Title:
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Link: PubMed (Epub ahead of print)

Please cite this article as:

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

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INTRODUCTION
In Europe, the conflict between endoscopists and anesthesiologists was at a peak in 2010 when a Guideline about non-anesthesiologist administration of propofol (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) (1). 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.” (2). We were astonished that the ESA endorsement of the Guideline was withdrawn for political reasons and not on the basis of new evidence that contradicted the Guideline. Thus, the motives of the retraction of endorsement were not “por ser sumamente peligroso para la seguridad y calidad de los procedimientos endoscópicos”, words mentioned by Álvarez et al. within quotation marks but which are absent from retraction letters (2,3).
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 still mention errors made by Álvarez et al. when they state “Afirma que solo uno de los 10 pacientes falleció a causa de la sedación es un monumento a la especulación, tal vez Vargo ignore que la mayor parte de las complicaciones que menciona pueden evitarse con una sedación adecuada realizada por un profesional correctamente formado.” In reality, only for EGD, 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)” (4). 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 “un estudio prospectivo en este ámbito sería poco práctico por la infrecuencia de los eventos adversos”, he stated “an appropriately powered randomized, prospective, controlled trial would be impractical because of the rarity of significant events” (4). 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) (5), desaturation (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) (6), 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) (7), 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 (8).

_Adequate provider for propofol sedation during digestive endoscopy_
In the second chapter, the authors state “Nuestra opinión es clara, pero las opiniones científicas deben justificarse cuidadosamente”. This chapter is confusing as the authors first state “el artículo de Adeyemo et al. (14) que atribuye un incremento del 2,5% de perforaciones cuando se utiliza propofol administrado por anestesiólogos. Hay algunos ejemplos más en esta línea, cuyo rigor científico no soporta la mínima crítica”. 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 have been outrageous (9). 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 (10-12).

Then the authors affirm “las exploraciones complejas como la CPRE deben ser sedadas o anestesiadas por un anestesiólogo, puesto que la sedación dirigida por anestesiólogos incrementa la eficacia de procedimientos endoscópicos avanzados”. The study cited to support this affirmation reported a lower success rate of ERCP in patients sedated by non-anesthesiologists compared with anesthesiologists (13). 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 (14).

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 (15). Participants in the elaboration of that Curriculum have reported that such a training allows them to
perform NAAP safely (16); they also developed and validated a test for assessing the qualifications of NAAP providers in gastrointestinal endoscopy (17).

With respect to the criticism of the study by Pambianco et al. who used the SEDASYS system, we cannot be surprised that Álvarez et al. again invented a quotation: “Lo más destacable fue una incidencia de complicaciones graves como la hipoxemia en un 5,8% en el grupo con SEDASYS, que aumenta hasta el 8,7% en el grupo control. Con estos resultados no se puede afirmar, como hace el autor, que ‘no hay ninguna evidencia científica que demuestre menor número de efectos adversos en la sedación endoscópica dirigida por el anestesiólogo respecto del endoscopista o de otros sistemas de administración de los sedantes’. Esta afirmación no es correcta porque no hay estudios que hayan comparado la sedación por anestesiólogos frente a la sedación por no anestesiólogos empleando los mismos fármacos, a las mismas dosis, en los mismos pacientes, y para los mismos procedimientos. No tiene sentido realizar afirmaciones tan categóricas cuando no hay evidencia científica que las respalde”.

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 (5-7). 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 (18,19).

To help in reducing costs, Álvarez et al. mention that the ASGE supports the performance of endoscopy 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” (20). Sigmoidoscopy for screening colorectal cancer has become outdated.

Finally, the authors themselves destroy their own arguments as they state “La sedación por parte de no-anestesiólogos a pacientes ASA I-II, empleando midazolam y fentanilo, fármacos con antagonistas específicos, empleando una escala definida de sedación con valores registrados en gráfica cada 5 minutos, que evite sedación profunda y las complicaciones derivadas de la misma, podría ser aceptable, puesto que en nuestra opinión garantiza la seguridad de los enfermos”. 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. (8).

**Conclusion**

Propofol sedation is underused (21), and a better allocation of anesthesiology resources would benefit the patients and the community globally. Honest discussion is a prerequisite for a better collaboration. Corporatist 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 anesthesiologist 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.
References


6. Ferreira AO, Torres J, Barjas E, et al. Non-anesthesiologist administration of


