Sedation in patients above 60 years of age undergoing urological surgery under spinal anesthesia: Comparison of propofol and midazolam infusions

Yaddanapudi S, Batra YK, Balagopal A, Nagdeve NG

Department of Anesthesia and Intensive Care, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Correspondence:
Sandhya Yaddanapudi
E-mail: sandhya.yaddanapudi@gmail.com

Received : 11-12-06
Review completed : 01-03-07
Accepted : 11-05-07
PubMed ID : ????
J Postgrad Med 2007;53:171-5

ABSTRACT

Context: Propofol and midazolam are commonly used sedatives during regional anesthesia in adults. Smaller doses of these drugs are required in older age due to altered pharmacokinetics and pharmacodynamics. **Aims:** To study the sedation, side-effects and the costs involved with smaller doses of propofol and midazolam in patients aged above 60 years during spinal anesthesia. **Settings and Design:** A randomized single-blind study was conducted in 60 ASA I-II patients aged ≥60 years undergoing urological surgery under spinal anesthesia. **Materials and Methods:** Sedation was administered after spinal anesthesia using propofol (bolus 0.4 mg/kg; infusion 3 mg/kg/hr) or midazolam (bolus 0.02 mg/kg; infusion 0.06 mg/kg/hr) and titrated to achieve a sedation score of 3 on the modified Observer's Assessment of Alertness/Sedation Scale. Perioperative sedation, hemodynamics and respiratory events were monitored. **Statistical Analysis:** The analysis for parametric data was done using Student's unpaired t test and the incidence data using Chi-square test. **Results:** The onset (13.0±4.2 vs. 18.8±4.2 min, $P<0.001$) and offset (8.9±2.8 vs. 12.5±3.5 min, $P<0.001$) of sedation were faster and the duration of adequate sedation longer (44.7±12.5 vs. 29.8±12.9% of total infusion time, $P<0.001$) with propofol than midazolam. More patients receiving propofol compared to midazolam had hypotension (16 [50%] vs.4 [14.3%], $P=0.003$). Airway obstruction occurred frequently in both the groups. Sedation was significantly more expensive with propofol than midazolam (US$ 9.83 ± 2.80 vs. US$ 0.33 ± 0.06, $P<0.001$). **Conclusions:** Propofol provided better titration and adequacy of sedation than midazolam in patients above 60 years of age, but caused hypotension. Lighter sedation is recommended in this age group.

KEY WORDS: Anesthesia, patient age, regional, sedation, spinal, surgery, TURP, urological

Both propofol and midazolam are commonly used for sedation during regional anesthesia in young adults and provide good and easily controllable sedation.[1-5] Elderly patients require smaller boluses of these drugs due to lower initial distribution volume of propofol[6] and age-related pharmacodynamic sensitivity to midazolam.[7,8] In addition, prolonged elimination half-life of the drugs necessitates about 25% decrease in their infusion rates in the elderly.[2,9] Due to paucity of literature in older patients, we studied the sedation, hemodynamic and respiratory effects and the costs involved with smaller doses of propofol and midazolam in patients aged above 60 years undergoing urological surgery under spinal anesthesia.

Materials and Methods

After approval of the Institute Ethics Committee, 60 ASA Grade I and II patients with age ≥ 60 years undergoing elective urological procedures of 45-120 min duration under spinal anesthesia were included in a prospective randomized single-blind study. Patients with any contraindication to spinal anesthesia and those chronically using benzodiazepines were excluded from the study.

A written informed consent for the study was obtained from the patients. No sedative premedication was used. Fluid preloading was done with 500 ml of 0.9% saline solution intravenously. Spinal anesthesia was administered with a 26G Quincke spinal needle at the L3-4 intervertebral space using 2.5 to 3 ml of 0.5% hyperbaric bupivacaine. The upper level of sensory block was ascertained after 10 min by assessing the cold sensation to an alcohol swab.

The patients were randomly assigned to receive either propofol or midazolam for sedation and were blinded to the drug used. Random numbers were generated using Microsoft Excel version 4.0 and simple randomization technique by the first author. Sealed coded envelopes were used to conceal the random

numbers. The envelope was opened after the patient had been enrolled in the study by the third author. The investigator was not blinded to the sedative drug. A bolus of 0.4 mg/kg of propofol was administered followed by a continuous infusion at the initial rate of 3 mg/kg/hr. One ml of 2% lignocaine was given intravenously prior to the injection of propofol. Midazolam was given as a bolus of 0.02 mg/kg followed by an infusion at the initial rate of 0.06 mg/kg/hr. One percent solution of propofol and 0.1% solution of midazolam was administered using a syringe infusion pump (JMS syringe infusion pump). The infusion was started approximately 5 min after the spinal anesthesia. The patients received oxygen with a Hudson's face mask (4 L/min) throughout the procedure.

Sedation was assessed using the responsiveness component of the modified Observer's Assessment of Alertness/Sedation Scale (OAA/SS) (Appendix).[10] A score of 3, i.e., patient asleep but responding to name spoken loudly or repeatedly, was defined as the target sedation. Sedation was measured just before the start of sedative infusion and every 5 min thereafter. The infusion rate was altered by one-third of the initial infusion rate to achieve the target sedation. The infusion was terminated about 5 min before the end of the surgical procedure. The primary outcome measures were the onset and offset of sedation and the duration of adequate sedation. The time taken from the start of infusion to reach the target sedation was defined as the onset time and the time from the end of infusion to complete patient awakening (a score of 5 on OAA/SS) was defined as the offset time. The percentage of total infusion time for which the patients stayed at the target sedation was termed as the duration of adequate sedation. The number of patients in whom the target sedation was not attained (undersedation) or exceeded (oversedation), was classified as inappropriate sedation. The cost of sedation was calculated based on the total amount of drug used.

Intraoperative monitoring consisted of heart rate, noninvasive blood pressure, ECG, oxygen saturation using pulse oximetry (SpO_2) and respiratory rate. Heart rate < 60 bpm or 20% less than the baseline was defined as bradycardia and treated with 0.25 mg of i.v. atropine. Systolic blood pressure < 90 mmHg or 20% less than the baseline was defined as hypotension and treated with i.v. boluses of 3 mg of mephenteramine, i.v. fluids and if required, decreasing the infusion rate of the sedative drug. The infusion rate was decreased by a third of the initial rate if hypotension did not respond to fluid bolus and three doses of mephenteramine or lasted for five or more minutes. Any episodes of hypoxia (SpO_2 < 95%), apnea or airway obstruction were recorded and treated by administering 100% oxygen (using an anesthesia mask and a Magill breathing system), awakening the patient, relieving the airway obstruction, mask ventilation and if required, decreasing the infusion rate of the sedative drug. The infusion rate was decreased by a third of the initial rate if the airway obstruction was not relieved by awakening or lasted for five or more minutes. The incidence of hemodynamic and respiratory side-effects were the secondary outcome measures.

Severity of nausea and number of episodes of vomiting were monitored intra- and postoperatively for 24h. The severity of nausea was scored on a 0-10 verbal numerical rating scale with 0 representing no nausea and 10 representing the worst imaginable nausea. Any patient with a nausea score of 3 or more or an episode of vomiting was treated with 4 mg of i.v. ondansetron. Occurrence of other side-effects such as pain on injection and shivering was recorded.

A mean difference in onset of sedation of 4 min with a standard deviation of 4 min was considered significant and was used to calculate the sample size. A total of 27 patients per group were required to detect this difference with an α error of 0.05 and a power of 95%. A total of 60 patients were enrolled to adjust for exclusion of patients.

Parametric data were expressed as mean ± standard deviation (SD) and analyzed using Student's unpaired t test. Nonparametric data were expressed as median and interquartile range (IQR) and analyzed using Mann-Whitney U test. Incidence of inappropriate sedation and of side-effects were analyzed using Chi-square test. A P value < 0.05 was considered statistically significant.

Results

Sixty patients were enrolled in the study during the period April 2002 to March 2003. Of these, 32 received propofol and 28 received midazolam for sedation. No patient was excluded from the study after enrollment. Patients in the two groups were comparable with respect to age, weight, gender distribution and duration of sedative infusion and surgery [Table 1]. The median (IQR) upper level of sensory block attained after spinal anesthesia was T10 (T8 - T10) in both the groups. The various surgical procedures that the patients underwent are listed in Table 1. The distribution of various surgical procedures in the two groups was not significantly different ($P = 0.067$, Chi-square test).

The onset and offset times and the duration of adequate sedation were found to be normally distributed (onset time: SEM 0.66, skewness –0.075, kurtosis –0.452; offset time: SEM 0.46, skewness 0.4, kurtosis 0.328; duration of adequate sedation: SEM 1.89, skewness 0.609, kurtosis –0.408)). Thus parametric statistical methods were applied for these parameters. The onset as well as the offset of sedation were significantly faster with propofol than with midazolam. The duration of adequate sedation was significantly longer in the propofol group compared to the midazolam group [Table 2]. Three patients in the propofol group and seven in the midazolam group remained undersedated throughout the procedure. Two patients in each group were oversedated. The incidence of inappropriate sedation was statistically similar in the two groups [Table 2].

The incidence of hypotension was significantly higher in the propofol group than the midazolam group [Table 3]. There were 21 episodes of hypotension in 16 patients in the propofol group and four episodes in as many patients in the midazolam group. All episodes of hypotension were initially treated with 3 mg of mephenteramine. Two patients in the propofol group required an additional 6 mg of mephenteramine and a decrease

Table 1: Demographic data

		Propofol (n = 32)	Midazolam (n = 28)
Age (years)*		70.8 ± 7.9	70.2 ± 6.7
Weight (kg)*		62.3 ± 12.4	64.1 ± 8.3
Male patients†		31 (96.9)	26 (92.9)
Duration of sedative infusion (minutes)*		60.0 ± 13.1	63.2 ± 11.6
Duration of surgery (minutes)*		62.3 ± 12.3	58.9 ± 12.6
{Median [25-75% interquartile range]}		{60 [52.8 - 73.8]}	{55[50 - 68.8]}
Surgical procedures†	Transurethral resection of prostate	14 (43.8)	6 (21.4)
	Transurethral resection of bladder tumor	6 (18.8)	11 (39.3)
	Cystopanendoscopy	8 (25)	5 (17.9)
	Others	4 (12.5)	6 (21.4)

*Values expressed as mean ± SD and analyzed using Student's t test; †Values expressed as number (%) of patients and analyzed using Chi-square test; Other surgical procedures included total penectomy, cystolithotomy, open prostatectomy, ureteric stenting and bilateral orchidectomy

Table 2: Sedation: onset and offset of sedation, duration of adequate sedation and incidence of inappropriate sedation

Sedation	Propofol (n = 32)	Midazolam (n = 28)
Onset of sedation (min) (mean ± SD)	13.0 ± 4.2	18.8 ± 4.2*
Offset of sedation (min) (mean ± SD)	8.9 ± 2.8	12.5 ± 3.5†
Duration of adequate sedation (% of total infusion time) (mean ± SD)	44.7 ± 12.5	29.8 ± 12.9‡
Number (%) of patients with inappropriate sedation [95% Confidence Interval]	5 (15.6) [9.2-22.0]	9 (32.1) [23.3-41.0]

Onset of sedation: The time from start of infusion to the time of attaining the target sedation (a score of 3 on the responsiveness component of the modified OAA/SS). Offset of sedation: The time from end of infusion to the time of awakening (a score of 5 on the responsiveness component of the modified OAA/SS). Inappropriate sedation: Sedation more or less than the target sedation. *$P < 0.001$, degrees of freedom 58, confidence interval -7.96 to -3.60; †$P < 0.001$, degrees of freedom 58, confidence interval -5.21 to -1.98; ‡$P < 0.001$, degrees of freedom 58, confidence interval 8.26 to -21.42

Table 3: Number of patients with side-effects

Side effects	Propofol (n = 32)	Midazolam (n = 28)
Hypotension	16 (50.0) [32.7-67.3]	4 (14.3)* [1.3-27.2]
Bradycardia	1 (3.1) [-2.9-9.2]	1 (3.6) [-3.3-10.4]
Airway obstruction	7 (21.9) [7.6-36.2]	7 (25) [9.0-41.0]
Agitation	0 (0)	1 (3.6) [-3.3-10.4]
Pain on injection	1 (3.1) [-2.9-9.2]	0 (0)
Nausea	1 (3.1) [-2.9-9.2]	1 (3.6) [-3.3-10.4]
Shivering	1 (3.1) [-2.9-9.2]	0 (0)

$P = 0.003$ (Chi-square test), Figures represent number (%) [95% confidence inverval]

in the rate of propofol infusion for the treatment of hypotension. One patient each in the propofol and midazolam group had an episode of bradycardia requiring treatment with atropine.

Seven patients in each group had intraoperative airway obstruction. A decrease in the rate of sedative infusion was required to relieve obstruction in two patients in each group. No patient had airway obstruction postoperatively. There were no episodes of apnea or hypoxia in any patient. None of the patients had nausea or vomiting in either group intraoperatively. One patient in each group had nausea postoperatively with nausea scores being 1 and 2 and did not require any treatment.

One patient in the midazolam group became restless and agitated 20 min after the start of midazolam infusion. These symptoms persisted on increasing the rate of infusion, but disappeared within 10 min of stopping the infusion. One patient in the propofol group complained of pain in the forearm after the start of propofol infusion which subsided within 5 min. One patient in the propofol group had shivering intra- and postoperatively.

The total amount of propofol used for sedation was 221.3 ± 62.9 mg and that of midazolam was 4.2 ± 0.8 mg. The cost of a vial containing 200 mg of propofol at the time of the study was US$ 8.89 and that of 5 mg of midazolam was US$ 0.39. The total cost of propofol sedation (US$ 9.83 ± 2.80) was significantly higher than that of midazolam sedation (US$ 0.33 ± 0.06) (Student's t test, *P<0.001*, degree of freedom 58, confidence interval 8.45 to 10.57).

Discussion

The goals of sedation during regional anesthesia include rapid achievement of adequate sedation, its maintenance at a constant level during the surgical procedure and awakening the patient quickly at the end. This can be attained by continuous infusion of sedative drugs preceded by a bolus. A wide range of doses of propofol (0.25-0.5 mg/kg; 1.5-4.5 mg/kg/hr) and midazolam (0.025-0.5 mg/kg; 0.05-0.5 mg/kg/hr) have been used for this purpose.[11] We selected a smaller bolus and a slower infusion rate for both the drugs.

We found that the target sedation was achieved much faster with propofol than with midazolam. It has been reported that when infusions are used without a prior bolus, the onset of sedation is similar with the two drugs.[4]

In our study, the target sedation was maintained for a longer period with propofol than midazolam (45 vs. 30% of infusion time). Also, sedation was maintained at the target level for only a fraction of the total infusion time unlike most of the earlier reports where adequate sedation lasted almost throughout the infusion.[2,4,5,12]

Approximately 16 and 32% of the patients in the propofol and midazolam groups were inappropriately sedated during the procedure. However, this was not statistically significant. Power analysis showed that this observed difference would have been statistically significant in a sample of 100 patients. Fanard *et al* also reported similar levels of inappropriate sedation during regional anesthesia (propofol-12%; midazolam-24%).[3] The factors that may have contributed to inadequate sedation in our study include: inability to increase the infusion rate due to hypotension or airway obstruction; prolonged time to reach target sedation due to small bolus, low infusion rate and slow circulation in the elderly patients; and difficulty in titrating the infusion rate of midazolam due to hysteresis in its concentration-response curve.[6]

A wide variation in recovery from sedation is reported in the literature. The recovery times in the elderly in our study were similar to those observed earlier in young adults.[3] Shinozaki found similar initial clinical recovery in young adults and elderly after similar infusion rates and levels of sedation, but delayed psychomotor recovery in the elderly.[13] On the other hand, Wilson *et al.* found shorter offset times than our observations with both propofol and midazolam in young adults (2.3 and 9.2 min).[4] The variation in different studies may be due to the use of different premedicants and wide interpatient variability of benzodiazepines.[6] We observed that recovery from sedation was much faster after propofol infusion than after midazolam. Similar findings are reported in young adults.[3,4]

We used a validated, well-discriminating clinical scoring method (OAA/SS) to assess sedation.[10] Such clinical methods necessitate stimulation of the patient for each assessment. However, Bispectral Index (BIS) and other EEG-based monitors cannot reliably distinguish between light and deep sedation and are agent-specific[14-17] and were not appropriate for this study.

The incidence of hypotension with propofol was three times higher than with midazolam, similar to earlier observations.[18] It was also higher than that reported in the literature (15.7%).[19] The elderly have diminished cardiovascular adaptation and reduced blood volume because of which both propofol infusion and spinal anesthesia result in frequent and profound episodes of hypotension.[19-21]

Both propofol and midazolam are known to cause apnea, arterial desaturation and airway obstruction in sedative doses.[22-25] Although none of our patients developed apnea or desaturation, airway obstruction occurred frequently in both the groups.[3,4] Benzodiazepines cause greater depression of upper airway muscle tone in the elderly resulting in a higher incidence of airway obstruction.[26] Administration of oxygen to all the patients during sedation and immediate relief of airway obstruction prevented the occurrence of oxygen desaturation in our study. The small size of the bolus and a slow infusion rate avoided apnea.

Since hypotension and airway obstruction were frequent in the elderly, it would be prudent to reduce the dosages of the sedative drugs further in these patients and maintain sedation at a lighter level (a score of 4 instead of 3 on OAA/SS).

Restlessness and agitation developed in one patient 20 min after the start of midazolam infusion and resolved on stopping it. Midazolam sometimes causes agitation and violence instead of tranquility (midazolam paradox). It is more frequent in the elderly and is completely reversible with flumazenil.[27]

Our incidence of nausea (3.3%) is much lower than the 9% reported in patients over the age of 60 years undergoing surgery under regional anesthesia.[28] Nausea and vomiting are not frequent following urologic procedures. Also, both propofol and midazolam are antiemetic.[28,29]

Sedation was 30 times more expensive with propofol than midazolam. However, the absolute cost of sedation with propofol (US$ 9.83 ± 2.80) was not very high. In addition, the cost of propofol in India has decreased markedly from US$ 8.89 per 200 mg of the drug at the time of the study to approximately US$ 3.33 presently. A limitation of this analysis is that only the costs of the sedative drugs are used. The prolonged offset time of midazolam or hypotension due to propofol may necessitate a longer stay in the post-anesthesia care unit (PACU) and thus increase the total costs. We did not compute these latter costs, as in our hospital the patient pays only for the drugs and disposables used and the surgical procedure. He is not charged for the stay in the PACU. Staffing patterns in the PACU are constant and not dependent on the patient load.

Conclusion

Propofol provides better sedation than midazolam in terms of easy titration and adequacy of sedation in patients above 60 years of age, but has the disadvantage of causing more hypotension. We recommend a lighter level of sedation in these patients to avoid side-effects. Further studies are required to determine whether light sedation is consonant with patient comfort.

References

1. McClure JH, Brown DT, Wildsmith JAW. Comparison of the i.v. administration of midazolam and diazepam as sedation during spinal anaesthesia. Br J Anaesth 1983;55:1089-93.
2. Mackenzie N, Grant IS. Propofol for intravenous sedation. Anaesthesia 1987;42:3-6.
3. Fanard L, van Steenberge A, Demeire X, van der Puyl F. Comparison between propofol and midazolam as sedative agents for surgery under

regional anaesthesia. Anaesthesia 1988;43:87-9.
4. Wilson E, David A, MacKenzie N, Grant IS. Sedation during spinal anaesthesia: Comparison of propofol and midazolam. Br J Anaesth 1990;64:48-52.
5. Urquhart ML, White PF. Comparison of sedative infusions during regional anesthesia - methohexital, etomidate and midazolam. Anesth Analg 1989;68:249-54.
6. Kirkpatrick T, Cockshott ID, Douglas EJ, Nimmo WS. Pharmacokinetics of propofol (Diprivan) in elderly patients. Br J Anaesth 1988;60:146-50.
7. Albrecht S, Ihmsen H, Hering W, Geisslinger G, Dingemanse J, Schwilden H, *et al*. The effect of age on the pharmacokinetics and pharmacodynamics of midazolam. Clin Pharmacol Ther 1999;65:630-9.
8. Jacobs JR, Reves JG, Marty J, White WD, Bai SA, Smith LR. Aging increases pharmacodynamic sensitivity to the hypnotic effects of midazolam. Anesth Analg 1995;80:143-8.
9. Greenblatt DJ, Abernethy DR, Locniskar A, Harmatz JS, Limjuco RA, Shader RI. Effect of age, gender and obesity on midazolam kinetics. Anesthesiology 1984;61:27-35.
10. Chernik DA, Gillings D, Laine H, Hendler J, Silver JM, Davidson AB, *et al*. Validity and reliability of the observer's assessment of alertness/sedation scale: Study with intravenous midazolam. J Clin Psychopharmacol 1990;10:244-51.
11. Chiu JW, White PF. Nonopioid intravenous anesthesia. *In*: Barash PG, Cullen BF, Stoelting RK, editors. Clinical anesthesia. 4th ed. Lippincott, Williams and Wilkins: Philadelphia, PA; 2001. p. 341-2.
12. Frizelle HP, Duranteau J, Samii K. A comparison of propofol with a propofol-ketamine combination for sedation during spinal anesthesia. Anesth Analg 1997;84:1318-22.
13. Shinozaki M, Usui Y, Yamaguchi S, Okuda Y, Kitajima T. Recovery of psychomotor function after propofol sedation is prolonged in the elderly. Can J Anesth 2002;49:927-31.
14. Glass PS, Bloom M, Kearse L, Rosow C, Sebel P, Manberg P. Bispectral analysis measures sedation and memory effects of propofol, midazolam, isoflurane and alfentanil in healthy volunteers. Anesthesiology 1997;86:836-47.
15. Ibrahim AE, Taraday JK, Kharasch ED. Bispectral index monitoring during sedation with sevoflurane, midazolam and propofol. Anesthesiology 2001;95:1151-9.
16. Buyukkocak U, Ozcan S, Daphan C, Apan A, Koc C. A comparison of four intravenous sedation techniques and bispectral index monitoring in sinonasal surgery. Anaesth Intensive Care 2003;31:164-71.
17. Chisholm CJ, Zurica J, Mironov D, Sciacca RR, Ornstein E, Heyer EJ. Comparison of electrophysiologic monitors with clinical assessment of level of sedation. Mayo Clin Proc 2006;81:46-52.
18. Hasen KV, Samartzis D, Casas LA, Mustoe TA. An outcome study comparing intravenous sedation with midazolam/fentanyl (conscious sedation) versus propofol infusion (deep sedation) for aesthetic surgery. Plast Reconstr Surg 2003;112:1683-9.
19. Hug CC Jr, McLeskey CH, Nahrwold ML, Roizen MF, Stanley TH, Thisted RA, *et al*. Hemodynamic effects of propofol: Data from over 25,000 patients. Anesth Analg 1993;77:S21-9.
20. Larsen R, Rathgeber J, Bagdahn A, Lange H, Rieke H. Effects of propofol on cardiovascular dynamics and coronary blood flow in geriatric patients. A comparison with etomidate. Anaesthesia 1988;43 (Supplement):25-31.
21. Tarkkila P, Isola J. A regression model for identifying patients at high risk of hypotension, bradycardia and nausea during spinal anesthesia. Acta Anesthesiol Scand 1992;36:554-8.
22. Montravers P, Dureuil B, Desmonts JM. Effects of i.v. midazolam on upper airway resistance. Br J Anaesth 1992;68:27-31.
23. Blouin RT, Seifert HA, Babenco HD, Conard PF, Gross JB. Propofol depresses the hypoxic ventilatory response during conscious sedation and isohypercapnia. Anesthesiology 1993;79:1177-82.
24. Nozaki-Taguchi N, Isono S, Nishino T, Numai T, Taguchi N. Upper airway obstruction during midazolam sedation: Modification by nasal CPAP. Can J Anaesth 1995;42:685-90.
25. Yamakage M, Kamada Y, Toriyabe M, Honma Y, Namiki A. Changes in respiratory pattern and arterial blood gases during sedation with propofol or midazolam in spinal anesthesia. J Clin Anesth 1999;11:375-9.
26. Leiter JC, Knuth SL, Krol RC, Bartlett D Jr. The effect of diazepam on genioglossal muscle activity in normal human subjects. Am Rev Respir Dis 1985;132:216-9.
27. Weinbroum AA, Szold O, Ogorek D, Flaishon R. The midazolam induced paradox phenomenon is reversible by flumazenil. Epidemiology, patient characteristics and review of the literature. Eur J Anaesthesiol 2001;18:789-97.
28. Borgeat A, Ekatodramis G, Schenker CA. Postoperative nausea and vomiting in regional anesthesia: A review. Anesthesiology 2003;98:530-47.
29. Splinter WM, MacNeill HB, Menard EA, Rhine EJ, Roberts DJ, Gould MH. Midazolam reduces vomiting after tonsillectomy in children. Can J Anaesth 1995;42:201-3.

Appendix: Responsive component of the modified Observer's Assessment of Alertness/Sedation Scale

Score	Responsiveness
5	Awake and responds readily to name spoken in normal tone
4	Awake but lethargic response to name spoken in normal tone
3	Asleep but responds to name spoken loudly or repeatedly
2	Asleep but responds to mild prodding or shaking
1	Does not respond to mild prodding or shaking
0	Does not respond to noxious stimuli

Source of Support: Nil, **Conflict of Interest:** None declared.