Sedation levels during propofol administration for outpatient colonoscopies

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The levels of sedation required for patients to comfortably undergo colonoscopy with propofol were examined. One hundred patients undergoing colonoscopy with propofol were enrolled. In addition to standard-of-care monitoring, sedation level was monitored with the Patient State Index (PSI) obtained from a brain function monitor, transcutaneous carbon dioxide (tcpCO₂) was monitored with the TCM TOSCA monitor, and end-tidal carbon dioxide was monitored via nasal cannula. The Ramsay Sedation Score (RSS) was also assessed and recorded. After baseline data were obtained from the first 40 consecutive patients enrolled in the study, the remaining 60 patients were randomized into two groups. In one group the PSI value was blinded from the anesthesiologist and in the second group the PSI was visible and the impact of this information on the management of the sedation was analyzed. Overall 96% of patients reached levels of deep sedation and 89% reached levels of general anesthesia. When comparing the blinded to PSI versus unblinded groups, the blinded group had a significantly lower PSI and higher RSS and tcpCO₂, indicating the blinded group was maintained at a deeper sedation level with more respiratory compromise than the unblinded group. Patients undergoing colonoscopy under propofol sedation delivered by a bolus technique are frequently taken to levels of general anesthesia and are at risk for respiratory depression, airway obstruction, and hemodynamic compromise.

Propofol sedation for outpatient endoscopy has become a popular technique in place of midazolam and opioids, although the combination technique still has its proponents (1). Propofol alone has been associated with improved patient satisfaction and faster recovery with less nausea and vomiting (2) and has been recommended as a safe technique for patients when administered by nurses under the supervision of a physician-endoscopist (3–6). It has a very short onset of action and has a plasma half-life of 2 to 4 minutes, leading to a rapid recovery. However, a number of potential adverse effects are associated with propofol. It has no analgesic effects; therefore, when used for moderate sedation, propofol frequently has to be administered in amounts to provide deep levels of sedation to allow a painful procedure to be performed. Propofol-induced respiratory and cardiac depression is dose dependent and may put patients at risk, particularly if they have significant comorbidities, so that supportive interventions may be necessary. However, the short duration of action will allow many patients to recover before

any lasting untoward effects occur. Patients are typically administered supplemental oxygen during the endoscopy procedure. Pulse oximetry (SpO₂) is frequently used as an indicator of the patient's ventilatory status; however, supplemental oxygen limits the usefulness of SpO₂ in this regard (7–9). We examined the levels of sedation required for patients to comfortably undergo routine colonoscopy using bolus doses of propofol as a sole agent in the manner described by Rex, Overley, and Walker (3). Additional monitoring systems were also utilized to determine the depth of sedation and degree of respiratory depression.

METHODS

Institutional review board (IRB) approval was obtained at Baylor University Medical Center at Dallas to enroll patients undergoing outpatient colonoscopies during a 9-month period. One hundred patients scheduled for an outpatient colonoscopy were enrolled in this prospective trial. Patients were recruited from the practice of two gastroenterologists and were eligible if they were scheduled for an outpatient colonoscopy with a specific anesthesiologist, who planned to administer propofol only for sedation. The patients were over 18 years of age and had an American Society of Anesthesiologists (ASA) risk class of 1, 2, or 3. Informed consent was obtained prior to the start of the procedure using an IRB-approved consent form.

Propofol was administered with an initial bolus of 30 to 50 mg given over 5 to 10 seconds through a rapid running intravenous catheter. Approximately 50 to 70 seconds after the first dose, a second dose was administered, consisting of 10 to 30 mg depending on how the patient reacted to the initial dose. This was similar to the nurse-administered propofol sedation (NAPS) technique described by Rex et al (3), who noted that the dose of propofol required to initiate the colonoscopy may vary from 30 to >200 mg. If the patient seemed to experience discomfort during the procedure, a 10- to 20-mg bolus was delivered. The NAPS technique excluded ASA 3 patients, those with sleep apnea or

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other signs of a difficult airway, and those at an increased risk of reflux. No other sedatives or pain medications were administered. All patients received supplemental oxygen via nasal cannulae. The safety record of the NAPS technique has been reported to be good, with less than 1 in 500 cases having a need for brief periods of mask ventilation. In that review of more than 17,000 patients, no other adverse events were recorded (5).

In addition to standard-of-care monitoring of vital signs, sedation levels were monitored with the Ramsay Sedation Scale (RSS) (*Table 1*), and brain function was monitored using the Patient State Index (PSI) obtained from a brain function monitor (Hospira, Inc., Lake Forest, IL). Transcutaneous carbon dioxide (tcpCO₂) was monitored with the TCM TOSCA® monitor (Radiometer Copenhagen, Basel, Switzerland), and end-tidal carbon dioxide (EtCO₂) was monitored via nasal cannulae. Blood pressure was recorded every 5 minutes, and heart rate, respiratory rate, PSI, RSS, and oxygenation by SpO₂, EtCO₂, and tcpCO₂ were displayed continually and recorded at the top of every minute during the course of the procedure.

The anesthesiologist was privy to the PSI data for the first 40 subjects enrolled so that a baseline level of sedation could be ascertained as complemented by the PSI. The next 60 patients were numbered sequentially as they were enrolled and randomized to a blinded or unblinded group. All even-numbered patients were randomized to a blinded group where the anesthesiologist was blinded to the PSI data. The anesthesiologist was able to view the PSI data for odd-numbered subjects. The goal of this second part of the study was to see if information from a brain function monitor would affect the management of the sedation technique.

Each patient was monitored according to the standards of the ASA by the anesthesiologist who performed all necessary airway interventions. Airway interventions were designated as any action taken to improve or restore ventilation and included chin lifts, jaw thrust, the addition of an oxygen mask, insertion of nasal or oral airways, and ventilatory assist maneuvers. Airway interventions were recorded along with the total bolus doses of propofol. Airway interventions were always made at the judgment of the anesthesiologist.

For the purposes of this study, a PSI of 70 to 51 was considered deep sedation and a PSI of 50 or below was considered general anesthesia. General anesthesia as defined by the ASA occurs when a patient is not arousable, airway interventions

may be required, spontaneous breathing is often inadequate, and cardiovascular function may be impaired.

A Fisher's exact analysis was utilized to evaluate the categorical variables of ASA classification and gender. A nonparametric Wilcoxon two-sample test was used to evaluate the difference between the blinded and unblinded groups for vital signs, patient age, length of procedure, and propofol administration. Stepwise logistic regression was applied to see if a combination of measurements or drop or rise of a measurement in the minutes prior to the intervention was predictive of the intervention. A *P* value < 0.05 was considered significant.

RESULTS

A total of 100 patients were enrolled in this study. One subject was withdrawn from the study due to differing opinions on ASA physical status, and data from one subject were incomplete due to a data collection error and thus were not included. A total of 46 women and 52 men with a mean age of 59.9 ± 11.7 years were evaluated.

Of the 98 subjects undergoing colonoscopy using this NAPS technique, 94 patients (96%) were under deep sedation accounting for 68% of the total procedure time, and 87 patients (89%) were under general anesthesia accounting for 47% of total procedure time as graded by the ASA classification of sedation, the RSS, and the PSI data. During the endoscopy, 65 patients (66%) required at least one airway intervention.

The demographic characteristics and procedure data of the two study groups was similar with the exception of procedure length (*Table 2a*). The unblinded-to-PSI group had a significantly longer procedure time (*P* = 0.002) than the blinded group, with the mean total amount of propofol used similar between the groups. The percentage of subjects requiring an airway intervention was higher in the unblinded group, which also had more aggressive interventions (*Table 2b*). No interventions beyond a jaw thrust were performed in the blinded group. Subjects in the blinded group spent 18.3% of total procedure time with an airway intervention, and subjects in the unblinded group spent 18.2% of total procedure time with an airway intervention.

The vital signs of the blinded and unblinded groups are shown in *Table 2c*. The blinded group was kept at a deeper sedation level than the unblinded group, with a lower mean PSI (*P* < 0.001) and a higher RSS (*P* < 0.001). There were no significant differences between the two groups for three of the four indicators of respiratory status, although tcpCO₂ demonstrated that the blinded-to-PSI subjects had a significantly higher tcpCO₂ (48 vs 43, *P* < 0.001), indicating respiratory depression not detected in the other three monitoring methods.

The sedation levels and respiratory data of the blinded and unblinded groups were compared at the time of an airway intervention (*Table 2d*). When the anesthesiologists were blinded to the PSI, the interventions occurred when the patient was more sedated with a higher RSS (*P* = 0.02). During the interventions, the blinded group had a significantly higher tcpCO₂ than the unblinded group (*P* = 0.003). *Figure 1a* shows that 68% of airway interventions occurred at a PSI of 70 or below, and 44% occurred at a PSI of 50 or below; *Figure 1b* shows the ranges of EtCO₂ at

Table 1. Ramsay Sedation Scale

Score	Response
1	Anxious and agitated or restless or both
2	Cooperative, oriented, and tranquil
3	Responds to commands only
4	Brisk response to light glabellar (forehead) tap or auditory stimulus
5	Sluggish response to light glabellar (forehead) tap or loud auditory stimulus
6	No response

Table 2. Data in the groups where the anesthesiologist was blinded to the PSI or unblinded to the PSI

	Blinded group (n = 29)	Unblinded group (n = 69)	P value
a. Demographic and procedure data			
Age (years)	56 ± 12	61 ± 11	0.05
Male	19 (66%)	33 (48%)	0.13
Female	10 (34%)	36 (52%)	
Length of procedure (minutes)	24 ± 14	32 ± 13	0.002
ASA classification			
1	9 (31%)	17 (25%)	0.44
2	15 (52%)	32 (46%)	
3	5 (17%)	20 (29%)	
Total propofol use (mg)	340 ± 174	350 ± 155	0.67
b. Airway intervention*			
Chin lift	17 (59%)	43 (62%)	
Jaw thrust	3 (10%)	4 (6%)	
Nasal airway	0	1 (1%)	
Oral airway	0	3 (4%)	
Oxygen mask	0	1 (1%)	
c. Vital signs			
PSI	47 ± 15	60 ± 15	<0.001
RSS	6 ± 0.2	5 ± 1	<0.001
SpO ₂ (%)	97 ± 3	98 ± 2	0.20
RR (breaths/min)	18 ± 5	17 ± 3	0.99
tcpCO ₂ (mm Hg)	48 ± 3	43 ± 7	<0.001
EtCO ₂ (mm Hg)	35 ± 12	35 ± 11	0.96
d. Vital signs at the time of airway intervention			
PSI	47 ± 16	55 ± 17	0.06
RSS	6 ± 0	6 ± 0	0.02
SpO ₂ (%)	94 ± 5	96 ± 4	0.08
RR (breaths/min)	19 ± 6	17 ± 4	0.24
tcpCO ₂ (mm Hg)	49 ± 4	44 ± 7	0.003
EtCO ₂ (mm Hg)	36 ± 13	34 ± 12	0.58
e. Adverse events			
Bradycardia	1	—	
Hypertension	1	—	
Airway obstruction	—	1	

*Three subjects had more than one intervention concurrently, i.e., a nasal airway and oxygen mask at the same time.

Data are presented as mean ± standard deviation or n (%). ASA indicates American Society of Anesthesiologists; PSI, Patient State Index; RSS, Ramsay Sedation Scale; SpO₂, oxygen saturation; RR, respiratory rate; tcpCO₂, transcutaneous carbon dioxide; EtCO₂, end-tidal carbon dioxide.

the time the airway intervention occurred. Sixty-three percent of the interventions occurred when the respiratory rate was >15 breaths per minute, 63% when the SpO₂ was >95%, 58% when the tcpCO₂ was >45, and 38% when the EtCO₂ was <30.

Table 3. Patient statistics in those with airway intervention or no airway intervention

Test	No airway intervention	Airway intervention	P value
PSI	58 ± 17	53 ± 17	<0.001
RSS	5 ± 1	6 ± 0	<0.001
SpO ₂ (%)	97 ± 2	96 ± 6	<0.001
RR (breaths/min)	17 ± 4	18 ± 5	0.95
tcpCO ₂ (mm Hg)	45 ± 7	45 ± 7	0.19
EtCO ₂ (mm Hg)	35 ± 10	34 ± 12	0.88

Data are presented as mean ± standard deviation. PSI indicates Patient State Index; RSS, Ramsay Sedation Scale; SpO₂, oxygen saturation; RR, respiratory rate; tcpCO₂, transcutaneous carbon dioxide; EtCO₂, end-tidal carbon dioxide.

The subjects with an airway intervention were significantly more sedated, with a lower SpO₂, than those with no airway intervention (Table 3). The mean PSI was also significantly lower during the intervention ($P < 0.001$), and the RSS was higher ($P < 0.001$). As the mean SpO₂ was above 95%, the differences in SpO₂ between the two groups did not have clinical significance. The same is true with the RSS; the differences may not be clinically detectable, as the subjects were all in the deep sedation/general anesthesia range.

Three adverse events occurred in three different patients, two in the blinded group and one in the unblinded group (Table 2e). One subject experienced bradycardia with a heart rate of 39 beats per minutes. The subject was then treated with 0.2 mg of glycopyrrolate, and no further interventions were needed. Hypertension (a blood pressure of 173/78 mm Hg) was noted in one patient who was treated with 3 mg of metoprolol with no further interventions required. One subject required oxygen via a nonrebreather oxygen mask 5 minutes into the colonoscopy procedure and then required a nasal airway. The nasal airway was removed 4 minutes after insertion at the request of the subject with no further interventions required.

DISCUSSION

Greater than 88% of patients undergoing propofol sedation using a bolus technique, as described by Rex et al (6) for NAPS, for routine colonoscopy procedures are taken to levels of deep sedation or general anesthesia for some part of the procedure and are subsequently at risk for respiratory depression, airway obstruction, and hemodynamic compromise. Therefore, the health care provider administering the propofol in this manner must be trained in recognizing and managing respiratory compromise and rescuing patients with obstructed airways.

When the anesthesiologist was privy to the PSI value, the intervention occurred before the subject reached a level of general anesthesia. Additionally, the subjects were kept at a lighter sedation level with monitors of respiratory status such as RR, SPO₂, tcpCO₂ and EtCO₂ being closer to normal ranges than when the PSI was not available, even at the time when an airway

Figure 1. Measurements at the onset of airway interventions: (a) cumulative percentage of airway intervention as Patient State Index value decreases and (b) end-tidal carbon dioxide level at the time of an airway intervention.

intervention occurred. If interventions were deemed to be appropriate for the blinded subjects, the intervention occurred when the mean PSI was considered to be general anesthesia and with significantly higher tcpCO_2 , indicating a prolonged hypoventilation. In addition, a larger number of airway interventions, and more aggressive interventions, were performed in the group where the anesthesiologist had access to PSI data.

The use of supplemental oxygen during the procedure keeps the SpO_2 in the high 90s and minimizes its usefulness as a sensitive monitor of respiratory depression (7–9). Downs and his team have clearly demonstrated how the administration of supplemental oxygen can allow arterial carbon dioxide levels to reach dangerously high levels before oxygen saturation declines significantly (8). Data from this study are consistent with Downs' work, as airway interventions were generally made by anesthesiologists while the SpO_2 was still within acceptable levels but the tcpCO_2 was elevated. The mean tcpCO_2 of 48 mm Hg in the blinded group versus 43 mm Hg in the unblinded group indicates the blinded group experienced significant respiratory compromise, as the physiological rate of the increase of the partial pressure of arterial carbon dioxide is 3 to 6 mm Hg per minute during apnea (10).

The study was designed knowing that supplemental oxygen limits the usefulness of SpO_2 and, therefore, EtCO_2 and tcpCO_2 were monitored to determine if the CO_2 level change was predictive of respiratory distress. Stepwise logistic regression was performed on all measures of respiratory status and sedation levels to see if a combination of measurements in the minutes prior to an airway intervention was predictive of the intervention. None of the statistically significant measurements were related strongly enough to be predictive of the need for an intervention.

All colonoscopies were performed by one of two gastroenterologists. Ideally, future studies should be done utilizing a single gastroenterologist to ensure consistency. In addition, baseline vital signs including baseline CO_2 should be recorded immediately prior to the start of the procedure in order to determine changes from baseline rather than protocol-driven parameters.

In conclusion, although none of the monitors were predictive of an airway intervention, the data showed that subjects undergoing

colonoscopy were frequently taken to levels of general anesthesia and more patients required an airway intervention at deeper levels of sedation. When anesthesiologists were privy to PSI, the patients were maintained at a lighter sedation level, received more interventions to improve or restore ventilation, and had other measures of sedation and respiratory status that are closer to the normal ranges than when anesthesiologists were not privy to PSI data.

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