

# ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

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## Patient-controlled Sedation for Endoscopic Procedures

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### G&H Could you explain what is meant by patient-controlled sedation?

**JV** Patient-controlled sedation usually involves a target-controlled method, which is a pharmacokinetically based model that utilizes an infusion system that may be computer-controlled. There are two types of patient-controlled sedation. In the open-loop system, the sedation is adjusted according to a target drug concentration. In the closed-loop system, the patient directs the infusion system to release medication up to a set point known as a “lockout,” which minimizes oversedation. Delivery of medication in a closed-loop system may be based on the patient’s perception of pain or feedback from the physiologic parameters monitored during the procedure. In the first scenario, the target is the plasma concentration of the medications, with override by the procedural team, whereas in the second scenario, the dosage is determined by both the patient and the machine-physician interface.

### G&H In which patients and endoscopic procedures is patient-controlled sedation normally used?

**JV** It is important to point out that the studies evaluating patient-controlled sedation have been conducted mainly in healthy patients undergoing ambulatory procedures such as colonoscopy. There are very little data for prolonged procedures such as endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound (EUS), both of which require deep sedation. At present, there have been approximately 10 randomized

controlled trials, which, although quite small, offer an indication as to where patient-controlled sedation may be optimal. At this point, however, it is not possible to make an overall recommendation for patient-controlled sedation overtaking traditional sedation. At Digestive Disease Week 2008, Pambianco and colleagues will present results from a large study examining patient-controlled sedation in over 1,000 patients that will help answer these questions.

### G&H Which sedation agents have been used in patient-controlled sedation?

**JV** Although various sedation agents have been used, most scenarios of patient-controlled sedation involve a combination of a short-acting narcotic such as remifentanyl (Ultiva, Abbott) and propofol or, to a lesser extent, the combination of fentanyl and midazolam. In patient-controlled sedation, a combination of medications is normally used. Although several small case series have examined the use of propofol alone, this experience has essentially been relegated to a handful of colonoscopy and ERCP trials.

### G&H How prevalent is the use of patient-controlled sedation, as opposed to more traditional forms of sedation, for endoscopic procedures?

**JV** Patient-controlled sedation is quite uncommon, though its utilization appears to be gaining momentum. I believe that we are now seeing an evolution in patient-controlled sedation, and there is a very real possibility in the near future that we will see gastroenterologists administer patient-controlled sedation platforms, across many

procedures, that will have similar safety profiles compared to traditional sedation. These platforms may also have the advantage of improved efficiency in terms of recovery profiles and improved patient satisfaction.

**G&H** What have studies shown regarding the efficacy of patient-controlled sedation as compared to gastroenterologist- or nurse-administered sedation?

**JV** The efficacy of patient-controlled sedation depends upon the type of procedure performed and the type of sedation agents used. Mandel and associates recently conducted a study that examined patient-controlled sedation for ambulatory colonoscopy. The patients received a loading dose of the combination of either propofol and remifentanyl or midazolam and fentanyl and then were able to self-administer additional medication as needed, up to the lockout point, to ensure that patients were not overmedicated. The patients who received the propofol and remifentanyl combination demonstrated superiority in terms of time to sedation and recovery parameters such as recovery room time and time to ambulation. There was no difference between the sedation groups in terms of the length of the colonoscopy or the polyp detection rate.

**G&H** How safe is patient-controlled sedation compared to other forms of sedation?

**JV** The safety of patient-controlled sedation depends mainly on the type of system used. In the study by Mandel and colleagues, it was quite difficult to obtain a good understanding of safety issues, as only 50 patients were enrolled in the study and one anesthesiologist was involved. However, other studies have shed some light on safety issues in patient-controlled sedation. Several studies have examined the use of propofol infusion in a target-controlled fashion for ERCP; in one case series, the infusion device was tied to reaching a plasma concentration of propofol. Some patients were oversedated, whereas others were undersedated.

Another important study in terms of safety was a case series conducted by Pambianco and associates in the United States and Belgium, which used a computerized propofol infusion machine to administer a bolus dose of fentanyl and propofol infusion directed by physiologic monitoring. This study used an automated responsiveness-monitoring device, which has been shown to detect the presence of deep sedation. Among 48 patients undergoing upper endoscopy and colonoscopy, Pambianco and colleagues found that the safety and efficacy of the sedation were excellent and the majority of sedation levels were in

the mild-to-moderate range. These results triggered the recent multicenter US study that Pambianco and associates conducted in over 1,000 patients, which also used an automated responsiveness-monitoring device.

**G&H** Has patient-controlled sedation shown positive results for patient and physician satisfaction compared to other forms of sedation?

**JV** Patient satisfaction has essentially been equivalent in most studies. In some studies, physician satisfaction has been superior in the patient-controlled arm, but it is very difficult to remove bias from these studies to determine whether there is actual improvement. In the study by Mandel and coworkers, which blinded gastroenterologists as well as nurses to the type of patient-controlled sedation, the perceptions of satisfaction of the patient, nurse, and gastroenterologist were equivalent between the two groups.

**G&H** Have any cost-effectiveness studies been performed in patient-controlled sedation?

**JV** There have not been any studies examining the cost-effectiveness of patient-controlled sedation. Further studies are needed to answer this important question. One could reasonably expect that patient-controlled sedation may be more costly than standard sedation and most likely less expensive than anesthesiologist-administered sedation. Gains in efficiency throughout the procedure will be needed to offset the higher costs when compared to standard sedation, which is administered by the gastroenterologist. As most of the patients studied with patient-controlled sedation have undergone colonoscopy, we have very little data regarding patients undergoing upper endoscopic procedures. Efficacy outcomes in these studies have not been standardized and have ranged from recovery times to patients' ability to resume ambulation and normal oral intake. Additional costs associated with each of these measures, such as the need for overnight admission, lost work productivity, and the length of follow-up, should also be considered, as they contribute to the cost of the procedure. In the future, we may find that patient-controlled sedation could decrease the number of personnel in the procedure room.

**G&H** What are the main side effects and complications of this type of sedation?

**JV** Most studies are randomized, controlled trials that involve colonoscopy and are designed to detect differences in recovery parameters. The available data have used dif-

ferent drug combinations, infusion machines, and lock-out parameters, thereby producing heterogeneous data. As procedural sedation is, fortunately, extremely safe, a very large group of patients is needed in order to detect any difference in safety. At this point, I would conclude that the data thus far are positive for patient-controlled sedation in colonoscopy. However, the worldwide experience remains too limited to detect any obvious difference in safety profiles.

### G&H What are the next steps for future research in patient-controlled sedation?

**JV** Patient-controlled sedation should be further investigated in different patient populations, including the elderly, those with significant comorbidities, and, in particular, obese patients, as there is a dearth of information regarding sedation outcomes in these patients.

In addition, it is important to further investigate the use of patient-controlled sedation in patients undergoing upper endoscopy. Although the bulk of studies has been conducted in colonoscopy, the average clinical practice performs a mixture of both upper endoscopy

and colonoscopy. Other applications that require further study include prolonged procedures such as ERCP and EUS, in which deep sedation is often necessary.

### Suggested Reading

Mandel JE, Tanner JW, Lichtenstein GR, Metz DC, Katzka DA, et al. A randomized, controlled, double-blind trial of patient-controlled sedation with propofol/remifentanyl versus midazolam/fentanyl for colonoscopy. *Anesth Analg*. 2008;106:434-439.

Pambianco DJ, McRorie J, Martin J, Poltilove R, Whitten CJ. Feasibility assessment of computer assisted personalized sedation: a sedation delivery system to administer propofol for gastrointestinal endoscopy. *Gastrointest Endosc*. 2006;63:AB189.

Vargo JJ. Big NAPS, little NAPS, mixed NAPS, computerized NAPS: what is your flavor of propofol? *Gastrointest Endosc*. 2007;66:457-459.

Vargo JJ. Minimizing complications: sedation and monitoring. *Gastrointest Endosc Clin N Am*. 2007;17:11-28, v-vi.

Agostoni M, Fanti L, Arcidiacono PG, Gemma M, Strini G, et al. Midazolam and pethidine versus propofol and fentanyl patient controlled sedation/analgesia for upper gastrointestinal tract ultrasound endoscopy: a prospective randomized controlled trial. *Dig Liver Dis*. 2007;39:1024-1029.

Bright E, Roseveare C, Dalglish D, Kimble J, Elliott J, Shepherd H. Patient-controlled sedation for colonoscopy: a randomized trial comparing patient-controlled administration of propofol and alfentanil with physician-administered midazolam and pethidine. *Endoscopy*. 2003;35:683-687.