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EDITORIAL

Non-anesthesiologist Administered Propofol With or Without Midazolam for Moderate Sedation—the Problem Is Not "Which Regimen" but "Who's Regimen"

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Propofol is a unique sedative that combines a rapid onset of action (30–45 s) with a short duration of effect (4–8 min), which makes it an ideal agent for relatively short outpatient procedures such as esophagogastroduodenoscopy (EGD) and colonoscopy. There is no doubt that propofol-based sedation has additional benefits compared to traditional sedation. When compared with traditional sedation in previous meta-analyses, propofol-based sedation had similar rates of adverse effects, provided higher patient satisfaction for most endoscopic procedures, decreased time to sedation, decreased recovery time (and may therefore decrease discharge time compared with traditional sedation) and increased the quality of endoscopic examination [1–3]. Recently, in Western countries, the main issue with propofol-based sedation has been, not "which regimen" is used but "who administers" the sedation. Non-anesthesiologist administration of propofol (NAAP) retains the advantages of propofol-based sedation while maintaining patient safety and lowering costs [4].

With regard to safety, Rex et al. [5] reported the largest safety data with NAAP, including 223,656 published and 422,424 unpublished cases. Propofol may cause hypoventilation, hypotension, and bradycardia relatively frequently, but severe adverse effects are extremely rare. Deaths occurred in two patients with pancreatic cancer, a severely handicapped patient with mental retardation, and a patient with severe cardiomyopathy. NAAP has a lower mortality rate than published data on endoscopist-delivered benzodiazepines and opioids and a comparable rate to published data on general anesthesia by anesthesiologists.

In the author's opinion, the main point of controversy regarding NAAP is the cost. Two indirect calculation studies found that propofol was at least as cost-effective as traditional sedation for colonoscopy and EUS [6, 7]. The indirect cost-effectiveness was attributable to a higher daily number of procedures due to shorter post-procedure recovery times. Although propofol is more efficient than conventional regimens in terms of induction and recovery times, it is only cost-effective compared with standard sedation when administered by a registered nurse under the supervision of the endoscopist [8]. Anesthesia professional-delivered sedation has become increasingly common when performing colonoscopy and EGD in both the United States and European countries. From 2003 to 2007 in the USA, the involvement of anesthesiologists in colonoscopy almost tripled, from 9 to 25 % of colonoscopies, and this will be increased >50 % by 2015 [9]. Hassan et al. [10] calculated the costs related to NAAP implementation at a national level for a screening colonoscopy program in the USA—propofol administration by nurses rather than by anesthesiologists would result in savings of 3.2 billion USD over a 10-year period. Their calculations assumed 28.3 million screening colonoscopies over 10 years, including 9.8 million colonoscopies (34.8 %) with propofol-based sedation. This would translate into savings per colonoscopy of 326.5 USD (3.2 billion/9.8 million). In France, fecal testing has been chosen for colorectal cancer screening; it is the most cost-effective method since 90 % of colonoscopies there are performed with intravenous sedation which may only be administered by anesthesiologists [11]. Anesthesiologist involvement adds 285 % to the cost of a colonoscopy (EUR 740 vs. EUR 192, respectively, for a colonoscopy with vs. without an anesthesiologist).

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In this issue of *Digestive Disease and Science*, Molina-Infante et al. [12] report the feasibility of moderate sedation with two different regimens, NAAP with or without midazolam, for colonoscopy. They assessed the depth of sedation by the OAA/S (Observer Assessment of Alertness/Sedation) scale throughout the procedure (mean 9 per case). Deep sedation occurred at least once more often with NAAP with midazolam at minute 4 which coincides with the peak effect of midazolam. There were 17 minor adverse events (10 transient oxygen desaturations, 3 bradycardic events and 5 transient hypotensive events) associated with the deep sedation. However, neither mechanical ventilation nor endotracheal intubation were necessary during the study. Additionally, patients that underwent colonoscopy with moderate sedation from single agent propofol by NAAP did not experience deep sedation and 95 % were willing to undergo repeat colonoscopy. In summary, moderate sedation for routine colonoscopy was feasible with both NAAP regimens. However, the NAAP with midazolam regimen promotes a deeper and longer moderate sedation, improving patient satisfaction rates but prolonging early recovery time. Although the authors want to address a comparison between propofol alone and balanced propofol sedation (BPS) targeted to moderate sedation for outpatient colonoscopy, many gastroenterologists (myself included) would get their confidence that NAAP be the recommended sedation method for their daily practice from this issue. The use of midazolam combined with propofol has been somewhat controversial; however, it seems that both NAAP regimens are suitable and reasonable for routine colonoscopy with regard to patient safety and endoscopic unit's efficiency. The decision to use propofol alone or BPS should be determined according to the characteristics of each patient, procedure type and endoscopic unit. In endoscopy units with large recovery rooms, good patient performance status or more complicated cases, the BPS regimen may be more suitable due to longer and deeper sedation. Furthermore, BPS would allow for both an increased early recovery time and an increased amnesia, thereby improving patient satisfaction rates. On the other hand, primary practitioners with small recovery rooms or for patients with a poor performance status may prefer the single propofol regimen since it may result in a safer procedure and shorter recovery time.

Recently, policies for endoscopic procedure-related moderate or deep sedation in many developed countries have been "shifting from NAAP to AAP." In the author's experience, almost all experienced endoscopists agree that this shift may not be appropriate in all cases. Although some would argue that AAP provides better patient safety monitoring, simple procedures such as diagnostic EGD or colonoscopy can certainly be done safely using NAAP. A recent large volume (over 1,000 cases) study from Lucendo et al. concluded that colonoscopy under endoscopist-controlled propofol sedation in low-risk patients is safe and effective, allowing for a complete exploration. However, patients over 65 years old and/or classified as ASA II are more likely to have a decrease in blood pressure and a prolonged recovery time [13]. In addition, Poincloux et al. [14] recently reported the first direct comparative study with NAAP (propofol only) moderate sedation and AAP deep sedation for colonoscopy. The NAAP group expressed a good level of satisfaction (95 vs. 75 %; $p = 0.03$) more frequently, a willingness to undergo further colonoscopies under the same conditions (95 vs. 79 %; $p = 0.02$), and experienced fewer side-effects (16 vs. 3, respectively; $p < 0.008$). As a result of these and many previous reports, NAAP has been gaining support (at least in moderate sedation) because of its safety and cost-effectiveness.

In the author's opinion, the decision between NAAP and AAP should be made based on the sedation level and procedure type. Diagnostic or shorter procedures (diagnostic endoscopy, polypectomy, or simple endoscopic mucosal resection) requiring moderate sedation may be conducted using the NAAP method. On the other hand, therapeutic or longer procedures (endoscopic submucosal dissection, endoscopic ultrasonography or endoscopic retrograde cholangiopancreatography) could be performed using the AAP method. Additional considerations are each country's healthcare finance policy and status. Although many Western anesthesiologists have claimed that AAP is required for deep sedation for complex procedures, many Asian countries, including South Korea and Japan, still use NAAP (mainly BPS) for therapeutic procedures because the national health insurance has refused to approve medical reimbursement for anesthesiological care during endoscopic procedures. In our previous report, compared with conventional sedation (midazolam and meperidine), non-anesthesiologist administrated BPS (propofol in combination with midazolam and meperidine) provides higher health care provider satisfaction, better patient cooperation, and similar adverse event profiles in patients undergoing therapeutic endoscopic procedures [15]. None of the patients required assisted ventilation or premature termination of a procedure using this method. Therefore, NAAP may play an important role in complex procedures requiring deep sedation in some countries.

The only way to definitively end the debate of "who's regimen" between NAAP and AAP is for gastroenterologists and anesthesiologists to collaborate on the issue. The decision should be made based on patient safety and the efficient use of limited resources and not based on political imperatives. Furthermore, it is important for endoscopists to seek out NAAP training courses, since specific skills and knowledge are necessary for both endoscopists and nursing

staff in order to ensure patient safety and comfort during NAAP procedures. This collaboration and training will ensure that the use of NAAP remains a feasible and more frequently used method of sedation.

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