

Editor,

In a recent paper, Ferreira and Riphaut<sup>1</sup> advocate the use of propofol for sedation of patients during colonoscopy not only by the pharmacokinetic characteristics of this compound, which gives it great versatility to adjust the depth of sedation to the endoscopy, but also by the security they attribute to propofol, stating that 'Propofol sedation has been gaining momentum in the last decade in several European countries .... but is still underused in most countries. There are several reasons behind this phenomenon. One is the theoretical possibility of clinically significant side effects that include respiratory and circulatory depression, despite the evidence gathered so far, that understates that nonanesthesiologist administration of propofol is as safe as endoscopist directed 'traditional sedation', as shown in several meta-analysis'. These dangerous statements deserve some pharmacological comments.

1 - Propofol side effects of respiratory and circulatory depression are not theoretical possibilities, as the recent death of Michael Jackson, sadly testifies the dangerous respiratory depression induced by propofol.

2 - Propofol is a GABA mimetic drug, which like thiopental hyperpolarizes neurons by an increased chloride conductance, which causes a dose-dependent depression of the central nervous system, varying from a simple sedation to an anesthetic coma and death. For this reason, propofol is classified as a general anesthetic, in the same pharmacological group as thiopental, which is used in anesthesia, but also as a lethal injection for criminal executions. Unlike thiopental, propofol is rapidly cleared, which makes it suitable not only for induction of anesthesia but also for its maintenance as well as for long-term sedation.

3 - The anesthetic coma resultant from the central nervous system depression implies several dangers: 1) cardiovascular depression, 2) depression of the respiratory center (ranging from bradipnea to apnea), 3) relaxation of the oropharyngeal muscles that may induce also obstructive apnea in patients with predisposing airways (retrognathia, obesity, short/thick necks or a history of heavy snoring or sleep apnea), and finally 4) the absence of airway's protective reflexes predispose to the aspiration of HCl from gastric regurgitation or vomiting.

Jones et al<sup>2</sup> in an excellent video published by The New England Journal of Medicine, considers sedation to be a continuum with three different levels. 1 - Minimal sedation provides a drug-induced state of anxiolysis during which patients respond normally to verbal commands. 2 - Moderate sedation or analgesia, or conscious sedation, is a drug-induced depression of consciousness during which patients respond purposefully to verbal commands when aroused by the sound of a voice or light tactile stimulation. No interventions are required to maintain a patent airway during conscious sedation. 3 - Deep sedation or analgesia is a drug-induced depression of consciousness during which patients cannot be easily aroused but respond purposefully after the administration of repeated or painful stimulation.

Having in mind the pharmacological profile of the drugs used to sedate patients, Jones aware that invasive or painful procedures require this deep sedation and that the ventilatory function may be impaired during deep sedation.

Jones also recommend that the procedure should be contraindicated when the patient has a history of allergic reaction to analgesic or sedative medications, has unstable cardiorespiratory function, or is in a nonfasting state. Patients undergoing conscious sedation should have had no liquids by mouth for 2 hours before the procedure and no food for 6 to 8 hours before the procedure. Finally, Jones et al. advises that "since sedation is a continuum and a patient's level of sedation can change rapidly, the clinician should have the ability to monitor the patient's level of consciousness, hemodynamics, ventilation, and oxygenation. The patient must have a working intravenous catheter before conscious sedation is initiated. Emergency equipment for intubation and resuscitation must be immediately available, and the clinician must know how to use this equipment and how to administer appropriate medications in case cardiopulmonary resuscitation is required.

I agree that the use of propofol is a very good choice for sedation, but we must be aware of adverse effects and we must never neglect the danger.

## REFERENCES

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**Keywords:** Colorectal Neoplasms; Hypnotics and Sedatives; Propofol; Endoscopy, Gastrointestinal; Colonoscopy.

**Palavras-chave:** Neoplasia Colo-Rectal; Hipnóticos e Sedativos; Propofol; Endoscopia Gastrointestinal; Colonoscopia.

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I write to support the comments of Ferreira and Riphaut regarding propofol administration by non-anesthesia specialists.<sup>1</sup> Endoscopist supervision of propofol administration by trained registered nurses is safe and remarkably cost-effective,<sup>2</sup> and has been successfully instituted in Switzerland and Germany. Endoscopist supervised propofol is particularly safe for colonoscopy, which does not need the greater depth of sedation often required for upper endoscopy.<sup>2</sup> Propofol can be titrated to moderate sedation by combining it with low doses of opioid and/or midazolam.<sup>3</sup> This approach further enhances its safety for administration by non-anesthesia personnel.

The European Society of Anesthesiology initially endorsed the use of propofol by non-anesthesia specialists for endoscopy based on evidence review,<sup>4</sup> and then withdrew the endorsement based on non-evidenced based objections from its members. The American Association of Anesthesiologists also has a history of non-evidence based positions with regard to propofol.<sup>5</sup> Inevitably, the comments made by Ferreira and Riphaut will be rejected by a substantial fraction of Portuguese anesthesiologists, who in doing so will again reject available evidence.

One way to develop an evidence-based policy regarding propofol would be to remove both anesthesiologists and endoscopists from the discussion and let independent medical experts evaluate the evidence. Such an approach could eliminate bias and facilitate an evidence-based decision regarding whether, when, and under what circumstances the administration of propofol by non-anesthesia specialists is appropriate.

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**Reply to the Letters to the Editor Concerning the Article: Alexandre Oliveira Ferreira, Andrea Riphaut. Propofol to Increase Colorectal Cancer Screening in Portugal. Acta Med Port 2014;27:541-42.**

**Resposta às Cartas ao Editor Relativas ao Artigo: Alexandre Oliveira Ferreira, Andrea Riphaut. Propofol como Forma de Aumentar o Rastreio Endoscópico do Cancro do Cólon e Reto em Portugal. Acta Med Port 2014;27:541-42.**

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Reply to the letter by Figueiredo Lima JJ:

The sedation frequency for endoscopic examinations was very low in the mid 90's in Germany and Switzerland compared to the USA and Great Britain. While up to 88% of patients were sedated in the USA and Great Britain much fewer patients, about 9%, had premedication in Germany and Switzerland. However, a current survey 'Nationwide Evaluation of Sedation in Gastrointestinal Endoscopy in Germany' shows that there is a pronounced increase in sedation frequency for endoscopic intervention of up to 88%.<sup>1</sup> This is most likely due, on the one hand, to the increase in interventional measures and, on the other hand, to the patients' preferences e.g. for colon carcinoma prevention.

Every patient has the right to an endoscopic examination that is as painless and as free of stress as possible. Therefore, ethically it is not justifiable to withhold sedation from patients.

In a study by Rex DK et al 65% of the patients refused to be randomized in a trial comparing colonoscopy with and without sedation. Male gender, higher education, and low anxiety are positive predictive factors for the patient's preference for unsedated colonoscopies.

Indeed, there is very robust data from nine randomized controlled trials (RCTs) that were pooled in four meta-analysis, including a Cochrane systematic review. This is the best available evidence and it clearly supports the use of propofol sedation for colonoscopy, since it not only increases patients comfort but also procedure quality as measured by cecal intubation rates. Furthermore, in the meta-analysis by Qadeer et al,<sup>2</sup> the risk of hypoxemia or hypotension during colonoscopy was actually lower with propofol than with traditional sedation 0.4 (95% CI, 0.2-0.79). None of the meta-analysis showed an increased risk for adverse events in the propofol sedation arms.

Above this, it seems that the author is unfamiliar with the developments of the last decade. Since the year 2000 an overwhelming amount of data was published, showing that sedation and especially propofol sedation performed by non-anaesthesiologists, is a safe and very cost-effective procedure. On top of the available data focusing on colonoscopy, there is even more data for upper endoscopy and ERCP/EUS.

There is also very compelling 'real life' data which include the study by Rex on the worldwide experience of propofol sedation by non-anaesthesiologists of 646080 cases.<sup>3</sup> The incidence of endotracheal intubations, permanent neurologic injuries, and death were 11, 0, and 4, respectively. Deaths occurred in 2 patients with pancreatic cancer, a severely handicapped patient with mental retardation and a patient with severe cardiomyopathy. Mask ventilation was required in less than 1:1000 cases.

The cost effectiveness of propofol sedation by an anaesthesiologist instead of a trained team has been estimated by Cesare Hassan to be in the range of \$1.5 million/life year gained (if they had adjusted for quality the value would be even greater). This figure is considerably

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