Propofol Compared With Combination Propofol or Midazolam/Fentanyl for Endoscopy in a Community Setting

John E. Poulos, MD, MSci, FACG, AGAF, FACP
Peter T. Kalogerinis, MMS, PA-C
Jeffrey N. Caudle, CRNA, MSN

This retrospective cohort study evaluated procedural efficiency and patient satisfaction in patients who had received propofol, midazolam/fentanyl/propofol (MFP), or midazolam/fentanyl, as sedation for either esophagastroduodenoscopy or colonoscopy. Questionnaires about procedural times and patient satisfaction were administered.

Use of propofol for colonoscopy resulted in shorter time (minutes) from induction to start of procedure (mean ± standard deviation: propofol, 1.3 ± 0.57; MFP, 3.2 ± 2.2; midazolam/fentanyl, 3.8 ± 2.7; P < .04) and shorter procedure time (propofol, 13 ± 0.36; MFP, 15 ± 0.004; midazolam/fentanyl, 15 ± 0.005 minutes; P < .05). Recovery time was less for patients receiving propofol for their colonoscopy compared with the other groups (propofol, 9 ± 8; MFP, 15 ± 9; midazolam/fentanyl, 18 ± 11 minutes; P < .05). Patients undergoing esophagastroduodenoscopy who received propofol had a shorter recovery time (9 ± 7 minutes vs MFP, 14 ± 9 minutes, and midazolam/fentanyl, 19 ± 11 minutes; P < .05). Patients receiving propofol felt less discomfort and need for adjustment in the sedation, and remembered less of the procedure compared with the MFP group.

Propofol resulted in less time in the endoscopy unit, quicker recovery and discharge, and greater patient satisfaction than did balanced or conscious sedation.

Keywords: Balanced sedation, conscious sedation, endoscopy, endoscopy unit efficiency, propofol.

Studies have indicated that propofol provides better sedation for endoscopy than an opioid/benzodiazepine combination because of faster recovery, improved sedation, and greater efficiency in the endoscopy unit.1–4 Combination or balanced anesthesia using propofol in combination with fentanyl and midazolam is believed to reduce the risk of deep sedation.5,6 Propofol as a sole agent is increasingly being used for endoscopic sedation. Comparative trials have shown propofol’s clear-cut superiority in terms of recovery time and physician satisfaction7–11; however, endoscopic efficiency and improvement in patient satisfaction between balanced sedation and the sole use of propofol requires further evaluation. The aim of this study was to evaluate the efficiency of a community-based endoscopy unit and patient satisfaction using propofol as a single agent compared with a balanced sedation regimen of midazolam, fentanyl, and propofol (MFP) or conscious sedation using midazolam and fentanyl.

Patients and Methods
This retrospective cohort trial evaluated data obtained from quality indicators and performance measurements involving 951 patients undergoing either colonoscopy or esophagastroduodenoscopy (EGD) at a community-based ambulatory endoscopy center from 2007 to 2010.

Forty-six patients were excluded because they underwent both EGD and colonoscopy on the same day.

Sedation Protocols and Patient Monitoring. Patients were evaluated from 3 forms of sedation used at our site consisting of propofol (n = 330), midazolam/fentanyl/propofol (MFP; n = 282), or midazolam/fentanyl (n = 339). Registered nurses (RNs) were responsible for administration of midazolam/fentanyl and Certified Registered Nurse Anesthetists (CRNAs) were responsible for administration of propofol-based regimens. The end point of sedation was to provide adequate analgesia in the absence of substantial pain or grimacing. Standard monitoring included continuous assessment of blood pressure, peripheral oxygen saturation, and heart rate.

Patients in the propofol group received propofol as an initial 50-mg bolus, with 20-mg boluses given at the discretion of the CRNA and endoscopist. The MFP group underwent sedation using an initial dose of 10 mg of propofol, 50 μg of fentanyl, and 2 mg of midazolam, with boluses of propofol given in 10-mg increments given at the discretion of the CRNA. Those in the midazolam/fentanyl group received 2 mg of midazolam and 50 μg of fentanyl as a bolus and increments of 25 μg of fentanyl and 1 mg of midazolam at 2-minute increments at the discretion of the endoscopist. An assistant measured the Modified Observer’s Assessment of Alertness/Sedation (MOAA/S).12
The responsibilities of the CRNAs (for propofol-based sedation) and RNs (for midazolam/fentanyl) were limited to sedating and monitoring the patient, including continuous clinical monitoring of ventilatory effort.

A technician started a stopwatch with the first administration of any sedative medication. All times recorded were from the continuously running stopwatch and included the initiation of sedation (time 0:00), the time of endoscope insertion, the time the endoscope was withdrawn, and the times to an Aldrete score of 9. On visualization of the antrum for EGD and cecum for colonoscopy, the provider determined the MOAA/S score. After recovery, patients completed a postprocedure satisfaction questionnaire about their satisfaction, memory of awake-ness, and discomfort with the procedure, as previously described.6,9

**Statistical Analysis.** Data are presented as means and standard deviations. The Student t test was used when 2 means were compared, and the χ² test was used for categorical data. Small-sample tests were applied when appropriate, and analysis of variance was used when 3 or more means were compared. A value of P < .05 was regarded as significant. Bonferroni adjustments for multiple testing were incorporated.

**Results**

- **Study Population and Mean Total Dose of Drugs.** There were no significant differences among the groups for age, ASA score, or gender (Table 1). Of the 951 cases, 56% were colonoscopies and 24% were upper endoscopy procedures. The remaining 20% of cases were excluded because patients underwent combined procedures. The mean (± standard deviation) propofol doses for colonoscopy were 151.0 ± 92.7 mg (propofol group) and 69.0 ± 58.6 mg (MFP group; Table 2). For those undergoing colonoscopic evaluation, patients in the propofol group received more propofol than did the MFP group (P < .05) on average. For EGD the mean dose of propofol for the propofol group was 153.0 ± 59.2 mg and was 43.0 ± 15.1 mg for the MFP group. Similar to colonoscopic sedation, patients undergoing EGD in the propofol group received more propofol than did those in the MFP group (P < .05). Mean doses of midazolam and fentanyl for colonoscopy were 6.2 ± 1.4 mg and 119.0 ± 29.2 μg, respectively, and for EGD were 4.3 ± 0.77 mg and 88.0 ± 29.0 μg, respectively (see Table 2). The midazolam/fentanyl group received more midazolam and fentanyl than did the MFP group (P < .05) in the colonoscopy and EGD groups.

- **Sedation Scores and Safety Profile.** Table 3 shows the average sedation scores (MOAA/S) for patients in the 3 groups. No significant differences in MOAA/S scores were seen between patients undergoing colonoscopy or EGD, and thus combined data are presented. Patients receiving propofol alone had substantially lower MOAA/S scores than did the MFP or midazolam/fentanyl groups (P < .05). Those receiving MFP had significantly lower MOAA/S scores compared with those receiving midazolam/fentanyl (P < .05). There was 1 hospitalization for postpolypectomy bleeding in the midazolam/fentanyl group. Three patients who received propofol underwent evaluation for abdominal pain in the emergency department, and none required hospitalization. No complications requiring assisted ventilation or treatment of bradycardia or hypotension were noted.

![Table 1](image1.png)

**Table 1. Demographics and ASA Scores of Patients**

Abbreviation: MFP, midazolam/fentanyl/propofol.

![Table 2](image2.png)

**Table 2. Mean Doses of Administered Agents by Procedure**

Abbreviations: EGD, esophagogastroduodenoscopy; F, fentanyl; M, midazolam; MFP, midazolam/fentanyl/propofol; MF, midazolam/fentanyl; dash, not applicable.

a Data are presented as mean ± standard deviation.

b P < .05 between the propofol group and MFP group.

c P < .05 between MFP group and MF group.

![Table 3](image3.png)

**Table 3. Sedation Scores**
• Procedure-Related Times. For patients undergoing EGD who received only propofol, time from induction to start of procedure was significantly less (1.5 ± 0.37 minutes) than patients receiving either MFP (3.6 ± 2.7 minutes) or midazolam/fentanyl (4.8 ± 3.2 minutes; P < .05; Figure 1). Initiation of EGD after sedation with MFP was quicker than for patients receiving midazolam/fentanyl (P = .01). No significant difference was observed in procedure time among the 3 groups. Patient receiving propofol reached an Aldrete score of 9 faster (9 ± 7 minutes) than did patients in either the MFP or midazolam/fentanyl group (P < .05), whereas patients in the MFP group recovered quicker than those in the midazolam/fentanyl group (14 ± 9 minutes vs 19 ± 11 minutes; P = .007).

Similar to patients undergoing EGD, those undergoing colonoscopy had a faster initiation of the procedure (Figure 2) with propofol (1.3 ± 0.57 minutes) than with MFP (3.2 ± 2.2 minutes) or midazolam/fentanyl (3.8 ± 2.7 minutes; P < .05). The MFP regimen showed a modest but significantly quicker procedural start time after administration of anesthesia than did the midazolam/fentanyl group (P < .05). The propofol group undergoing colonoscopy also had a shorter procedure time (13 ± 6 minutes) than did the MFP (15 ± 6 minutes) and midazolam/fentanyl group (15 ± 7 minutes), with no significant difference in procedure duration between the MFP and midazolam/fentanyl groups (P = .44). Patients receiving propofol alone had a significantly shorter time from the end of the procedure to recovery (9 ± 8 minutes) than did those receiving MFP (15 ± 9 minutes) or midazolam/fentanyl (18 ± 11 minutes; P = .26). However, patients receiving MFP recovered more quickly than those receiving midazolam/fentanyl (P < .05). The procedure (P < .05), rated their satisfaction with the procedure higher than did those receiving midazolam/fentanyl (P < .05), and believed they needed less adjustment in their medication dose (P < .05). Patients in the propofol group tended not to remember the start of the procedure or being awake during the procedure or the end of the procedure compared with those receiving MFP or midazolam/fentanyl (P < .05). There were no differ-

<table>
<thead>
<tr>
<th>Sedation arm</th>
<th>MOAA/S score^b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propofol</td>
<td>0.9 ± 0.4^c,d</td>
</tr>
<tr>
<td>MFP</td>
<td>3.8 ± 0.6^c</td>
</tr>
<tr>
<td>Midazolam/fentanyl</td>
<td>4.3 ± 0.3</td>
</tr>
</tbody>
</table>

Table 3. Intraprocedural MOAA/S Scores for Sedation Arms^a
Abbreviations: MOAA/S, Modified Observer’s Assessment of Alertness/Sedation; MFP, midazolam/fentanyl/propofol.
^a Data are presented as mean ± standard deviation.
^b Scale is as follows: 6 = agitated; 5 = responds to name in normal tone; 4 = lethargic response to name in normal tone; 3 = responds to name called loudly; 2 = responds to mild prodding/shaking; 1 = does not respond to mild prodding/shaking; and 0 = does not respond to deep-stimulus “sternal rub.”
^c Significant (P < .05) vs midazolam/fentanyl.
^d Significant (P < .05) vs MFP.

Figure 1. Results of EGD Procedural Times for Patients Receiving 1 of 3 Sedative Regimens^a
Abbreviations: EGD, esophagogastroduodenoscopy; P, propofol; MFP, midazolam/fentanyl/propofol; MF, midazolam/fentanyl; and Aldrete 9, Aldrete score of 9.
^a Data are presented as mean ± standard deviation.
^b Significant (P < .05) vs MF.
^c Significant (P < .05) vs MFP.

Figure 2. Results of Colonoscopy Procedural Times for Patients Receiving 1 of 3 Sedative Regimens^a
Abbreviations: P, propofol; MFP, midazolam/fentanyl/propofol; MF, midazolam/fentanyl; and Aldrete 9, Aldrete score of 9.
^a Data are presented as mean ± standard deviation.
^b Significant (P < .05) vs MF.
^c Significant (P < .05) vs MFP.

• Satisfaction Survey. The patients’ satisfaction with the procedure and recollection of pain were recorded before discharge from the procedure. Patients in the propofol and MFP groups had less discomfort during

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ences among the satisfaction scores between procedural types (data not shown). The MFP regimen was superior to midazolam/fentanyl regarding satisfaction with sedation, need for adjustment in medication dose, or memory of procedure (Table 4).

**Discussion**

In a previous American Gastroenterology Association guideline paper, it was recommended that further studies be performed to determine which sedation regimens would be best suited for use in endoscopic procedures. With this concept in mind the goal of this study was to evaluate the efficiency of a community-based endoscopy unit using propofol compared with a regimen of balanced sedation with propofol in combination with fentanyl/midazolam or standard sedation using fentanyl and midazolam. The results of this study indicate that the sole use of propofol for both EGD and colonoscopy resulted in faster induction, shorter procedure duration, and speedier recovery compared with balanced sedation with propofol in combination with fentanyl/ midazolam or standard sedation using fentanyl and midazolam. The results of this study indicate that the sole use of propofol for both EGD and colonoscopy resulted in faster induction, shorter procedure duration, and speedier recovery compared with balanced sedation with propofol or conscious sedation with midazolam/fentanyl. However, MFP did show faster induction with EGD and faster recovery for EGD and colonoscopies compared with midazolam/fentanyl. Overall patient satisfaction appeared to be equal for propofol and MFP but greater than that seen in the midazolam/fentanyl group. Satisfaction questionnaires also indicated that patients were less aware during the procedure but recovered faster with the sole use of propofol compared with MFP. The depth of sedation produced by propofol was significantly greater; however, this was not associated with significant adverse cardiorespiratory events. Similar to previous studies, time to induction with the sole use of propofol was faster than with conscious sedation. However, our times from the administration of anesthesia to start of procedure were much less than times previously reported, as was colonoscopic procedure duration. This may be related to our use of higher boluses of propofol at the initiation of the procedure, as well as other factors such as ASA status and body mass index (BMI). However, Sipe et al did show that colonoscopic procedural time was less with the sole use of propofol compared with conscious sedation and was most likely related to faster induction. Similar loading doses of propofol were employed by Horiuchi et al and Drake et al; unfortunately time to initiation of procedure was not reported in the Horiuchi trial, and the Drake study only examined the sole use of propofol as an anesthetic.

In accordance with previous trials and meta-analysis evaluating propofol for sedation, we also observed significant reductions in recovery time with the sole use of propofol for both EGD and colonoscopies. Although the use of propofol resulted in rapid recovery after the procedure, the greatest effect was seen with the sole use of propofol compared with MFP or midazolam/ fentanyl. However, unlike a previous study comparing MFP to the sole use of propofol for colonoscopy, we found quicker recovery time with the sole use of propofol. This may be related to our use of the Aldrete score of 9 as a measure of recoverability as well as the fact that patients in this study received lower doses of propofol as a sole agent (151 mg vs 215 mg) and higher doses of propofol in the balanced propofol group (69 mg vs 82.5 mg). A recent study failed to reveal any difference in onset to sedation or recovery time between conscious sedation using meperidine and midazolam vs balanced se-

<table>
<thead>
<tr>
<th>Question</th>
<th>Rating scale</th>
<th>Propofol</th>
<th>MFP</th>
<th>Midazolam/fentanyl</th>
</tr>
</thead>
<tbody>
<tr>
<td>On a scale of 1-10 how would you rate your procedure?</td>
<td>1-10</td>
<td>9.9a</td>
<td>9.8a</td>
<td>9.5</td>
</tr>
<tr>
<td>How was sedation for your procedure?</td>
<td>Excellent and good</td>
<td>99a</td>
<td>99a</td>
<td>95</td>
</tr>
<tr>
<td>Fair and poor</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Do you think you needed any adjustment in medication?</td>
<td>Just right</td>
<td>95.3a,b</td>
<td>92.1a</td>
<td>80.6</td>
</tr>
<tr>
<td>Needed less</td>
<td>2.6a</td>
<td>2.9a</td>
<td>5.6a</td>
<td></td>
</tr>
<tr>
<td>Needed more</td>
<td>2.1</td>
<td>5.0</td>
<td>13.8</td>
<td></td>
</tr>
<tr>
<td>Do you remember being awake during the procedure?</td>
<td>No</td>
<td>86.9a,b</td>
<td>71.6a</td>
<td>62.8</td>
</tr>
<tr>
<td>Yes</td>
<td>13.1</td>
<td>28.4</td>
<td>37.2</td>
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</tr>
<tr>
<td>Do you remember the end of the procedure?</td>
<td>No</td>
<td>97.3a,b</td>
<td>76.6a</td>
<td>67.1</td>
</tr>
<tr>
<td>Yes</td>
<td>2.7</td>
<td>23.4</td>
<td>32.9</td>
<td></td>
</tr>
<tr>
<td>How much discomfort or pain did you experience during the procedure?</td>
<td>None to mild</td>
<td>99.2a,b</td>
<td>98.3a</td>
<td>90.8</td>
</tr>
<tr>
<td>Moderate to severe</td>
<td>0.8</td>
<td>1.7</td>
<td>9.2</td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Satisfaction Questionnaire Results (percent)

Abbreviation: MFP, midazolam/fentanyl/propofol.
a Significant (P < .05) vs midazolam/fentanyl.
b Significant (P < .05) vs MFP.
dation with propofol/midazolam/meperidine. However, as pointed out in an accompanying editorial, failure to detect differences in sedation onset or recovery may have been due to the use of intramuscular meperidine, and higher doses of midazolam.

Limitations to our study included the inability to control bias because neither investigators nor subjects were blinded. Other limitations included the inability to randomize study participants to each sedation group and the retrospective nature of chart review. The strength of this study was its use of patient satisfaction scores similar to those used in previous propofol studies. There appeared to be no significant differences between propofol and MFP regarding patient satisfaction, however, both propofol regimens resulted in greater patient satisfaction than midazolam/fentanyl. Compared with the propofol group, patients in the MFP group tended to remember the initiation of the procedure, being awake during the procedure, and remembering the end of the procedure. This may be related to greater depth of sedation with the sole propofol regimen, as evident by lower MOAA/S scores in the propofol group. Our patient satisfaction surveys using propofol either as a sole agent or as part of a balanced anesthesia regimen compared with conscious sedation are consistent with previous studies.

The administration of propofol by nonanesthesiologists (“nonanesthesiologist-administered propofol,” or NAAP) continues to spark controversy. Several state nursing boards including our own (North Carolina) prohibit the administration of propofol by RNs. Due to the ability of propofol to induce deep sedation and the absence of an antagonist, its package insert, ASA guidelines, and rulings by the Centers for Medicare and Medicaid Services state that propofol should be administered by individuals who are trained to rescue patients from deep sedation and not performing the endoscopic procedure. Data from more than 600,000 endoscopic procedures using NAAP indicates comparable adverse events to that published by anesthesiologists and a lower mortality rate compared with conscious sedation. Sentiment among physicians performing endoscopy is that the estimated cost of using an anesthesiologist to administer propofol for procedures may drive up healthcare cost in the absence of improvements in safety. The cost of having anesthesiologist-administered propofol may increase the cost per case of the procedure and lead to estimated increased annual costs for endoscopic procedures of $1.5 billion per year. Thus, with the potential medical legal risks involved with NAAP, the prohibition of RNs to administer propofol in several states and the high economic cost of using an anesthesiologist, we used CRNAs to administer propofol. Research studies have found no significant differences in rates of anesthesia complications or mortality between CRNAs and anesthesiologists. The ability to replace an RN as a deliverer of conscious sedation with CRNAs providing propofol as a sedative may lead to improved efficiency with the ability to perform greater numbers of procedures per day in the endoscopy suite and greater patient satisfaction. Evidence is also accumulating in the literature that the use of propofol as a sedative during colonoscopy may improve the technical performance of the procedure and polyp detection rate. Higher endoscopic case volume due to improved efficiency and the loss of an RN as a conscious sedation provider could offset increased costs associated with the use of a CRNA. However, future analysis as to whether this is cost neutral merits further examination. Until guidelines can be established and agreed on for the administration of propofol by nonanesthesia providers, CRNAs may be an option for the delivery of propofol.

Conclusion

The results of this study indicate that the use of propofol as a sole sedative resulted in less patient time in the endoscopy unit, quicker recovery, and faster discharge from the endoscopy unit than did regimens using either balanced or conscious sedation. Propofol as a sole agent in endoscopic sedation resulted in greater patient satisfaction, less pain and awareness during the procedure, and increased awareness at the end of the procedure compared with the other anesthetic techniques.

REFERENCES

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AUTHORS

John E. Poulos, MD, MSci, FACG, AGAF, FACP, is employed by Fayetteville Gastroenterology Associates, Fayetteville, North Carolina. His email is poulosj@pol.net.

Peter T. Kalogerinis, MMS, PA-C, is employed by Cape Fear Physical Medicine and Rehabilitation Associates, Fayetteville, North Carolina.

Jeffrey N. Caudle, CRNA, MSN, is a chief nurse anesthetist at Carolina Anesthesia Associates, Hickory, North Carolina.

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