

## Adequate provider for propofol sedation during digestive endoscopy

In the second chapter, the authors state “Our opinion is crystal clear, but scientific opinions must be carefully demonstrated”. This chapter is confusing as the authors first state “the paper by Adeyemo et al. (14), which attributes a 2.5% increase in perforations to propofol administration by anesthesiologists. Other claims along these lines have been published, whose scientific rigor cannot stand up to the slightest analysis.”. Indeed, the study by Adeyemo et al. reported incidences of colonic perforation of 2.7/10,000 vs. 6.9/10,000 with traditional vs. propofol-based sedation, respectively, corresponding to an absolute increase in incidence of 4.2/10,000; a 2.5% perforation rate would indeed have been outrageous (10). It is unclear to me what the authors mean by this but, for their information, three other retrospective studies (2536, 6371, and 1144 900 colonoscopies) have found no association between propofol sedation and perforation (11-13).

Then the authors affirm “for complex procedures such as ERCP, patients must be sedated or anesthetized by an anesthesiologist as anesthesiologist-directed sedation increases efficacy for advanced endoscopic procedures”. The study cited to support this affirmation reported a lower success rate of ERCP in patients sedated by non-anesthesiologists compared with anesthesiologists (14). However, non-anesthesiologists used fentanyl, midazolam, and diphenhydramine, not propofol, as opposed to anesthesiologists. The difference was indeed in the drug used, not in the profession of the caregiver who administered the drug. Multiple studies have reported good results with NAAP for ERCP; also, in a Cochrane review that analyzed four RCTs, NAAP was found to be as safe as traditional sedation (midazolam and meperidine) for ERCP (15).

With regard to the lack of evidence supporting that a training program allows the performance of NAAP safely, Álvarez et al. should look into the multiple studies showing that NAAP is safe as non-anesthesiologists underwent training before performing NAAP. Progress must be made to standardize and validate training for NAAP. At the ESGE, we have developed together with anesthesiologists and nurses a Curriculum for sedation training in gastrointestinal endoscopy (16). Participants in the elaboration of that Curriculum have reported that such a training allows them to perform NAAP safely (17); they also developed and validated a test for assessing the qualifications of NAAP providers in gastrointestinal endoscopy (18).

With respect to the criticism to the study by Pambianco et al. who used the SEDASYS system, we cannot be surprised that Álvarez et al. again invented a quotation: “Most interesting was an incidence of serious complications, including hypoxemia, of 5.8% in the SEDASYS group, which increased to 8.7% in the control group. With these results one cannot claim, as the authors do, that *no scientific evidence shows fewer adverse events for endoscopic sedation when managed by an anesthesiologist rather than an endoscopist or a sedation delivery system*”. This statement is incorrect because no studies have compared sedation by an anesthesiologist *versus* a non-anesthesiologist using the same drugs, at the same doses, in the same patients, for the same procedures. There is no sense in providing such categoric statements in the absence of supporting scientific evidence”. Ironically, the last sentence applies to Álvarez et al. themselves as the three RCTs detailed above compared propofol administered by an anesthesiologist vs. a non-anesthesiologist (6-8). The argument of identical dose is irrelevant as the aim of sedation is to obtain a safe, high-quality, examination to the satisfaction of all intervenants. Higher satisfaction may be obtained with lower drug doses as shown by Poincloux et al. in their RCT, for example by administering it at different moments of the procedure and this is known only after some practice of endoscopy.

## Economic aspects

Everybody will agree with the authors that cost concerns should not prevail over patient safety. As the safety of NAAP performed under strict conditions has now been well demonstrated, thus costs have become a relevant concern. Nobody could negate that saving 40% of total costs would be extremely important from a health care perspective. This is particularly true for screening colonoscopy because a test used for screening the general population must be cost-effective. The additional cost of indiscriminate anesthesiologist involvement in colonoscopy is a serious concern (19,20).

To help in reducing costs, Álvarez et al. mention that the ASGE supports the performance of endoscopy by non-medical personal with a 1B evidence level but they fail to state that this support is only for flexible sigmoidoscopy for colorectal cancer screening and accompanied by the statement “There are insufficient data to support nonphysician endoscopists to perform colonoscopy and upper endoscopy” (21). Sigmoidoscopy for screening colorectal cancer has become outdated.

Finally, the authors themselves destroy their own arguments as they state “Sedation by non-anesthesiologists for ASA I-II patients using midazolam and fentanyl (drugs for which specific antagonists are available) and a well-defined sedation scale with graphically recorded values every five minutes, avoiding deep sedation and the complications deriving thereof, may be acceptable as it will, in our view, guarantee patient safety.” As outlined above, multiple studies have shown that NAAP is as safe as sedation based on midazolam and fentanyl, an option that is “acceptable” by Álvarez et al. (9).

## CONCLUSION

Propofol sedation is underused (22), and a better allocation of anesthesiology resources would benefit the patients and the community globally. Honest discussion is a prerequisite for a better collaboration. Corporatism should have no place in it. I encourage anesthesiologists, nurses and endoscopists to engage in such a debate at a local level. This may be easier than at a Society level and may induce changes. Reading the European training Curriculum, which was written by gastroenterologists, nurses and anesthesiologists, could serve as a basis. The process to achieve a better collaboration is difficult but rewarding. Some anesthesiologists may have something to lose in such a process but they should think that, on the other hand, the endoscopists have nothing to gain.

The train of NAAP has started and the collaboration of anesthesiologists to implement NAAP in proper conditions is a must. Hopefully, Anesthesiology Societies will seize this opportunity and engage in a fair discussion with their counterparts in the Endoscopy and Nurse assistant fields to improve endoscopic sedation.

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## REFERENCES

1. Álvarez J, Cabadas R, De la Matta M, et al. Patient safety under deep sedation for digestive endoscopic procedures. *Rev Esp Enferm Dig* 2017;109(2):137-43. DOI: 10.17235/reed.2016.4572/2016
2. Dumonceau JM, Riphaus A, Aparicio JR, et al. European Society of Gastrointestinal Endoscopy, European Society of Gastroenterology and Endoscopy Nurses and Associates, and the European Society of Anaesthesiology Guideline: Non-anesthesiologist administration of propofol for GI endoscopy. *Endoscopy* 2010;42(11):960-74. DOI: 10.1055/s-0030-1255728
3. Pelosi P, Board of the European Society of Anaesthesiology. Retraction of endorsement: European Society of Gastrointestinal Endoscopy, European Society of Gastroenterology and Endoscopy Nurses and Associates and the European Society of Anaesthesiology Guideline - non-anesthesiologist administration of propofol for gastrointestinal endoscopy. *European Journal of Anaesthesiology* 2012;29(4):208, author reply 208-9. DOI: 10.1097/EJA.0b013e32834f5e5a
4. Perel A. Non-anesthesiologists should not be allowed to administer propofol for procedural sedation: a Consensus Statement of 21 European National Societies of Anaesthesia. *European Journal of Anaesthesiology* 2011;28(8):580-4. DOI: 10.1097/EJA.0b013e328348a977
5. Vargo JJ, Niklewski PJ, Williams JL, et al. Patient safety during sedation by anesthesia professionals during routine upper endoscopy and colonoscopy: an analysis of 1.38 million procedures. *Gastrointest Endosc* 2017;85(1):101-8. DOI: 10.1016/j.gie.2016.02.007
6. Poincloux L, Laquière A, Bazin J-E, et al. A randomized controlled trial of endoscopist vs. anesthetist-administered sedation for colonoscopy. *Dig Liver Dis* 2011;43(7):553-8. DOI: 10.1016/j.dld.2011.02.007
7. Ferreira AO, Torres J, Barjas E, et al. Non-anesthesiologist administration of propofol sedation for colonoscopy is safe in low risk patients: results of a noninferiority randomized controlled trial. *Endoscopy* 2016;48(8):747-53. DOI: 10.1055/s-0042-105560
8. Pambianco DJ, Kudo S-E, Martin J. A comparison of propofol sedation by an anesthesiologist versus a gastroenterologist-led team using the SEDASYS® System. *Gastrointest Endosc* 2015;81(S):AB192. DOI: 10.1016/j.gie.2015.03.1946
9. Goudra BG, Singh PM, Gouda G, et al. Safety of non-anesthesia provider-administered propofol (NAAP) sedation in advanced gastrointestinal endoscopic procedures: comparative meta-analysis of pooled results. *Dig Dis Sci* 2015;60(9):2612-27. DOI: 10.1007/s10620-015-3608-x
10. Adeyemo A, Bannazadeh M, Riggs T, et al. Does sedation type affect colonoscopy perforation rates? *Dis Colon Rectum* 2014;57(1):110-4. DOI: 10.1097/DCR.0000000000000002
11. Amornyotin S, Prakanrattana U, Kachintorn U, et al. Propofol-based sedation does not increase rate of perforation during colonoscopic procedure. *Gastroenterol Insights* 2010;2(1):4. DOI: 10.4081/gi.2010.e4
12. Bielawska B, Day AG, Lieberman DA, et al. Risk factors for early colonoscopic perforation include non-gastroenterologist endoscopists: a multivariable analysis. *Clin Gastroenterol Hepatol* 2014;12(1):85-92. DOI: 10.1016/j.cgh.2013.06.030
13. Okholm C, Hadikhadem T, Andersen LT, et al. No increased risk of perforation during colonoscopy in patients undergoing Nurse Administered Propofol Sedation. *Scand J Gastroenterol* 2013;48(11):1333-8. DOI: 10.3109/00365521.2013.837951
14. Buxbaum J, Roth N, Motamedi N, et al. Anesthetist-directed sedation favors success of advanced endoscopic procedures. *Am J Gastroenterol* 2016. DOI: 10.1038/ajg.2016.285
15. Garewal D, Powell S, Milan SJ, et al. Sedative techniques for endoscopic retrograde cholangiopancreatography. *Cochrane Database Syst Rev* 2012;(6):CD007274. DOI: 10.1002/14651858.CD007274.pub2

16. Dumonceau JM, Riphaus A, Beilenhoff U, et al. European curriculum for sedation training in gastrointestinal endoscopy: position statement of the European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Gastroenterology and Endoscopy Nurses and Associates (ESGENA). *Endoscopy* 2013;45(6):496-504. DOI: 10.1055/s-0033-1344142
17. Slagelse C, Vilmann P, Hornslet P, et al. Nurse-administered propofol sedation for gastrointestinal endoscopic procedures: first Nordic results from implementation of a structured training program. *Scand J Gastroenterol* 2011;46(12):1503-9. DOI: 10.3109/00365521.2011.619274
18. Jensen JT, Savran MM, Møller AM, et al. Development and validation of a theoretical test in non-anaesthesiologist-administered propofol sedation for gastrointestinal endoscopy. *Scand J Gastroenterol* 2016;51(7):872-9. DOI: 10.3109/00365521.2016.1141433
19. Hassan C, Rex DK, Cooper GS, et al. Endoscopist-directed propofol administration versus anesthesiologist assistance for colorectal cancer screening: a cost-effectiveness analysis. *Endoscopy* 2012;44(5):456-64. DOI: 10.1055/s-0032-1308936
20. Dumonceau JM. Nonanesthesiologist administration of propofol: it's all about money. *Endoscopy* 2012;44(5):453-5. DOI: 10.1055/s-0031-1291658
21. American Society for Gastrointestinal Endoscopy, Ikenberry SO, Anderson MA, et al. Endoscopy by nonphysicians. *Gastrointest Endosc* 2009;69(4):767-70. DOI: 10.1016/j.gie.2008.11.006
22. Riphaus A, Macias Gomez C, Deviere J, et al. Propofol, the preferred sedation for screening colonoscopy, is underused. Results of an international survey. *Dig Liver Dis* 2012;44(5):389-92. DOI: 10.1016/j.dld.2011.10.019