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Original Article

Endoscopist-directed balanced propofol sedation is safe and effective in patients undergoing outpatient colonoscopy

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Abstract

Background and Aims: Propofol administered in combination with other moderate sedation medications (balanced propofol sedation [BPS]) is an appealing and effective sedation regimen for gastrointestinal (GI) endoscopy procedures. However, product labeling dictates propofol be administered only by anesthesiology personnel. We evaluated the safety of endoscopist-directed as well as anesthesiologist-administered BPS during outpatient colonoscopy. **Methods:** We performed a retrospective cohort study using prospectively collected endoscopy data where endoscopist-directed BPS is standard practice. Measured patient outcomes included: BPS drug dosages, postcolonoscopy oxygen saturation levels, pulse, and systolic/diastolic blood pressures, need for mask bag ventilation or endotracheal intubation, aborted colonoscopy due to sedation, hospital admission postcolonoscopy, and mortality. **Results:** From April 1 to November 30, 2013, 1036 patients undergoing outpatient colonoscopy (mean age 56.4 years, 55% males, 32% American Society of Anesthesiologists [ASA] I, 59% ASA II, 9% ASA III) received endoscopist-directed BPS. During the same time period, 40 patients (mean age 66.6 years, 55% males, 33% ASA II, 67% ASA III) received anesthesiologist-administered BPS. Indications for colonoscopy for the endoscopist-directed BPS included 352 (34%) colorectal cancer screening/surveillance, 404 (39%) evaluation of lower GI symptoms, 156 (15%) positive fecal occult blood, and 124 (12%) inflammatory bowel disease. BPS dosages (mean ± standard deviation) per patient were Fentanyl 0.05 mg (fixed dose), midazolam 1.6 mg ± 0.5 mg (range: 1–5 mg), and propofol 104 mg ± 62 mg (range: 10–460 mg). Propofol doses correlated inversely with patient age ($r = -0.35$; $P < 0.001$), and the mean Propofol dose was lower as ASA score increased: ASA I – 115 mg, ASA II – 103 mg, and ASA III – 75 mg ($P < 0.01$). No patient required bag mask ventilation, endotracheal intubation, or hospital admission. There were no aborted colonoscopies secondary to sedation and no mortality. All patients were discharged directly to home. **Conclusions:** Endoscopist-directed BPS appears safe and effective for low-, intermediate- and high-risk patients undergoing outpatient colonoscopy.

Key words

Anesthesiology, balanced propofol sedation, colonoscopy, conscious sedation, endoscopy, moderate sedation, monitored anesthesia care, propofol

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Introduction

The increasing use of monitored anesthesia care (e.g., anesthesiologists, nurse anesthetists) for sedation during gastrointestinal (GI) endoscopic procedures is directly correlated with the rising utilization of propofol.[1] This is occurring for routine endoscopic procedures such as esophagogastroduodenoscopy and screening/surveillance colonoscopy, as well as for more complex endoscopic procedures such as endoscopic retrograde cholangiopancreatography and endoscopic ultrasound. Monitored anesthesia care is occurring because current product labeling dictates that the administration of propofol be only in the presence of personnel trained in administering general anesthesia.[2] Propofol was introduced in the 1980's and has expanded into the realm of moderate sedation use for GI endoscopic procedures, reaching high adoption levels during the past decade.[3] Compared to traditional moderate sedation regimens, propofol-based sedation has a similar rate of adverse events but provides additional benefits including reduced time to induction of sedation, shorter duration of action, faster patient recovery time, higher postprocedure patient satisfaction, and greater patient willingness to repeat endoscopy in the future.[4-6] Rapid recovery and return to baseline behavior allows for faster patient discharge from the endoscopy unit following outpatient procedures and may facilitate procedural and endoscopy unit efficiency.[7]

Studies have shown that propofol can be safely administered in combination with fixed doses of benzodiazepines and/or opioids to enhance hypnotic and sedative effects.[8,9] The co-administration of propofol with other sedative agents allows for a substantial reduction in the propofol dose, thereby improving its safety profile.[10,11] This moderate sedation regimen is also known as "balanced propofol sedation" (BPS). In BPS, an opioid and benzodiazepine are each given as a single dose, which is complemented by small incremental doses of propofol (10–20 mg/push) administered to obtain a target level of moderate sedation.[12]

However, there is ongoing controversy and lack of consensus regarding the safety and efficacy of endoscopist-directed BPS in the absence of monitored anesthesia care during GI endoscopy procedures. On August 19th 2010, the US Food and Drug Administration (FDA) upheld the recommendations of the American Society of Anesthesiologists (ASA) and denied a petition from the American College of Gastroenterology (ACG) to remove the warning that propofol administration should be only performed by personnel trained in administering general anesthesia.[13] The FDA summarized its reasoning by stating that the evidence provided by the ACG failed to demonstrate the necessary safety profile for changing the current product labeling. In this study, we aimed to evaluate the safety and efficacy of endoscopist-directed BPS consisting of fentanyl (fixed dose) + midazolam + propofol without monitored anesthesia care during outpatient colonoscopy procedures. During the same time period, we also evaluated a control group of patients that underwent anesthesiologist-administered BPS also consisting of fentanyl + midazolam + propofol during outpatient colonoscopy procedures.

Methods

This was a retrospective observational cohort study using prospectively collected endoscopy data from the electronic endoscopy procedures records in the Institute of Gastroenterology at Rambam Health Care Campus, Haifa, Israel. We included any patient undergoing outpatient colonoscopy who received endoscopist-directed BPS as well as the second cohort of patients (control group) that received BPS administered by an anesthesiologist. Rambam Health Care Campus is a tertiary care university hospital where endoscopist-directed BPS is the routine moderate sedation practice for the vast majority of routine endoscopic procedures. To administer/direct BPS, an endoscopist is required every 2 years to satisfactorily complete a 1-day didactic course on sedation that is sponsored by the Israel Gastroenterology Association and have up to date basic life-support and advanced cardiac life-support certification. Complete cardiopulmonary resuscitation equipment and medications are available within the endoscopy unit. Endoscopy nurses also maintain up to date certification in basic and advanced cardiac life-support.

During the endoscopy procedure, the endoscopist, and the endoscopy nurse as a team was responsible for monitoring patient vital signs (e.g., pulse, blood pressure, and oxygen saturation levels). The endoscopist was also responsible for directing the provision and dosing of the BPS.

In this study, we evaluated patient-level demographic variables including age, gender, ASA classification, and indication for colonoscopy. We also evaluated clinically relevant patient outcome variables including: BPS drug dosages, postcolonoscopy oxygen saturation levels, pulse, and systolic/diastolic blood pressures, need for mask bag ventilation or endotracheal intubation at any time during or immediately following colonoscopy, aborted colonoscopy procedure due to a sedation-related adverse event, hospital admission postcolonoscopy, and mortality. Before initiating our data collection, we received local Institutional Review Board (Rambam Health Care Campus Helsinki Committee) approval September 15, 2013, to review our endoscopic database and report upon these de-identified patient data.

Descriptive statistics for all parameters were calculated: For continuous variables this included mean, standard deviation (SD), median, minimum, maximum and range values. For noncontinuous variables, counts and percentages were reported. Comparison of categorical data was performed using the Student's *t*-test. An *a priori* determined $P < 0.05$ was considered statistically significant. All analyses were performed using Microsoft Excel 2010 (Microsoft Corp, Redmond, WA, USA).

Results

From April 1 to November 30, 2013, a total of 1,036 patients (mean age 56.4 years, 55% males) underwent an outpatient colonoscopy and received endoscopist-directed BPS from any one of 12 gastroenterologists who routinely perform endoscopy in the Rambam Health Care Campus GI endoscopy unit.

Indications for colonoscopy included [Table 1] 404 (39%) evaluation of lower GI symptoms, 352 (34%) colorectal cancer screening/surveillance, 156 (15%) positive fecal occult blood testing, and 124 (12%) inflammatory bowel disease endoscopic surveillance. Stratified by ASA classification [Table 1] 332 (32%) patients were classified as ASA I, 611 (59%) patients ASA II, and 93 (9%) patients ASA III. BPS dosages (mean ± SD) per patient were as follows [Table 2]: Fentanyl 0.05 mg (fixed dose), midazolam 1.6 mg ± 0.5 mg (range: 1–5 mg), and propofol 104 mg ± 62 mg (range: 10–460 mg). Propofol doses correlated inversely with patient age ($r = -0.35$; $P < 0.001$). Moreover, we found no statistical difference in propofol doses between females and males in the overall cohort nor when stratifying according to ASA score. We also found that the propofol dose (mean ± SD) was significantly lower as the ASA score increased: ASA I – 115 mg ± 62 mg, ASA II – 103 mg ± 64 mg, and ASA III – 75 mg ± 42 ($P < 0.01$). Postcolonoscopy (mean ± SD) oxygen saturation levels were 98% ±2%. Pre- and post-colonoscopy blood pressures were 133/77 mmHg versus 118/67 mmHg ($P < 0.001$), and pulse 75/min versus 66/min ($P < 0.001$) [Table 2].

Table 1: Indications for colonoscopy and ASA score stratification

Indication for colonoscopy	Endoscopist-directed BPS (*n*=1036) (%)	Anesthesiologist-administered BPS (*n*=40) (%)
Evaluation of lower GI symptoms	404 (39)	10 (25)
Colorectal cancer screening/ surveillance	352 (34)	17 (42.5)
Positive fecal occult blood testing	156 (15)	10 (25)
IBD endoscopic surveillance	124 (12)	3 (7.5)
ASA score		
ASA I	332 (32)	0
ASA II	611 (59)	13 (33)
ASA III	93 (9)	27 (67)

ASA=American Society of Anesthesiologists, BPS=Balanced propofol sedation, GI=Gastrointestinal, IBD=Inflammatory bowel disease

No patient required bag mask ventilation, endotracheal intubation, or hospital admission. There were no aborted colonoscopies secondary to a sedation-related adverse event and no mortality. All patients were discharged from the endoscopy unit recovery area directly to home.

Anesthesiologist-administered balanced propofol sedation

During the same study period, a total of 40 patients (mean age 66.6 years, 55% males) underwent outpatient colonoscopy with an anesthesiologist present who administered BPS. Here again, the colonoscopy procedures were performed by any one of the 12 aforementioned gastroenterologists.

Indications for colonoscopy included [Table 1] 10 (25%) evaluation of lower GI symptoms, 17 (42.5%) colorectal cancer screening/surveillance, 10 (25%) positive fecal occult blood testing, and 3 (7.5%) inflammatory bowel disease endoscopic surveillance. Stratified by ASA classification [Table 1]: There were no patients classified as ASA I, 13 (33%) patients were ASA II, and 27 (67%) patients were ASA III. BPS dosages (mean ± SD) per patient were [Table 2] fentanyl 0.08 mg ± 0.16 mg (range: 0–1 mg), midazolam 1.0 mg ± 0.8 mg (range: 0–2 mg), and propofol 105 mg ± 53 mg (range: 30–240 mg). Here again, we found no statistical difference in propofol doses between females and males in this cohort. Postcolonoscopy (mean ± SD) oxygen saturation levels were 97% ±2%. Pre- and post-colonoscopy blood pressures were 142/81 mmHg versus 123/68 mmHg ($P < 0.001$), and pulse 75/min versus 65/min ($P < 0.001$) [Table 2].

No patient required bag mask ventilation, endotracheal intubation, or hospital admission. There were no aborted colonoscopies secondary to a sedation-related adverse event and no mortality. All patients were discharged from the endoscopy unit recovery area directly to home.

Discussion

Moderate sedation for outpatient colonoscopy is standard practice in North America, Western Europe, and Israel.[14] The increasing popularity of propofol as an integral component of moderate sedation for GI endoscopic procedures is it offers

Table 2: Patient outcomes

Medications	Endoscopist-directed BPS (*n*=1036)			Anesthesiologist-administered BPS (*n*=40)		
	Fentanyl	Midazolam	Propofol	Fentanyl	Midazolam	Propofol
Mean dose (mg)±SD	0.05±0	1.6±0.5	104±62	0.08±0.16	1.0±0.8	105±53
Range (mg)	0.05 fixed dose	1-5	10-460	0-1	0-2	30-240
Postcolonoscopy oxygen saturation (%)		98			97	
Precolonoscopy blood pressure (mmHg)		133/77			142/81	
Postcolonoscopy blood pressure (mmHg)		118/67			123/68	
Precolonoscopy pulse (bpm)		75			75	
Postcolonoscopy pulse (bpm)		66			65	

BPS=Balanced propofol sedation, SD=Standard deviation, bpm=Beats per minute

rapid onset of action, quick patient recovery, and earlier time to patient discharge. All told, leading to a more efficient and patient-satisfied endoscopy experience.[15] However, despite the benefits of propofol, higher doses can induce deep sedation leading to respiratory depression, and apnea.[16] These potential untoward effects can be further complicated by the fact that there is currently no known propofol antagonist. Moreover, propofol product labeling states that "propofol should be administered only by persons trained in the administration of general anesthesia."[2] Thus, in the United States and in Western Europe, endoscopist-directed propofol is largely prohibited, and it is instead administered by anesthesiology professionals (e.g., monitored anesthesia care). This increasingly common clinical practice significantly increases medical costs, thereby making colonoscopy less affordable to health care systems, payors, and patients. The ASA and the Centers for Medicare and Medicaid Services interpretative guidelines on deep sedation both support this approach.[17] This despite data suggesting that nonanesthesiologist administered propofol is safe and effective. For example, a comprehensive review showed that colonoscopist-directed or nurse-administered propofol is safe and effective for colonoscopy procedures.[18] However, these data were from colonoscopy procedures in which specific training of the operator in the use of propofol was mandatory. In 2010, the European Society of GI Endoscopy (ESGE), the ESGE Nurses and Associates, and the European Society of Anaesthesiology issued guidelines for specific operator training that is required for nonanesthesiologist administration of propofol for colonoscopy.[4]

Our data on patients undergoing outpatient colonoscopy challenges the belief that patient safety is enhanced by anesthesiologist-administered propofol during endoscopic procedures. The results of this study indicate that endoscopist-directed BPS is safe for moderate sedation for outpatient colonoscopy procedures in ASA class I-III patients. In our study, the mean dose of propofol administered was 104 mg, which is higher than the doses reported (propofol dose 60–70 mg) in the literature for colonoscopy procedures using BPS.[10] Clarke *et al*.[19] evaluated 15,268 colonoscopies whereby the patient mean propofol dose was 60 mg, administered in combination with midazolam and fentanyl. However, the administration protocol was different from our study and sedation was administered by general medical practitioners. Although the pre- and post-colonoscopy pulses and blood pressures were statistically significant in this study, we found that not a single patient sustained any clinically relevant hemodynamic changes during colonoscopy. Moreover, no patient required bag-mask ventilation, endotracheal intubation, or hospital admission. There were no aborted colonoscopies secondary to a sedation-related adverse event or mortality, and all patients were discharged from the endoscopy unit recovery area directly to home.

We included a control group of patients that underwent outpatient colonoscopy with the presence of an anesthesiologist who administered BPS. The group of patients who underwent anesthesiologist-administrated BPS was relatively small, and not surprisingly was primarily comprised ASA III patients (67%). This likely reflects the success of endoscopist-directed BPS without monitored anesthesia care during outpatient colonoscopy procedures at our institution.

Endoscopist-directed BPS may have substantial economic advantages as the financial burden of anesthesiologist services for GI endoscopic procedures is estimated to be $5 billion annually in the USA.[20] Although endoscopist-directed propofol is endorsed by the GI professional societies in the US and in Europe, there are many caveats regarding its routine implementation into clinical gastroenterology practice (i.e., specific propofol training).[4,12,21] Moreover, the American Society for Gastrointestinal Endoscopy (ASGE) guideline on the use of propofol for GI endoscopy does not make a distinction with respect to the administration of moderate sedation in ASA III and IV patients. However, outside of the US this is not the case, for example, in Australia and Germany, the Australian Guidelines on sedation and/or analgesia for diagnostic and interventional medical, dental, or surgical procedures, and the Endoscopic Section of the German Society for Digestive and Metabolic Diseases Guideline for Sedation for GI Endoscopy require the presence of an anesthesiologist in ASA III or IV patients.[22,23] Although the patient numbers are limited in this study, our data on safety for ASA III patients (n = 93) undergoing outpatient colonoscopy is of importance since evidence for propofol safety in such "at risk" patients is limited.

This study has a number of limitations including its retrospective cohort design, and the analyzed data are from a single year at an academic university endoscopy unit. Moreover, it should be remembered that this study evaluated the use of "BPS". Propofol was not administered as a single moderate sedation agent during outpatient colonoscopy, and thus total propofol dosages were lower than what is administered when used alone.[10,11] Therefore, the results of this study are not able to be extrapolated to the practice of using propofol as a single sedation agent. Other limitations include that a Mallampati score was not routinely measured/documented before colonoscopy. We also restricted our data analysis to "hard endpoints" including postcolonoscopy oxygen saturation levels, pulse, and systolic/diastolic blood pressures, need for mask bag ventilation or endotracheal intubation at any time during or immediately following colonoscopy, aborted colonoscopy procedure due to a sedation-related adverse event, hospital admission postcolonoscopy, and mortality. Another limitation is that the overall n = 1036 is somewhat small and thus may be underpowered to definitively establish and extrapolate safety of endoscopist-directed BPS. Yet, these intriguing data should lay the foundation for a larger prospective trial. Last, we did not have follow-up data beyond patient discharge from the endoscopy unit's recovery area, and thus some late sedation-related adverse events may not have been captured.

Conclusions

We found that endoscopist-directed BPS was safe and effective for low, intermediate, and high-risk patients undergoing outpatient colonoscopy. There were no observed adverse events or mortality.

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Conflicts of interest

There are no conflicts of interest.

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