

Non-anaesthesiologists should not be allowed to administer propofol for procedural sedation: a Consensus Statement of 21 European National Societies of Anaesthesia

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Propofol, which is the most commonly used drug for induction of general anaesthesia, has also become a popular drug for procedural sedation. Because its use may be associated with serious and potentially fatal side-effects, the manufacturers of propofol restrict its use solely to personnel trained in general anaesthesia. In spite of this warning, the use of propofol for procedural sedation by non-anaesthesiologists is rapidly expanding in many countries. Recently, the US Food and Drugs Administration (FDA) denied a petition from gastroenterologists seeking the removal of this particular restriction. This unequivocal ruling of the FDA received strong support from the American Society of Anesthesiologists (ASA). At about the same time, the European Society of Anaesthesiology (ESA), together with various European gastroenterology societies, published new guidelines entitled 'Nonanaesthesiologist Administration of Propofol for

Gastrointestinal Endoscopy' (NAAP). Following publication of the NAAP guidelines, many reservations have been expressed by ESA member societies and individuals, dealing with professional, political, procedural and safety-oriented concerns. Out of concern for patient safety, and in order to officially and publicly dissociate themselves from the NAAP guidelines, 21 national societies of anaesthesiology in Europe, all of whom are ESA members, have signed a Consensus Statement confirming that due to its significant well known risks, propofol should be administered only by those trained in the administration of general anaesthesia.

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Introduction

Propofol, which is the most commonly used drug for induction of general anaesthesia, has also become a popular drug for procedural sedation because of shorter sedation effect and faster recovery time compared to midazolam. However, the use of propofol may be associated with serious and potentially fatal side-effects. These include cardiovascular effects such as hypotension and bradycardia, and respiratory effects such as hypoventilation, hypoxaemia and apnoea. In addition, at similar depths of sedation, propofol is more likely than midazolam to cause airway obstruction, due to upper airway collapsibility, suggesting that particular vulnerability exists after transition from conscious to unconscious sedation.¹

Rapid bolus dose administration of propofol during procedural sedation may result in undesirable cardio-respiratory depression, especially in the elderly, debilitated, and the American Society of Anesthesiologists (ASA) III/IV patients. Accordingly, the rates of administration should be individualised and titrated to clinical response, and an interval of 3–5 min must be allowed between clinical dosage adjustments in order to assess drug effects.² The principal risk of propofol use is its narrow therapeutic range, which carries the danger of

an unintentional slip into a state of deep sedation, or even anaesthesia, with loss of spontaneous ventilation. This is most likely to occur during prolonged or complex endoscopic procedures, which are often performed under deep sedation. For propofol, lack of an analgesic effect might possibly lead endoscopists to deepen the level of unconsciousness.² Last but not least, there are no specific pharmacologic antagonists that may reverse the undesirable side-effects of propofol when they do occur, necessitating active rescue measures if a disastrous outcome is to be prevented.

Because of the well-known risks of propofol administration, the manufacturers of the drug add the following restriction: 'For general anaesthesia or monitored anaesthesia care (MAC) sedation, DIPRIVAN Injectable Emulsion should be administered only by persons trained in the administration of general anaesthesia and not involved in the conduct of the surgical/diagnostic procedure.'

This special article is accompanied by the following Invited Commentary:

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The use of propofol in digestive endoscopy

Despite this warning, the use of propofol for procedural sedation by non-anaesthesiologists is rapidly expanding in many countries. The efficacy of propofol in achieving satisfactory procedural conditions, and its fast recovery time which allows a higher turnover of patients, has made this drug especially appealing to gastroenterologists who perform digestive endoscopy.

The 'dawning' ² of propofol in gastrointestinal endoscopy has been accompanied by dozens of publications in gastroenterology journals attesting to its safety when used by gastroenterologists. In addition, a large number of guidelines and consensus statements specifically concerning sedation by propofol have appeared in the gastroenterology literature.³⁻⁷ This multitude of publications may be ascribed, in part at least, to a medicolegal motive, namely, that non-anaesthesiologists who depart from the manufacturer's recommendations wish to shift the burden of proof that the method of use accords with recognised clinical practice, to the defendant.⁸ It is, therefore, understandable why, in 2005, the American College of Gastroenterologists presented the US Food and Drugs Administration (FDA) with a citizen's petition requesting a change in the propofol label.⁹ In August 2010, the FDA denied the petition and concluded its ruling with the following: 'In fact, we conclude that both components of the warning are appropriate in light of the significant risks associated with propofol, and we further conclude that the warning should help ensure that propofol is used safely. We therefore will not seek to have the warning removed, reduced, or otherwise amended.'⁹

The position of the American Society of Anesthesiologists

The ASA has devoted an enormous amount of effort to developing guidelines for establishing credentials that allow individual practitioners privileges to administer anaesthetic drugs to produce sedation.¹⁰ More than 10 years ago, after much debate, the 'Practice Guidelines for Sedation and Analgesia by Nonanaesthesiologists' were published.¹¹ Much of the controversy within the ASA concerned the wisdom of awarding privileges to non-anaesthesiologists to administer deep sedation, recognising that the margin between deep sedation and general anaesthesia was small, and that those who administer deep sedation must be prepared to rescue patients whose deep sedation becomes general anaesthesia.¹⁰ As a first step, the ASA approved a document that addresses only moderate sedation¹², and then followed with other statements, guidelines and standards, on the different aspects of sedation managed by non-anaesthesiologists. (www.ASAhq.org/publicationsAndServices/sgstoc.htm)

In 2004, the ASA and the American Association of Nurse Anesthetists issued a joint statement regarding propofol administration stating that 'Whenever propofol is used for sedation/anaesthesia, it should be administered only

by persons trained in the administration of general anaesthesia, who are not simultaneously involved in these surgical or diagnostic procedures.' The ASA has also actively urged the FDA to retain the warning limiting the use of propofol to clinicians trained in the administration of general anaesthesia and not involved in the conduct of the surgical/diagnostic procedure.¹³ One of the main arguments in the comments of the ASA was that 'Removal of the warning label from the propofol package insert may encourage the use of propofol by practitioners with inadequate training and experience in non-accredited facilities where credentialing is not required, such as private offices.' (see www.ASAhq.org/news/news111705.htm).

Recently, the ASA also addressed the problem of granting privileges for deep sedation to non-anaesthesiologists.¹⁴ In this statement from 2010, the ASA again expressed its 'genuine concern that individuals, however well intentioned, who are not anaesthesia professionals, may not recognize that sedation and general anaesthesia are on a continuum, and thus deliver levels of sedation that may, in fact, be general anaesthesia without having the training and experience to respond appropriately.'¹⁴ This statement includes detailed information regarding a formal education and training programme, licensure, and a mechanism for evaluation and improvement of performance, that are required from the non-anaesthesiologist sedation practitioner. More recently, the ASA has expressed strong support for the proposal of the US Drug Enforcement Agency to place propofol into schedule IV of the Controlled Substances Act due to its potential for abuse.

The position of the European Society of Anaesthesiology

In 2007, the Working Party on Sedation by non-anaesthesiology doctors of the Section and Board of Anaesthesiology of the European Union of Medical Specialists, published in this Journal guidelines for sedation and/or analgesia by non-anaesthesiologists.¹⁵ The initiative was prompted by the ever increasing demand for sedation for diagnostic and therapeutic procedures that cannot be fulfilled by the limited number and capacity of anaesthetists in most European countries. The Working Party felt there was an obligation to provide those non-anaesthesiologists, who wished to sedate patients with a high standard of safe care, with guidelines, and that our duty as anaesthesiologists was to provide such guidelines. Although the peer-review process of this document was not specified, and despite never being officially endorsed by the ESA, the efforts of the Working Party in improving patient safety through these guidelines were greatly appreciated. Yet, in the 'Drugs' section of these guidelines, it is stated that 'I.V. techniques using propofol may also be used (by non-anaesthesiologists) after appropriate training.'¹⁵ Following the publication of the FDA ruling in 2010, the

Guidelines Committee of the ESA was requested to re-assess the earlier guidelines of its Working Party and declare that the ESA condemns the use of propofol by non-anaesthesiologists.

In the meantime, however, the ESA, together with the European Society of Gastrointestinal Endoscopy and the European Society of Gastroenterology and Endoscopy Nurses and Associates, has co-authored a new set of guidelines, entitled 'Nonanaesthesiologist Administration of Propofol for Gastrointestinal Endoscopy' (NAAP), which was published simultaneously in this Journal⁸ and in a European gastroenterology journal.¹⁶ Following publication, the NAAP guidelines have been subject to much criticism from a number of National Societies of Anaesthesia in Europe, who feel that they have significantly damaged efforts to keep procedural sedation safe by keeping propofol out of the hands of non-anaesthesiologists. The matter has, therefore, been extensively discussed by the Board of the ESA, its Council, the National Anaesthesia Societies Committee (NASC) and the Guidelines Committee. From the ensuing deliberations has come an acknowledgement from the ESA Council that, indeed, the policy and procedures of guideline approval of the ESA should be reconsidered and revised. The call to retract the endorsement of the ESA and its participation in the NAAP guidelines was, however, rejected.

The Nonanaesthesiologist Administration of Propofol for Gastrointestinal Endoscopy guidelines

Although a detailed analysis of the NAAP guidelines is beyond the scope of this article, and despite the overt disagreement with endorsement of the use of propofol by non-anaesthesiologists, they are worthy of further consideration. The evidence on which the NAAP guidelines are based is classified according to the prevailing standards of evidence-based medicine (EBM), with evidence levels ranging from 1++ (the highest) to 4, and with four recommendation grades (A–D). Although this methodology seems to be appropriate and well accepted, and despite the appearance of the word 'evidence' 83 times within the text of the guidelines, some of the evidence levels and recommendation grades may seem questionable to the experienced anaesthesiologist. In addition, the proclaimed safety of propofol use by non-anaesthesiologists has to be assessed against the hazards of interpreting an incidence of adverse event that is either zero or has a very low numerator. As Hanley and Lippman-Hand¹⁷ asked close to 30 years ago, if nothing goes wrong, is everything all right? Finally, we have to honestly consider if it is appropriate to adopt strict EBM criteria, according to which expert opinion has the lowest merit, in writing clinical guidelines in areas in which evidence is scant to start with.

The NAAP guidelines present only four Grade A recommendations. These include that self-training in NAAP is strongly discouraged and that prolonged or complex procedures are frequently performed under deep sedation. Another Grade A recommendation is that patients should be continuously monitored by a member of staff with no other role. Although the evidence level for this recommendation was 1++, the authors hasten to add that this recommendation is based mostly on expert opinion, and that it has been recently challenged by reports that blood pressure was not monitored in a majority of patients, and it is, therefore, unclear how often patients might have presented critical hypotension.

It might be of greater interest to see which recommendations (seven in all) received the lowest grade (D). These include documenting the procedure of informed consent, that intravenous access is required, that the caregiver should undergo advanced cardiac life support (ACLS) training in locations where another ACLS provider is not immediately available, that the first procedural sedation patients of all practitioners be supervised by an anaesthesiologist or another person with previous experience of more than 300 sedations, that when patient-related risk factors for complications are present, the primary involvement of an anaesthesiologist is suggested, and that if a patient proves difficult to sedate adequately, endoscopy termination and referral to an anaesthesiologist should be considered.

The recommendations on patient monitoring may also seem inadequate to experienced anaesthesiologists. The NAAP guidelines recommend that routine patient monitoring is limited to continuous pulse oximetry and automated non-invasive blood pressure only. The rationale given is that although the clinical utility of these measures has not been demonstrated, these devices are widely available, relatively reliable, cheap and easy to use. As to the utility of blood pressure monitoring during NAAP, the authors say that it has not been studied but it is intuitively important to monitor because a decrease in blood pressure is one of the most frequent side-effects of propofol, and it may require intervention. On the contrary, continuous electrocardiography is recommended only for selected patients with a history of cardiac and/or pulmonary disease. Similarly, although it is admitted that visual assessment of respiratory activity during NAAP is not a reliable method of detecting apnoea, and that capnographic monitoring may reduce episodes of hypoxaemia, capnography is not recommended as standard because its use has not demonstrated any clinical impact. Last but not least, the danger of airway obstruction is not mentioned even once in these guidelines. In summary, it is hard to evade the impression that the NAAP guidelines challenge the essential safety standards and culture that have been so successfully developed by anaesthesiologists and that have made our profession a leader in patient safety.

A Consensus Statement regarding the Nonanaesthesiologist Administration of Propofol for Gastrointestinal Endoscopy guidelines

Although the NAAP guidelines bear the name of the ESA, they are inconsistent with the stance of many national societies of anaesthesia in Europe. These societies have expressed their reservations both verbally and in published form.¹⁸ These societies feel that the publication of the ESA NAAP guidelines has significantly damaged efforts to keep propofol out of the hands of non-anaesthesiologists and is detrimental to patient safety during procedural sedation. Those national societies who disagree with the NAAP guidelines have collectively written the following Consensus Statement, clearly and publicly expressing both disagreement and disassociation from these guidelines.

Non-anaesthesiologists should not be allowed to administer propofol for procedural sedation: a Consensus Statement of 21 European National Societies of Anaesthesia

- (1) The ESA, together with the European Society of Gastrointestinal Endoscopy and the European Society of Gastroenterology and Endoscopy Nurses and Associates, has issued guidelines concerning Non-Anaesthesiologist Administered Propofol for Gastrointestinal Endoscopy (NAAP). These guidelines have been published in the December 2010 issue of the *European Journal of Anaesthesia*⁸, the official journal of the ESA, and elsewhere.¹⁶
- (2) Following their publication, the NAAP guidelines have met with many professional, political, procedural and safety-oriented reservations on the part of ESA member societies and individuals, including a specific motion to retract said guidelines. On the 26 of November 2010, the ESA Board and Council decided not to withdraw the guidelines, although it was agreed that the ESA's policy and procedures for guideline approval would have to be reconsidered and revised.
- (3) The undersigned European National Societies of Anaesthesia declare their disagreement with the NAAP guidelines, which specifically allow and endorse the use of propofol by non-anaesthesiologists. This endorsement contradicts the official manufacturers' warning which clearly says: 'For general anesthesia or monitored anesthesia care (MAC) sedation, DIPRIVAN Injectable Emulsion should be administered only by persons trained in the administration of general anesthesia and not involved in the conduct of the surgical/diagnostic procedure'. We find it inconceivable that the ESA totally disregards this warning.
- (4) In August 2010, FDA denied a petition of the American College of Gastroenterologists seeking the removal of a warning from the package insert of propofol (Diprivan).⁹ The FDA clearly concluded

that, in light of the significant risks associated with propofol, both components of the drug warning (propofol should be administered only by those trained in the administration of general anaesthesia, and, that such individuals not be engaged in the conduct of the surgical or diagnostic procedure involved so that their full attention can be devoted to the state of the patient) are appropriate and warranted. The ASA has also clearly stated that propofol be given by anaesthesia-trained personnel only and has (successfully) urged the FDA to deny the petition of the gastroenterologists in the USA.¹³ We find it inconceivable that the endorsement by the ESA of the use of propofol by non-anaesthesiologists stands in such clear contrast to the stance of the FDA.

- (5) In addition to our disagreement with the NAAP concept, we find the NAAP guidelines to be lacking in evidence, in requirements for training and in requirements for monitoring. We feel that these guidelines do not comply with the ESA's Helsinki Declaration, which states that 'patients have the right to...be safe and protected during their medical care and anaesthesiology has a key role to play in improving patient safety'.¹⁹
- (6) In summary, we, the undersigned National Societies of Anaesthesia in Europe, believe that, due to its well known significant risks, propofol should be administered only by those trained in the administration of general anaesthesia. It is, therefore, out of concern for patient safety, that we strongly disagree with the practice of NAAP. We hereby, officially and publicly, dissociate ourselves from the NAAP guidelines and declare that our respective societies are not to be held responsible and accountable, in any way or form, for these guidelines and their potential impact on patient safety.

This Consensus Statement has been endorsed by the following undersigned European National Societies of Anaesthesia:

- (1) Society for Anesthesia and Resuscitation of Belgium (Professor Luc Barvais).
- (2) Bulgarian Society of Anaesthesiologists (Professor Ivan Smilov).
- (3) Czech Society of Anaesthesiology and Intensive Care Medicine (Professor Karel Cvachovec).
- (4) Danish Society of Anaesthesiology and Intensive Care Medicine (Dr Ole Nørregaard).
- (5) Estonian Society of Anaesthesiologists (Dr Indrek Rätsep).
- (6) Georgian Society of Anesthesiology and Critical Care Medicine (Dr Merab Tevzadze).
- (7) Hellenic Society of Anesthesiologists (Dr Anna Malissiova).
- (8) Israel Society of Anesthesiologists (Professor Azriel Perel).

- (9) Italian Society of Anaesthesia, Analgesia, Reanimation and Intensive Care (Professor Rosalba Tufano).
- (10) Association of Kosovar Anaesthesiologists (Dr Qamile Morina).
- (11) Latvian Association of Anaesthesiologists and Reanimatologists (Professor Indulis Vanags).
- (12) Lithuanian Society of Anaesthesiology and Intensive Care (Professor Juozas Ivaskevicius).
- (13) Macedonian Society of Anaesthesiologists (Professor Mirjana Shosholcheva).
- (14) Association of Anaesthesiologists of Malta (Dr Carmel Abela).
- (15) Polish Society of Anaesthesiology and Intensive Therapy (Professor Janusz Andres).
- (16) Portuguese Society of Anaesthesiology (Dr Lucindo Ormonde).
- (17) Romanian Society of Anaesthesia and Intensive Care (Professor Șerban Bubenek).
- (18) Serbian Association of Anesthesiologists and Intensivists (Professor Predrag Romić).
- (19) Slovenian Society of Anaesthesiology and Intensive Care Medicine (Professor Vesna Novak Jankovič).
- (20) Spanish Society of Anaesthesia, Reanimation and Pain Treatment (Professor Gilsanz Rodriguez).
- (21) Turkish Society of Anaesthesiology and Reanimation (Professor Sukran Sahin).

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