

Current role of non-anesthesiologist administered propofol sedation in advanced interventional endoscopy

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

Daniela Elena Burtea, Adrian Săftoiu, Research Center of Gastroenterology and Hepatology Craiova, University of Medicine and Pharmacy Craiova, 200639 Craiova, Romania

Daniela Elena Burtea, Endoscopy Department, Clinical County Emergency Hospital Craiova, 200639 Craiova, Romania

Anca Dimitriu, Anca Elena Maloş, Anesthesiology Department, Clinical County Emergency Hospital Craiova, 200639 Craiova, Romania

Adrian Săftoiu, Endoscopy Department, Gastrointestinal Unit, Copenhagen University Hospital Herlev, 2730 Herlev, Denmark

Author contributions: Burtea DE retrieved the references, carefully reviewed the literature and wrote the initial manuscript; Dimitriu A and Maloş AE contributed to the reviewing of the manuscript; Săftoiu A designed the content of the mini-review and wrote parts of the manuscript.

Supported by The Partnership program in priority areas - PN II, implemented with support from National Authority of Scientific Research (ANCS), CNDI - Uefiscdi, Romania, No. 2011-3.1-0252 (Nano-Ablation).

Conflict-of-interest statement: None.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Correspondence to: Adrian Săftoiu, MD, PhD, MSc, FASGE, Visiting Clinical Professor, Research Center of Gastroenterology and Hepatology Craiova, University of Medicine and Pharmacy Craiova, 2 Petru Rares str., 200639 Craiova, Romania. adrian.saftoiu@umfvcv.ro
Telephone: +40-744-823355
Fax: +40-251-310287

Received: May 7, 2015

Peer-review started: May 9, 2015

First decision: June 3, 2015

Revised: June 21, 2015

Accepted: July 21, 2015

Article in press: July 23, 2015

Published online: August 10, 2015

Abstract

Complex and lengthy endoscopic examinations like endoscopic ultrasonography and/or endoscopic retrograde cholangiopancreatography benefit from deep sedation, due to an enhanced quality of examinations, reduced discomfort and anxiety of patients, as well as increased satisfaction for both the patients and medical personnel. Current guidelines support the use of propofol sedation, which has the same rate of adverse effects as traditional sedation with benzodiazepines and/or opioids, but decreases the procedural and recovery time. Non-anesthesiologist administered propofol sedation has become an option in most of the countries, due to limited anesthesiology resources and the increasing evidence from prospective studies and meta-analyses that the procedure is safe with a similar rate of adverse events with traditional sedation. The advantages include a high quality of endoscopic examination, improved satisfaction for patients and doctors, as well as decreased recovery and discharge time. Despite the advantages of non-anesthesiologist administered propofol, there is still a continuous debate related to the successful generalization of the procedures.

Key words: Non-anesthesiologist administered propofol sedation; Advanced interventional endoscopy; Endoscopic ultrasound; Endoscopic retrograde cholangiopancreatography

© **The Author(s) 2015.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: A large amount of clinical research data demonstrated that propofol provides significant advantages over traditional sedation techniques during advanced endoscopic procedures like endoscopic retrograde cholangiopancreatography and/or endoscopic ultrasonography. Thus, propofol is more effective and safer than the combination of midazolam and meperidine to maintain an adequate level of sedation during advanced endoscopic procedures, with shorter recovery times and increased patient and endoscopist satisfaction. The trend of an increased usage of propofol and generalization of non-anesthesiologist administered propofol sedation in both hospital and private practice settings will certainly increase in the years to come.

Burtea DE, Dimitriu A, Maloş AE, Săftoiu A. Current role of non-anesthesiologist administered propofol sedation in advanced interventional endoscopy. *World J Gastrointest Endosc* 2015; 7(10): 981-986 Available from: URL: <http://www.wjgnet.com/1948-5190/full/v7/i10/981.htm> DOI: <http://dx.doi.org/10.4253/wjge.v7.i10.981>

INTRODUCTION

Most of the endoscopic procedures, either diagnostic or therapeutic, are nowadays performed under sedation, used as a standard practice in most of the centers^[1]. Non-complex endoscopic examinations can be performed safely without any sedation, but with thorough psychological preparation and pre-procedural care, which might be good enough for patients to decrease procedure related anxiety^[2]. However, the number and complexity of endoscopic procedures increased due to the generalized usage of sedation, which diminishes anxiety, discomfort and/or pain for the patients, thus improving patient acceptance and satisfaction^[3-7]. Sedation is also important to medical practitioners as it improves the quality of endoscopic examinations and completion rate, but also treatment outcomes in therapeutic endoscopy, thus increasing endoscopist's satisfaction^[3]. Sedation levels and medication types depend on a variety of factors, related to both patient characteristics (age, comorbidities, preference, *etc.*), as well as procedure types (simple diagnostic gastroscopy or colonoscopy, as opposed to prolonged complex therapeutic procedures)^[4].

Sedation levels are variable and include a continuum of states ranging from minimal and moderate sedation to deep sedation and general anesthesia^[4]. Conscious sedation assumes an *iv* administration of pharmacologic agents that lower the level of consciousness up to a state of drowsiness, relaxation, but the patient stays awake during the procedure retaining its ability to maintain an open airway and to breath spontaneously (patients do not require intubation and mechanical ventilation as with general anesthesia). Conscious sedation also helps to ensure adequate cardiac output,

to communicate with the medical team and to respond to verbal commands^[8,9]. Nevertheless, complex and lengthy procedures like endoscopic ultrasound (EUS) and endoscopic retrograde cholangiopancreatography (ERCP) usually require a deeper sedation level^[10]. Consequently, deep sedation makes the pain more tolerable, minimizes patient anxiety and/or discomfort, and has no memory effect (the patient will never recall any negative emotions) and thereby facilitates the procedure performance by the endoscopist^[4]. Current guidelines also support the use of propofol-based sedation as compared with traditional (conventional) sedation with benzodiazepines and/or opioids, thus offering higher patient and endoscopist satisfaction, decreasing procedure-related time, as well as recovery time, without increasing the rate of adverse events^[11].

On the other hand, the use of intravenous sedation has increased the demand of qualified medical providers to assess and intervene on behalf of the patient, before serious adverse events occur^[6].

Due to limited anesthesiology resources in most countries, non-anesthesiologist administered propofol (NAAP) sedation has started to be used extensively^[6]. Registered nurses have responded to this demand through implementation of educational programs, definition of clinical competencies and promulgation of recommended practice guidelines by professional practice organizations and nursing position statements^[12].

The aim of this article was to critically review the available evidence on deep sedation procedures necessary for complex therapeutic EUS and/or ERCP procedures, highlighting the controversies that still concern sedation by non-anesthesiologists (either endoscopists or nurses) based on structured multisociety sedation curriculum programs.

METHODS OF SEDATION

Sedation methods differ widely from one country to another, from one health system to another and, of course, they depend on local circumstances and both patient's and endoscopist's preferences that all increased the threshold on quality^[2]. On the other hand, the differences between various hospitals/departments, university/community hospitals, as well as public/private endoscopy units, and other systematic differences of practice, might influence a particular endoscopy unit concerning its own sedation practices. Various types and degrees of sedation techniques are thus used during gastrointestinal (GI) endoscopic procedures, although the optimal sedation is tailored according to the individual patient, based on the balance between clinical risks and type of procedure performed^[13]. Even nowadays, there is no standard system of sedation, while in the private institutions the choice of sedation depends on endoscopist and/or anesthesiologist preference, as well as the complexity of procedures to be performed.

Recent pharmacological researches and progresses have also contributed to the increased use of conscious sedation for specific patient populations. The introduction of "non-barbituric" intravenous anesthetics (propofol, remifentanyl, ketamine, etomidate) with shorter half-lives and having minimum cumulative active metabolites, have increased the safety and efficacy associated with the administration of sedation. Nevertheless, both propofol (alone or in combination with other agents), but also conventional/traditional sedation techniques (using benzodiazepines and/or opioids) can induce deep sedation, even though only moderate sedation is desired^[5].

Benzodiazepines

Benzodiazepines, such as midazolam, alprazolam, bromazepam, diazepam, *etc.*, are among the most commonly prescribed drugs^[2]. These drugs act as anxiolytics, sedatives, hypnotics, anesthetics, antiepileptic and muscle relaxants. Moderate sedation using midazolam and an opioid is still considered the standard method of sedation, although propofol is increasingly used in many countries, mainly because both the endoscopists', as well as patients' satisfaction are higher than for conventional sedation. Midazolam is currently considered the benzodiazepine of choice because of its shorter duration of action and better pharmacokinetic profile compared with diazepam. The duration of action of midazolam is dependent on the duration of its administration. Mental function returns to normal after approximately 4 h after administration, the drug being very useful for short procedures. One published meta-analysis reported that midazolam provided better patient satisfaction as compared to diazepam, and less frequent memory of procedures^[9]. The recovery time can be shortened after midazolam usage by using the benzodiazepine antagonist flumazenil^[14].

Opioids

Among the opioids, fentanyl and meperidine/pethidine are the most popular^[2]. Fentanyl is a synthetic narcotic analgesic characterized by a rapid onset and short duration of action. At the level of respiratory system, higher doses can cause respiratory depression, immediately, as well as late. It can induce chest muscle rigidity followed by a difficult or even impossible intubation. Also, the combination of fentanyl and midazolam that is used quite often in some endoscopy departments can produce apnea and cardiac arrest^[9]. Pethidine/meperidine is a weak opioid (7-10 times weaker than morphine) which relaxes smooth muscles, produces sedation and mild euphoria. The combination between midazolam and meperidine is safe and effective for GI endoscopy^[15]. Ketamine is also a suitable sedative for GI endoscopy^[16], although it might stimulate salivary and tracheobronchial secretion, while it sometimes gives a dissociative anesthesia that can produce hallucinations and delirium awakening^[17].

Propofol

Propofol is an ultra-short-acting, sedative-hypnotic agent that has multiple potential advantages compared with "traditional sedation" based upon administration of an opioid and benzodiazepine agents for endoscopic procedures^[18]. Propofol is a highly soluble phenol derivative, consisting of an *iv* emulsion for injection or infusion (1% concentration, 10 mg/mL) containing also 10% soybean oil, 2.25% glycerol and 1.2% purified egg phosphatide^[2]. Propofol has become undoubtedly the induction agent of choice in GI endoscopy, as it is really easy to administer and provides prompt awakening, with fewer side effects^[19]. Postprocedure, propofol reduces nausea and vomiting as well as the time required for the ability to walk, as compared with thiopental and methohexital. The pain on injection of propofol may be reduced by injecting it into large veins or by mixing with 20-40 mL of lidocaine anesthetic agents. Co-induction with midazolam reduces the dose of propofol, produce sedation and amnesia without prolonging hospitalization time^[20]. Nevertheless, recovery is slower, which for outpatient endoscopy cabinets can be an impediment.

ADVANCED ENDOSCOPY

Compared to standard diagnostic upper or lower GI endoscopy, advanced therapeutic procedures (EUS and/or ERCP) are often longer and complicated, thus requiring higher doses of sedatives for corresponding patient compliance, without recall of the procedure^[10].

ERCP

ERCP is a technically demanding, but highly important modality to diagnose and treat pancreaticobiliary disorders. ERCP has progressed from an initial diagnostic technique to an exclusively therapeutic procedure used for the management of common bile duct stones, as well as biliary strictures. Pancreatic stones, strictures or even pseudocysts can be also managed by ERCP in highly specialized tertiary centers^[21]. Traditional conscious (moderate) sedation with the combination between a benzodiazepine and an opiate is challenged nowadays by the use of propofol sedation. A Cochrane review on individual studies concluded that patients have a better recovery profile after propofol sedation, as compared to the combination midazolam - meperidine, with no difference in complication rate^[22]. The same conclusion has been reached by several meta-analyses that indicated clear advantages for propofol sedation, without increased risk of cardiopulmonary adverse events^[18,23]. In order to obtain the desired deep sedation effects, balanced propofol sedation (propofol in combination with midazolam and fentanyl) has been used showing a longer recovery time without any other difference in term of complications^[24]. The conclusion was that non-anesthesiologists propofol sedation can also be administered safely by trained, registered sedation nurses, with the same being

valid also in emergency ERCP^[25]. Although propofol is nowadays preferred, in high doses it induces a risk of cardiopulmonary complications (bradycardia, hypotension, apnea, hypoxemia, etc.), consequently various methods of administration have been designed. Target propofol infusion (TPI) consists of an initial bolus, followed by a rate of constant infusion controlled by a computer, and has been compared to self-administration of propofol through patient controlled sedation (PCS)^[26]. The later technique showed a reduced consumption of propofol and a faster recovery, but no significant benefits over TPI.

EUS

EUS is a state-of-the-art method for the assessment of GI pathology, especially for pancreaticobiliary lesions, but also GI tract or lung cancers. Moreover, the procedure allows the performance of EUS-guided fine needle aspiration (FNA) used to obtain a final diagnosis through cytology or histology exams of the obtained samples^[27]. While routine diagnostic or staging EUS carries a relatively low risk, it is usually more time consuming and more uncomfortable than a simple diagnostic upper GI tract endoscopy. Likewise, EUS-FNA procedures are more difficult and lengthier, therefore a deeper sedation is necessary. The same thing is valid for therapeutic procedures which start with the initial placement of a needle through EUS-guidance, for, *e.g.*, celiac plexus neurolysis or pancreatic pseudocyst drainage. Other therapeutic procedures performed under EUS-guidance or assistance, like hepaticogastrostomies, choledoco-duodenostomies or cholecystogastrostomies, are also performed under deep sedation or general anesthesia, even in high risk patients [American Society of Anesthesiologists (ASA) III-IV]^[28]. A large prospective study including 500 patients showed that administration of propofol by qualified persons, other than endoscopist, is safe and effective for patients with ASA less than 2, during upper GI EUS^[29]. Balanced propofol sedation techniques have been used also during EUS-FNA procedures without any major complications^[30]. Likewise, TCI during monitored anesthesia has been proven useful for safe sedation during EUS, without major complications^[31].

NAAP

NAAP propofol sedation caused major debates due to limited anesthesiology resources that determined administration of NAAP by trained nurses or endoscopists in selected endoscopy procedures^[6]. A comprehensive guideline endorsed by the European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Gastroenterology and Endoscopy Nurses and Associates established the role of NAAP in clinical endoscopy. Thus, trained registered nurses or endoscopists can safely administer propofol during ongoing endoscopy, with a very low rate of respiratory events requiring endotracheal intubation^[32]. The recommendations from the ESGE guidelines are clear,

indicating that propofol sedation has a similar rate of adverse events compared to conventional sedation (based on benzodiazepines ± opioids), with a high post-procedural satisfaction for both the patients, but also endoscopists. Moreover, the time for sedation decreases, with a higher quality of the endoscopic examination, while the recovery and discharge time will decrease^[6]. Even psychomotor ability after the procedure seems to be improved leading to a possible continuation of daily routine (including driving after recovery in the medical suites)^[33]. Because higher category of ASA physical status classification system leads to higher complication rate, an anesthesiologist is usually required on-site or for all patients with ASA category equal to or more than III^[34].

A dedicated person (usually a trained registered nurse) should be used for propofol administration, based on a clear protocol and adequate monitoring of the patient. An intravenous access should be maintained based on catheter with continuous supplemental oxygen, with careful continuous pulse oximetry and automated non-invasive blood pressure monitoring at 3-5 min intervals^[6]. While simple endoscopic procedures can be performed with moderate sedation, complex procedures like EUS and/or ERCP are usually performed with deep sedation^[10]. Currently, there is insufficient evidence that balanced propofol sedation with combination of drugs, beside propofol, has more beneficial effects^[35,36]. The preferred mode of administration is with intermittent bolus administration or PCS in a minority of patients, if available^[37]. Nevertheless, one large study from Germany showed that the combination of propofol and midazolam has a significantly lower sensation of pain, as well as reduced symptoms of dizziness, nausea and vomiting as compared to patients that received only propofol mono-sedation^[38]. There is a lot of data to support the usage of patient-selected music during the procedures, which can decrease the dosage of propofol administered^[39].

Both endoscopists and nurses should undergo a specific training program, which includes theoretical and practical parts on both basic life support and advanced cardiac life support^[6]. A structured training program followed by an implementation phase documented a low incidence of adverse events, while the independent risk factors were: type of intervention and level of staff experience^[40]. Thus, the patients had short duration hypoxia (4.7%), needed suction (2.4%) or bag-mask ventilation (0.9%), with only 0.3% of procedures that had to be discontinued^[12]. Anesthetic assistance was necessary for only 0.4% of patients. A recent meta-analysis compared pooled results for NAAP and AAP studies, and showed the same rates of hypoxia (oxygen saturation less than 90%) and airway intervention in both arms^[41]. Respiratory complications after endoscopist directed sedation were also shown to be important, with coughing or vomiting resulting in an increased risk of respiratory infections, thus requiring antibiotic treatment^[42]. However, pooled patient satisfaction and

pooled endoscopist satisfaction rate, as well as the dose of propofol administered were lower in the NAAP group, as compared to the AAP group. 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.

Nevertheless, cautious opinions on NAAP still exist, with more data required before transition of procedures from major hospitals to community practice^[43,44]. Retraction of endorsement for the NAAP guideline by the European Society of Anesthesiology (ESA) came in line with the concerns of using NAAP by trained nurses or endoscopists, mainly in view with the possible complications and their proper management^[45]. 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 bradycardia.

CONCLUSION

In conclusion, several large prospective studies and meta-analyses demonstrated that propofol provides significant advantages over benzodiazepine and opioid agents for deep patient sedation during advanced endoscopic procedures like ERCP and/or EUS: propofol was more effective and safer than the combination of midazolam and meperidine for achieving and maintaining an adequate level of sedation during endoscopic procedures, with better titration of the level of sedation and shorter recovery times. The trend of an increased usage of propofol and generalization of NAAP sedation in both hospital and private practice settings will certainly increase in the years to come.

REFERENCES

- 1 **Ferreira AO**, Cravo M. Sedation in gastrointestinal endoscopy: Where are we at in 2014? *World J Gastrointest Endosc* 2015; **7**: 102-109 [PMID: 25685266 DOI: 10.4253/wjge.v7.i2.102]
- 2 **Triantafyllidis JK**, Merikas E, Nikolakis D, Papalois AE. Sedation in gastrointestinal endoscopy: current issues. *World J Gastroenterol* 2013; **19**: 463-481 [PMID: 23382625 DOI: 10.3748/wjg.v19.i4.463]
- 3 **Obara K**, Haruma K, Irisawa A, Kaise M, Gotoda T, Sugiyama M, Tanabe S, Horiuchi A, Fujita N, Ozaki M, Yoshida M, Matsui T, Ichinose M, Kaminishi M. Guidelines for sedation in gastroenterological endoscopy. *Dig Endosc* 2015; **27**: 435-449 [PMID: 25677012 DOI: 10.1111/den.12464]
- 4 **Igea F**, Casellas JA, González-Huix F, Gómez-Oliva C, Baudet JS, Cacho G, Simón MA, De la Morena E, Lucendo A, Vida F. Sedation for gastrointestinal endoscopy. *Endoscopy* 2014; **46**: 720-731 [PMID: 25061964 DOI: 10.1055/s-0034-1377561]
- 5 **Vargo JJ**, DeLegge MH, Feld AD, Gerstenberger PD, Kwo PY, Lightdale JR, Nuccio S, Rex DK, Schiller LR. Multisociety sedation curriculum for gastrointestinal endoscopy. *Gastroenterology* 2012; **143**: e18-e41 [PMID: 22624720 DOI: 10.1053/j.gastro.2012.05.001]
- 6 **Dumonceau JM**, Riphaus A, Aparicio JR, Beilenhoff U, Knappe JT, Ortmann M, Paspatis G, Ponsioen CY, Racz I, Schreiber F, Vilman P, Wehrmann T, Wientjes C, Walder B. 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**: 960-974 [PMID: 21072716 DOI: 10.1055/s-0030-1255728]
- 7 **Riphaus A**, Wehrmann T, Weber B, Arnold J, Beilenhoff U, Bitter H, von Delius S, Domagk D, Ehlers AF, Faiss S, Hartmann D, Heinrichs W, Hermans ML, Hofmann C, In der Smitten S, Jung M, Kähler G, Kraus M, Martin J, Meining A, Radke J, Rösch T, Seifert H, Sieg A, Wigglinghaus B, Kopp I. S3-guidelines--sedation in gastrointestinal endoscopy. *Z Gastroenterol* 2008; **46**: 1298-1330 [PMID: 19012203 DOI: 10.1055/s-2008-1027850]
- 8 **Müller M**, Wehrmann T. How best to approach endoscopic sedation? *Nat Rev Gastroenterol Hepatol* 2011; **8**: 481-490 [PMID: 21750516 DOI: 10.1038/nrgastro.2011.122]
- 9 **McQuaid KR**, Laine L. A systematic review and meta-analysis of randomized, controlled trials of moderate sedation for routine endoscopic procedures. *Gastrointest Endosc* 2008; **67**: 910-923 [PMID: 18440381 DOI: 10.1016/j.gie.2007.12.046]
- 10 **Cheriyian DG**, Byrne MF. Propofol use in endoscopic retrograde cholangiopancreatography and endoscopic ultrasound. *World J Gastroenterol* 2014; **20**: 5171-5176 [PMID: 24833847 DOI: 10.3748/wjg.v20.i18.5171]
- 11 **Ellett ML**. A literature review of the safety and efficacy of using propofol for sedation in endoscopy. *Gastroenterol Nurs* 2010; **33**: 111-117 [PMID: 20389224 DOI: 10.1097/SGA.0b013e3181d601fb]
- 12 **Slagelse C**, Vilman P, Hornslet P, Hammering A, Mantoni T. Nurse-administered propofol sedation for gastrointestinal endoscopic procedures: first Nordic results from implementation of a structured training program. *Scand J Gastroenterol* 2011; **46**: 1503-1509 [PMID: 22050137 DOI: 10.3109/00365521.2011.619274]
- 13 **Fanti L**, Testoni PA. Sedation and analgesia in gastrointestinal endoscopy: what's new? *World J Gastroenterol* 2010; **16**: 2451-2457 [PMID: 20503443 DOI: 10.3748/wjg.v16.i20.2451]
- 14 **Mathus-Vliegen EM**, de Jong L, Kos-Foekema HA. Significant and safe shortening of the recovery time after flumazenil-reversed midazolam sedation. *Dig Dis Sci* 2014; **59**: 1717-1725 [PMID: 24563235 DOI: 10.1007/s10620-014-3061-2]
- 15 **Lee BS**, Ryu J, Lee SH, Lee MG, Jang SE, Hwang JH, Ryu JK, Do SH, Kim YT. Midazolam with meperidine and dexmedetomidine vs. midazolam with meperidine for sedation during ERCP: prospective, randomized, double-blinded trial. *Endoscopy* 2014; **46**: 291-298 [PMID: 24671858 DOI: 10.1055/s-0033-1358909]
- 16 **Varadarajulu S**, Eloubeidi MA, Tamhane A, Wilcox CM. Prospective randomized trial evaluating ketamine for advanced endoscopic procedures in difficult to sedate patients. *Aliment Pharmacol Ther* 2007; **25**: 987-997 [PMID: 17403003 DOI: 10.1111/j.1365-2036.2007.03285.x]
- 17 **Chudnofsky CR**, Weber JE, Stoyanoff PJ, Colone PD, Wilkerson MD, Hallinen DL, Jaggi FM, Boczar ME, Perry MA. A combination of midazolam and ketamine for procedural sedation and analgesia in adult emergency department patients. *Acad Emerg Med* 2000; **7**: 228-235 [PMID: 10730829 DOI: 10.1111/j.1553-2712.2000.tb01064.x]
- 18 **Sethi S**, Wadhwa V, Thaker A, Chuttani R, Pleskow DK, Barnett SR, Leffler DA, Berzin TM, Sethi N, Sawhney MS. Propofol versus traditional sedative agents for advanced endoscopic procedures: a meta-analysis. *Dig Endosc* 2014; **26**: 515-524 [PMID: 24354404 DOI: 10.1111/den.12219]
- 19 **Vargo JJ**, Zuccaro G, Dumot JA, Shermock KM, Morrow JB, Conwell DL, Trolli PA, Maurer WG. Gastroenterologist-administered propofol versus meperidine and midazolam for advanced upper endoscopy: a prospective, randomized trial.

- Gastroenterology* 2002; **123**: 8-16 [PMID: 12105827 DOI: 10.1053/gast.2002.34232]
- 20 **Molina-Infante J**, Dueñas-Sadornil C, Mateos-Rodríguez JM, Perez-Gallardo B, Vinagre-Rodríguez G, Hernandez-Alonso M, Fernandez-Bermejo M, Gonzalez-Huix F. Nonanesthesiologist-administered propofol versus midazolam and propofol, titrated to moderate sedation, for colonoscopy: a randomized controlled trial. *Dig Dis Sci* 2012; **57**: 2385-2393 [PMID: 22615015 DOI: 10.1007/s10620-012-2222-4]
 - 21 **Bakman Y**, Freeman ML. Update on biliary and pancreatic sphincterotomy. *Curr Opin Gastroenterol* 2012; **28**: 420-426 [PMID: 22782017 DOI: 10.1097/MOG.0b013e32835672f3]
 - 22 **Garewal D**, Powell S, Milan SJ, Nordmeyer J, Waikar P. Sedative techniques for endoscopic retrograde cholangiopancreatography. *Cochrane Database Syst Rev* 2012; **6**: CD007274 [PMID: 22696368 DOI: 10.1002/14651858.CD007274]
 - 23 **Bo LL**, Bai Y, Bian JJ, Wen PS, Li JB, Deng XM. Propofol vs traditional sedative agents for endoscopic retrograde cholangiopancreatography: a meta-analysis. *World J Gastroenterol* 2011; **17**: 3538-3543 [PMID: 21941422 DOI: 10.3748/wjg.v17.i30.3538]
 - 24 **Lee TH**, Lee CK, Park SH, Lee SH, Chung IK, Choi HJ, Cha SW, Moon JH, Cho YD, Hwangbo Y, Kim SJ. Balanced propofol sedation versus propofol monosedation in therapeutic pancreaticobiliary endoscopic procedures. *Dig Dis Sci* 2012; **57**: 2113-2121 [PMID: 22615018 DOI: 10.1007/s10620-012-2234-0]
 - 25 **Ikeuchi N**, Itoi T, Gotoda T, Kusano C, Kono S, Kamada K, Tsuchiya T, Tominaga N, Mukai S, Moriyasu F. Feasibility of non-anesthesiologist-administered propofol sedation for emergency endoscopic retrograde cholangiopancreatography. *Gastroenterol Res Pract* 2015; **2015**: 685476 [PMID: 25883644 DOI: 10.1155/2015/685476]
 - 26 **Mazanikov M**, Udd M, Kylänpää L, Mustonen H, Lindström O, Färkkilä M, Halttunen J, Pöyhä R. A randomized comparison of target-controlled propofol infusion and patient-controlled sedation during ERCP. *Endoscopy* 2013; **45**: 915-919 [PMID: 24104763 DOI: 10.1055/s-0033-1344712]
 - 27 **Vilmann P**, Săftoiu A. Endoscopic ultrasound-guided fine needle aspiration biopsy: equipment and technique. *J Gastroenterol Hepatol* 2006; **21**: 1646-1655 [PMID: 16984583 DOI: 10.1111/j.1440-1746.2006.04475.x]
 - 28 **Redondo-Cerezo E**, Sánchez-Robaina A, Martínez Cara JG, Ojeda-Hinojosa M, Matas-Cobos A, Sánchez Capilla AD, López de Hierro Ruiz M, Pleguezuelo-Díaz J, de Teresa J. Gastroenterologist-guided sedation with propofol for endoscopic ultrasonography in average-risk and high-risk patients: a prospective series. *Eur J Gastroenterol Hepatol* 2012; **24**: 506-512 [PMID: 22330236 DOI: 10.1097/MEG.0b013e328350fcbf]
 - 29 **Yusoff IF**, Raymond G, Sahai AV. Endoscopist administered propofol for upper-GI EUS is safe and effective: a prospective study in 500 patients. *Gastrointest Endosc* 2004; **60**: 356-360 [PMID: 15332023 DOI: 10.1016/S0016-5107(04)01711-0]
 - 30 **Pagano N**, Arosio M, Romeo F, Rando G, Del Conte G, Carlino A, Strangio G, Vitetta E, Malesci A, Repici A. Balanced Propofol Sedation in Patients Undergoing EUS-FNA: A Pilot Study to Assess Feasibility and Safety. *Diagn Ther Endosc* 2011; **2011**: 542159 [PMID: 21785561 DOI: 10.1155/2011/542159]
 - 31 **Fanti L**, Agostoni M, Arcidiacono PG, Albertin A, Strini G, Carrara S, Guslandi M, Torri G, Testoni PA. Target-controlled infusion during monitored anesthesia care in patients undergoing EUS: propofol alone versus midazolam plus propofol. A prospective double-blind randomised controlled trial. *Dig Liver Dis* 2007; **39**: 81-86 [PMID: 17049322 DOI: 10.1016/j.dld.2006.09.004]
 - 32 **Rex DK**, Heuss LT, Walker JA, Qi R. Trained registered nurses/endoscopy teams can administer propofol safely for endoscopy. *Gastroenterology* 2005; **129**: 1384-1391 [PMID: 16285939 DOI: 10.1053/j.gastro.2005.08.014]
 - 33 **Vargo JJ**. Doc, can I drive home? *Am J Gastroenterol* 2009; **104**: 1656-1657 [PMID: 19574969 DOI: 10.1038/ajg.2009.262]
 - 34 **Frieling T**, Heise J, Kreysel C, Kuhlen R, Schepke M. Sedation-associated complications in endoscopy--prospective multicentre survey of 191142 patients. *Z Gastroenterol* 2013; **51**: 568-572 [PMID: 23740356 DOI: 10.1055/s-0032-1330441]
 - 35 **Lee SH**. Non-anesthesiologist administered propofol with or without midazolam for moderate sedation-the problem is not "which regimen" but "who's regimen". *Dig Dis Sci* 2012; **57**: 2243-2245 [PMID: 22833381 DOI: 10.1007/s10620-012-2268-3]
 - 36 **González-Santiago JM**, Martín-Noguerol E, Vinagre-Rodríguez G, Hernández-Alonso M, Dueñas-Sadornil C, Pérez-Gallardo B, Mateos-Rodríguez JM, Fernández-Bermejo M, Robledo-Andrés P, Molina-Infante J. Intermittent boluses versus pump continuous infusion for endoscopist-directed propofol administration in colonoscopy. *Rev Esp Enferm Dig* 2013; **105**: 378-384 [PMID: 24206547 DOI: 10.4321/S1130-01082013000700002]
 - 37 **Repici A**, Pagano N, Hassan C, Carlino A, Rando G, Strangio G, Romeo F, Zullo A, Ferrara E, Vitetta E, Ferreira Dde P, Danese S, Arosio M, Malesci A. Balanced propofol sedation administered by nonanesthesiologists: The first Italian experience. *World J Gastroenterol* 2011; **17**: 3818-3823 [PMID: 21987624 DOI: 10.3748/wjg.v17.i33.3818]
 - 38 **Sieg A**, Beck S, Scholl SG, Heil FJ, Gotthardt DN, Stremmel W, Rex DK, Friedrich K. Safety analysis of endoscopist-directed propofol sedation: a prospective, national multicenter study of 24441 patients in German outpatient practices. *J Gastroenterol Hepatol* 2014; **29**: 517-523 [PMID: 24716213 DOI: 10.1111/jgh.12458]
 - 39 **Lee DW**, Chan KW, Poon CM, Ko CW, Chan KH, Sin KS, Sze TS, Chan AC. Relaxation music decreases the dose of patient-controlled sedation during colonoscopy: a prospective randomized controlled trial. *Gastrointest Endosc* 2002; **55**: 33-36 [PMID: 11756911 DOI: 10.1067/mge.2002.120387]
 - 40 **Jensen JT**, Vilmann P, Horsted T, Hornslet P, Bodtger U, Banning A, Hammering A. Nurse-administered propofol sedation for endoscopy: a risk analysis during an implementation phase. *Endoscopy* 2011; **43**: 716-722 [PMID: 21811940 DOI: 10.1055/s-0030-1256515]
 - 41 **Goudra BG**, Singh PM, Gouda G, Borle A, Gouda D, Dravida A, Chandraskhara V. Safety of Non-anesthesia Provider-Administered Propofol (NAAP) Sedation in Advanced Gastrointestinal Endoscopic Procedures: Comparative Meta-Analysis of Pooled Results. *Dig Dis Sci* 2015 Mar 3; Epub ahead of print [PMID: 25732719]
 - 42 **Friedrich K**, Scholl SG, Beck S, Gotthardt D, Stremmel W, Rex DK, Sieg A. Respiratory complications in outpatient endoscopy with endoscopist-directed sedation. *J Gastrointest Liver Dis* 2014; **23**: 255-259 [PMID: 25267952 DOI: 10.15403/jgld.2014.1121.233.kfl]
 - 43 **Cohen LB**. Nurse-administered propofol sedation for upper endoscopic ultrasonography: not yet ready for prime time. *Nat Clin Pract Gastroenterol Hepatol* 2009; **6**: 76-77 [PMID: 19092792 DOI: 10.1038/ncpgasthep1332]
 - 44 **Vargo JJ**. Big NAPS, little NAPS, mixed NAPS, computerized NAPS: what is your flavor of propofol? *Gastrointest Endosc* 2007; **66**: 457-459 [PMID: 17725935 DOI: 10.1016/j.gie.2007.03.1035]
 - 45 **Perel A**. Non-anaesthesiologists should not be allowed to administer propofol for procedural sedation: a Consensus Statement of 21 European National Societies of Anaesthesia. *Eur J Anaesthesiol* 2011; **28**: 580-584 [PMID: 21705907 DOI: 10.1097/EJA.0b013e328348a977]

P- Reviewer: Giannopoulos GA, Skok P, Sieg A
S- Editor: Tian YL L- Editor: A E- Editor: Wu HL





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>

