#### **ADVANCES IN ENDOSCOPY**

Current Developments in Diagnostic and Therapeutic Endoscopy

Section Editor: John Baillie, MB ChB, FRCP

#### Sedation in Colonoscopy



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#### **G&H** Which agents are currently available for use as sedatives for colonoscopy?

**AS** The sedative agents that are currently available for colonoscopy include midazolam, propofol, diazepam, diphenhydramine, promethazine, meperidine, and fentanyl. Among these, midazolam and propofol are the most commonly used sedatives, whereas fentanyl is the most frequently administered analgesic.

### **G&H** What differentiates conscious sedation from deep sedation?

**AS** With conscious sedation, patients typically remain arousable at all times. Deep sedation with propofol allows most patients to sleep through the procedure, and it is administered by an anesthesiologist or a nurse anesthetist. However, the above demarcation between conscious and deep sedation may not hold true for all patients, as some may sleep through the procedure with conscious sedation or remain arousable with deep sedation.

#### **G&H** What advantages and disadvantages are associated with sedatives?

**AS** The main advantages of sedative agents are that they allow patients to feel comfortable and relaxed during the endoscopic procedure and to experience little to no pain. Deep sedation, in most cases, allows patients to sleep through the procedure without remembering any medical activity upon waking up. The disadvantages relate to the aftereffects, which include drowsiness and impaired

cognitive function for 4 to 24 hours afterwards. Therefore, patients are unable to work or operate a motor vehicle, and require an accompanying person to drive them home after the endoscopy.

# **G&H** Are any adverse events related to these sedatives or to sedation for colonoscopy in general?

AS Each drug is associated with its own list of potential adverse events, but respiratory depression is the main adverse event associated with all sedatives. Physicians should monitor the respiration and heart rate of all patients undergoing conscious sedation to avoid this event. Propofol in particular can lead to apnea and has a relatively narrow therapeutic window, which is the main reason why the US Food and Drug Administration has decided that an anesthesiologist or nurse anesthetist, rather than a registered nurse or gastroenterologist, should administer the drug. Midazolam can cause retrograde amnesia, although amnesia in the context of conscious sedation is actually considered a beneficial outcome. Midazolam also leads to minor adverse events such as hiccups and nasal itching, and in rare instances can have paradoxical effects in that the patient becomes hyperactive and agitated. These adverse events typically resolve within minutes.

#### **G&H** How does each agent compare in terms of cost?

**AS** The main distinction in cost is between deep vs conscious sedation. Because administration of deep sedation

requires the involvement of a nurse anesthetist or anesthesiologist, its use tends to be more costly than conscious sedation.

### **G&H** Can you briefly explain the design of your study that evaluated practice patterns of sedation?

**AS** As clinical gastroenterologists, my colleagues and I were interested in learning how our practice patterns compared with those of other gastroenterologists. We used a database of endoscopic procedures among 100 gastroenterology practices located throughout the United States to evaluate how practice patterns of sedation for colonoscopy varied by demographic characteristics (patient age, sex, ethnicity) and how procedural characteristics determined the amount of conscious sedation given.

In the database, which is in the public domain and does not reveal patient identity, 77% of endoscopies were performed in community or private practices, 9% in academic centers, and 14% in hospitals affiliated with the US Department of Veterans Affairs. My colleagues and I looked at the use of the 7 most common drugs mentioned above (midazolam, diazepam, fentanyl, meperidine, diphenhydramine, promethazine, and propofol) and analyzed how patient demographics and colonoscopy outcomes affected the use of these drugs. We were able to analyze almost 1.4 million colonoscopies performed between 2000 and 2013 (Figure 1). Although this is only a small fraction of all colonoscopies performed in the United States, it still constitutes a fairly large sample representative of practice patterns throughout the United States.

#### **G&H** What trends did you identify for the use of specific agents over the study period?

AS The main outcome of our study was that practice patterns were fairly consistent and similar throughout the United States. As mentioned above, midazolam continued to be the most commonly used sedative and fentanyl remained the most common analgesic. A large fraction of patients were given a combination of these 2 drugs; the average dose was 4 mg of midazolam and 100 µg of fentanyl. In a much smaller group of patients, gastroenterologists added diphenhydramine as a third drug, and in approximately a quarter of patients, propofol was used as a sedative. Age was the most important factor that determined the dose amount. Gastroenterologists typically used a smaller dose in older patients, who tend to be more sensitive to conscious sedation or sedatives in general (Figure 2).

The second most important predictor for dose was the length of the procedure; the longer the procedure, the more sedatives were being used. This pattern applied to all individual drugs that we studied, particularly midazolam,

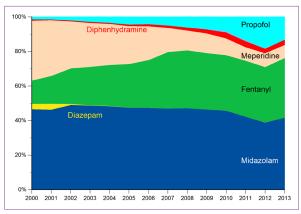


Figure 1. Proportional rates of individual sedative usage between 2000 and 2013.

fentanyl, meperidine, and propofol. Some of the trends concerning sex and ethnicity were also statistically significant, but they are probably less relevant in clinical practice. Overall, men and women tended to receive a similar dose, although diazepam and midazolam were given in slightly higher doses to women than men. Within ethnic distributions, there was a small trend for more sedatives (eg, midazolam and fentanyl) to be used in whites than blacks or Hispanics. Alternatively, propofol was used more frequently in Hispanics than in other ethnic groups, and meperidine was used more frequently in blacks than other groups. A variety of statistically significant patterns emerge whenever large numbers of patients are being studied, but such differences in dosing do not necessarily carry much or any clinical significance.

# **G&H** What role do diphenhydramine and promethazine play in modern endoscopic practice?

AS Diphenhydramine is beneficial in patients who may feel more anxious or agitated prior to a colonoscopy and require a more effective conscious sedation than the usual combination of fentanyl and midazolam. Likewise, diphenhydramine may be added to fentanyl and midazolam in patients who have a history of alcohol or drug abuse and are more difficult to sedate. Promethazine has recently fallen into disfavor due to the potential of vascular necrosis in instances of extravasation. Therefore, the majority of gastroenterologists would prefer to use diphenhydramine instead.

## **G&H** What do the results of your study mean for the future use of sedative agents?

**AS** One trend that became obvious in our study is the rising use of propofol in the United States. Most recently, its frequency of utilization has increased to 20% or even 25%

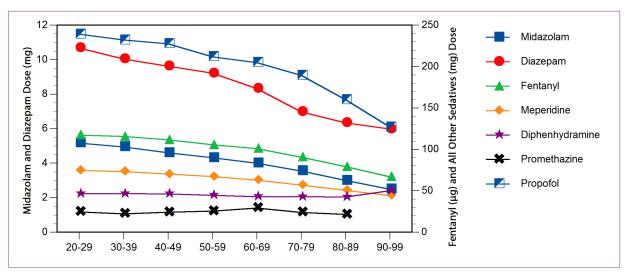


Figure 2. Average dose of sedation by age group of patients undergoing colonoscopy.

of all colonoscopies. Ultimately, gastroenterologists want their patients to be happy and to feel unafraid of repeat surveillance or screening colonoscopy. In that regard, propofol use may become more common in the future because it can meet these needs better than conscious sedation.

#### **G&H** What research is needed in this field?

AS It would be beneficial to compare patterns of conscious sedation in other endoscopic procedures, such as esophagogastroduodenoscopy, endoscopic retrograde cholangio-pancreatography, and endoscopic ultrasound. Other areas of research relate to the statistical distribution of practice patterns with respect to dose and procedural length in large groups of patients. It would be helpful to know whether the distribution is normal or lognormal, or whether it follows a power law with a very long tail. What are the reasons for potential outliers with respect to very long procedural times or high demands for sedation? Additionally, studies are needed on patient satisfaction as part of quality assur-

ance. Studies already exist that analyze various aspects of documentation, indication, or outcome associated with endoscopy and sedation; it might also be interesting to study quality with respect to other measures of endoscopy, such as procedural skills and dexterity of the endoscopist and how they affect the amount of sedation given.

Dr Sonnenberg has no relevant conflicts of interest to disclose.

#### **Suggested Reading**

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