Upper airway obstruction during midazolam sedation: modification by nasal CPAP

Natsuko Nozaki-Taguchi MD,* Shiroh Isono MD,†
Takashi Nishino MD,† Takeshi Numai MD,*
Noboru Taguchi MD†

We examined the depressant effect of midazolam on respiration in 21 healthy women undergoing lower abdominal surgery with spinal anaesthesia. Airway gas flow, airway pressure, and the sound of snoring were recorded together with arterial oxygen saturation (SpO₂). After spinal anaesthesia was established, subjects were deeply sedated with pentazocine 15 mg followed by incremental doses of midazolam 1 mg iv up to 0.1 mg · kg⁻¹. When SpO₂ decreased to <90% or snoring and/or apnoea was observed, continuous positive airway pressure applied through the nose (nasal CPAP) was increased until the respiratory deterioration was reversed. While one patient remained free of respiratory events, the other 20 patients were successfully treated with nasal CPAP restoring normal SpO₂ (95.5 ± 1.7%) without snoring. Stepwise reduction of nasal CPAP determined the minimally effective CPAP to prevent snoring to be 5.1 ± 2.1 cm H₂O. Further reduction of nasal CPAP induced snoring in 15 patients and obstructive apnoea in five patients with the latter accompanied by a severe reduction of SpO₂ (87.4 ± 6.1%). Patients with apnoea were older than those who snored (P < 0.05). We conclude that upper airway obstruction contributes considerably to decreases in SpO₂ during midazolam sedation for spinal anaesthesia.

Key words

AIRWAY: obstruction;

ANAESTHETIC TECHNIQUES: spinal;

HYPNOTICS: benzodiazepines;

VENTILATION: obstruction, oxygenation, continuous positive airway pressure.

From the Department of Anaesthesia, Funabashi Municipal Medical Centre,* and Department of Anaesthesiology, School of Medicine Chiba University.†

Address correspondence to: Dr. N. Nozaki-Taguchi, Department of Anaesthesiology, School of Medicine, Chiba University, 1-8-1 Inohana Chuo-ku Chiba-shi, Chiba 270 Japan.

Accepted for publication 14th April, 1995.

Nous avons étudié les effets déresseurs du midazolam sur la respiration chez 21 femmes bien portantes opérées pour une chirurgie abdominale basse sous anesthésie rachidienne. Le débit et la pression des voies aériennes, ainsi que le ronflement ont été enregistrés en même temps que la saturation en oxygène (SpO₂). Une fois l'anesthésie rachidienne établie, les patientes ont reçu une sédation profonde avec de la pentazocine 15 mg suivie par des doses répétées de midazolam 1 mg iv pour une dose totale de 0,1 mg · kg⁻¹. Lorsque la SpO₂ diminuait sous 90% ou qu'un ronflement avec ou sans apnée était observé, une pression positive était appliquée progressivement sur les voies aériennes par le nez (CPAP nasal) jusqu'au retour de la respiration normale. Tandis qu'une patiente ne manifestait aucun symptôme respiratoires, les 20 autres patientes étaient traitées avec succès par le CPAP nasal avec le rétablissement d'une SpO₂ normale (95,5 ± 1,7%). Une diminution en paliers du CPAP nasal a permis de déterminer le CPAP minimal requis pour prévenir le ronflement qui se situe à 5,1 ± 2,1 cm H₂O. La diminution subséquente du CPAP a provoqué du ronflement chez 15 des patientes et une apnée de type obstructif chez cinq des patientes qui s'est accompagnée d'une chute importante de la SpO₂ (87,4 ± 6,1%). Les patientes devenues apnéiques étaient plus âgées que celles qui ronflaient (P < 0,05). Nous concluons que l'obstruction des voies aériennes supérieures contribue considérablement aux baisses de SpO₂ pendant la sédation au midazolam pendant l'anesthésie rachidienne.

Patients undergoing surgery with spinal anaesthesia are frequently sedated to suppress awareness and to enhance comfort. However, reduction in arterial oxygen saturation (SpO₂)^{1,2} and cardiopulmonary arrest³ have been reported during sedation with spinal anaesthesia. Recently, Gauthier *et al.*⁴ showed that the combination of midazolam and spinal anaesthesia has a modest synergistic effect of depressing resting ventilation. However, they did not examine the influence of upper airway obstruction. Benzodiazepines used to induce overnight hypnosis reduce upper airway muscle tone which leads to upper air-

way collapse and may cause severe arterial oxygen desaturation.⁵ Hypoxaemia in patients receiving sedatives during spinal anaesthesia may also result from upper airway obstruction and, if so, continuous positive airway pressure through the nose (nasal CPAP) may improve oxygenation as well as breathing patterns.⁶

This study was designed to test the hypothesis that the combined use of sedation with midazolam and spinal anaesthesia compromises respiration, especially upper airway patency resulting in oxygen desaturation.

Methods

The protocol was approved by the Hospital Ethics Committee, and each patient gave informed consent. Twenty-one ASA physical status I female patients, ages 25–59 yr and having elective lower abdominal surgery, were studied. Their average heights and weights were 156.4 ± 4.8 cm and 55.8 ± 6.6 kg, respectively (means $\pm$ SD). None complained of habitual snoring at night.

All patients received, an hour before induction of anaesthesia, ranitidine 50 mg *iv* and, 30 min later, atropine 0.5 mg and hydroxyzine 50 mg *im*. In the operating room, spinal anaesthesia was established with dibucaine $0.096 \text{ mg} \cdot \text{kg}^{-1}$ (max. dose 5.76 mg for those >60 kg) through the L₃₋₄ interspace. Pulse oximetry and a side stream spirometer (Datex, Capnomac Ultima SV) were used for the monitoring of SpO₂, airway gas flow ($\dot{V}$) and mask pressure (P_m), which were recorded on a four-channel recorder (Graphtec, LINEARECORDER F WR3701). The snoring sound heard through the precordial stethoscope placed on the patient's neck was also recorded through a microphone and an amplifier (TOMY, Voice Changer).

After confirming the upper level of the subarachnoid block by loss of sensation to pinprick, pentazocine 15 mg *iv* was given followed by incremental doses of midazolam 1 mg *iv* every 30 sec to a maximum of $0.1 \text{ mg} \cdot \text{kg}^{-1}$ (max. dose 6 mg). A nasal CPAP mask (Respironics, BiPAP or Rescare, Sullivan Nasal CPAP system) was tightly fitted while breathing room air. The CPAP was increased when (1) SpO₂ was $<90\%$ or (2) changes in respiratory pattern such as snoring or apnoea occurred. Apnoea was diagnosed by an absence of inspiratory airflow for >10 sec. Airway pressure was increased until SpO₂ was $>90\%$ without apnoea or snoring. If SpO₂ values did not exceed 90% even with 10 cm H₂O CPAP, the patient was given oxygen and was withdrawn from the study. After midazolam $0.1 \text{ mg} \cdot \text{kg}^{-1}$ was given and respiratory pattern was stable with SpO₂ $>90\%$, surgery was started confirming no discomfort was felt by the patients. The CPAP was then reduced by 1 cm H₂O by every 30 sec until snoring was heard again. The minimally effective CPAP pressure to reverse

snoring (Psnore(–)) was determined. The pressure was further reduced to zero. However, if apnoea was observed, no further reduction of airway pressure was performed. Upon observing apnoea, if SpO₂ decreased to $<85\%$ with no sign of restoration of breathing, CPAP was raised.

Patients were divided into three groups according to the changes in respiratory patterns observed during CPAP reduction: SNORE; continuous snoring at CPAP 0 cmH₂O, APNOEA; occurrence of apnoea during the reduction of CPAP, and NORMAL; maintaining SpO₂ $>90\%$ with no change in the breathing pattern at CPAP 0 cmH₂O. Apnoea was further diagnosed as obstructive or central in its origin. Obstructive apnoeas were accompanied with (1) paradoxical chest wall movement during apnoea, (2) a characteristic snort with the restoration of respiration, and (3) effective reversal with nasal CPAP.

Data were analyzed with Student's *t* test and one way analysis of variance, difference being detected by Scheffe's test. A probability value of $P < 0.05$ was considered significant.

Results

One patient remained free of respiratory events after sedation and 20 were treated with nasal CPAP. All patients regained SpO₂ values $>90\%$ with nasal CPAP <10 cmH₂O and none was excluded from the study. The level of subarachnoid block was above Th 10 but below Th 6 in all patients at examination and surgery was performed without complaints. After the maximum dose of midazolam had been given, patients were deeply sedated responding to pain but not to verbal commands not allowing the insertion of any artificial airway.

Figure 1 is an example of changes in the breathing pattern observed during reduction of nasal CPAP. As P_m was reduced from 8 to 4 cmH₂O, maximum inspiratory flow decreased: gradually the typical flow pattern of inspiratory flow limitation, characterized by the flattening of the inspiratory flow curve accompanied with the snoring sound.⁷ The SpO₂ values also showed concomitant decreases with reduction of P_m. The Psnore(–) of this patient was 8 cmH₂O.

Figure 2 is a record of a patient with snore at CPAP 0 cmH₂O. Snoring was accompanied by a slight and constant decrease in SpO₂, and a limitation of the inspiratory flow. A record of a patient with apnoea is shown in Figure 3. A period of no airflow associated with severe but episodic decrease in SpO₂ was followed by a brief large airflow and a loud snort with restoration of SpO₂, a pattern typical of obstructive apnoea. During the apnoeic period, paradoxical movement of the chest wall was observed confirming that the inspiratory effort was present.

Patient characteristics, values of Psnore(–) and the

FIGURE 1 Effect of nasal CPAP on breathing patterns. As the Pm is reduced from 8 to 4 cmH₂O, maximum inspiratory flow shows a gradual decrease and limitations of inspiratory flow accompanying the snoring sound is seen with concomitant decrease in SpO₂. (SpO₂ = arterial oxygen saturation; Pm = mask pressure).

FIGURE 2 Record of a patient who snored at CPAP of zero. Snoring is accompanied with a slight decrease in SpO₂ and a limitation of the inspiratory flow. (SpO₂ = arterial oxygen saturation; Pm = mask pressure.)

breathing patterns are summarized in the Table. An average of 5.1 ± 2.1 cmH₂O was effective in the treatment of snoring and apnoea. Five patients were observed with apnoea while only snoring was observed in 15 patients when CPAP was reduced. All apnoeas observed were diagnosed obstructive. In four patients, spontaneous restoration of breathing was seen before SpO₂ < 85%, while in one patient increase in CPAP was necessary to establish patent airway to breathe. There was no difference

in Body Mass Index (BMI: kg · m⁻²) between patients with apnoea and patients who snored (22 ± 4.8 kg · m⁻² vs 22.9 ± 2.8 kg · m⁻², respectively), but patients with apnoea were older than patients who snored (49.0 ± 7.5 vs 39.9 ± 8.2 yr, $P < 0.05$).

The average SpO₂ value of all 20 patients at Psnore(–) was 95.5 ± 1.7 (range 92–98)%; SpO₂ values at Psnore(–) were similar between patients who snored and patients with apnoea ($95.3 \pm 1.6\%$ vs $95.8 \pm 2.2\%$, respectively) (Figure 4). These values decreased with snoring at CPAP zero ($95.0 \pm 1.8\%$, $P < 0.05$) or with the occurrence of apnoea ($87.4 \pm 6.1\%$, $P < 0.05$). The decrease in SpO₂ values was lower with apnoea than in snorers at CPAP zero ($P < 0.05$).

Values of Psnore(–) had no correlation with age or BMI, nor was there any difference in Psnore(–) between patients who snored and patients with apnoea (4.9 ± 1.9 vs 5.4 ± 3.0 cmH₂O, respectively).

Discussion

The present study demonstrated that the combined use of midazolam with spinal anaesthesia for lower abdominal surgery in otherwise healthy female patients caused apnoea and/or snoring which were accompanied with reductions in SpO₂ values suggesting that the critical effect of *iv* midazolam on respiration is upper airway obstruction.

After administration of midazolam and pentazocine, all patients showed a sedation level at which the patient responded to pain but not to verbal commands. A commonly used dose of midazolam for sedation during regional anaesthesia is $0.05\text{--}0.1$ mg · kg⁻¹.^{1,2,4} However, during lower abdominal surgery with spinal anaesthesia,

FIGURE 3 Record of a patient with apnoea. Attenuation of flow and episodic desaturation is followed by a brief large airflow and a loud snort. This pattern is characteristic of obstructive apnoea. (SpO_2 = arterial oxygen saturation; Pm = mask pressure.)

TABLE Patient characteristics, breathing patterns, $\text{Psnore}(-)$ and minimum SpO_2

Patient	Age (yr)	Height (cm)	Weight (kg)	BMI ($\text{kg} \cdot \text{m}^{-2}$)	Criteria	$\text{Psnore}(-)$ (cmH_2O)	Minimum $\text{SpO}_2(\%)$
1	47	153.5	53.0	22.5	Apnea	4	91
2	53	152.0	72.0	31.2	Apnea	4	86
3	29	169.5	62.0	21.6	Snore	2	95
4	41	155.0	53.0	22.1	Snore	6	91
5	36	162.0	54.2	20.7	Snore	2	93
6	59	156.0	51.0	21.0	Apnea	2	<85
7	44	155.0	65.8	27.4	Snore	3	96
8	41	158.0	59.0	23.6	Normal		
9	44	149.8	60.0	26.7	Snore	3	91
10	43	150.0	53.0	23.6	Snore	4	95
11	38	157.0	54.0	21.9	Snore	7	95
12	39	153.0	47.5	20.3	Apnea	9	94
13	47	153.0	53.0	22.6	Snore	5	97
14	54	156.5	58.0	23.7	Snore	7	94
15	36	163.0	48.0	18.1	Snore	6	96
16	27	163.0	53.0	19.9	Snore	5	90
17	42	159.0	59.0	23.3	Snore	6	96
18	42	155.8	49.0	20.2	Snore	4	94
19	25	157.4	56.5	22.8	Snore	6	92
20	50	152.5	65.5	28.2	Snore	8	87
21	47	154.0	46.0	19.4	Apnea	8	88

patients often complain of nausea or discomfort upon upper displacement of the intestines or traction of the viscera,⁸ requiring additional doses of analgesics or light general anaesthesia^{9,10} to produce profound sedation. The dose chosen for study was sufficient to produce such profound sedation, but patients were rousable after 1–1.5 hr of surgery.

Though decreases in SpO_2 values were observed with snoring, they remained $>90\%$. However, obstructive ap-

noea produced oxygen desaturation $<90\%$. Thus, it is important to predict the patient's airway response to sedative drugs. The occurrence of upper airway obstruction may be influenced by two different mechanisms; anatomical (i.e., a structurally narrow or highly compliant airway) and neuromuscular (i.e., central depression of neural mechanisms controlling upper airway muscles).¹¹ Patients in our study were all healthy female patients, none complained of habitual snoring at night. High BMI,

FIGURE 4 Comparison of SpO₂ values at Psnore(-) and at CPAP 0 cmH₂O(P(0)) or minimal SpO₂ values with apnoea. Values are expressed as means $\pm$ SD. * $P < 0.05$ vs. Psnore(-) § $P < 0.05$ between snore at CPAP 0 cmH₂O and apnoea.

a known risk factor for obstructive sleep apnoea did not predict the occurrence of apnoeas with sedative drugs. In our study, patients with apnoea were older than those who snored. Burger *et al.*¹² have reported that in normal men, age was not associated with decrease in diameter or collapse of the upper airway. These facts suggest that there was no anatomical background for the airway obstruction.

Anatomical factors being equal, the sensitivity the neuromuscular mechanisms of each patient to sedative drugs may play an important role. Benzodiazepines are known to depress motor activity of upper airway muscles selectively,¹³⁻¹⁵ increasing sleep-disorder breathing patterns, such as obstructive apnoea and hypopnea even in asymptomatic subjects when used to induce hypnosis.¹⁶ Leiter *et al.*¹⁵ have found greater sensitivity to diazepam in older subjects, who showed a decrease in genioglossal EMG activity. Old age suggests higher sensitivity to sedative drugs, greater depression of upper airway neuromuscular mechanisms, that leads to complete obstruction.

A decrease in SpO₂ during midazolam sedation with spinal anaesthesia is considered to be a result of central respiratory depression.^{2,3,5} Under profound sedation, however, several factors such as central depression of the ventilation, a decrease in functional residual capacity (FRC), and upper airway obstruction, all contribute to the decrease in SpO₂. In our study, low levels of nasal CPAP resolved upper airway obstruction and snoring and restored SpO₂ values to normal, which in turn suggests that the upper airway obstruction contributes to the oxygen desaturation.

In conclusion, profound sedation induced by midazolam and pentazocine combined with spinal anaesthesia caused obstruction apnoea and/or snoring which were accompanied with decreases in arterial oxygen saturation. Low levels of nasal CPAP used to prevent upper airway obstruction was effective in the restoration of SpO₂ suggesting that the critical effect of midazolam sedation on respiration is upper airway obstruction.

Acknowledgement

Our thanks to Mr. T. Sato, medical engineer of our hospital, for his help with setting up the monitoring system. We also thank the surgeons of the Gynaecology Department and the nursing staff of Funabashi Municipal Medical Centre for their co-operation.

References

- 1 Manara AR, Smith DC, Nixon C. Sedation during spinal anaesthesia: a case for the routine administration of oxygen. *Br J Anaesth* 1989; 63: 343-5.
- 2 Smith DC, Crul JF. Oxygen desaturation following sedation for regional analgesia. *Br J Anaesth* 1989; 62: 206-9.
- 3 Caplan RA, Ward JR, Posner K, Cheney FW. Unexpected cardiac arrest during spinal anesthesia: a closed claims analysis of predisposing factors. *Anesthesiology* 1988; 68: 5-11.
- 4 Gauthier RA, Dyck B, Chung F, Romanelli J, Chapman KR. Respiratory interaction after spinal anesthesia and sedation with midazolam. *Anesthesiology* 1992; 77: 909-14.
- 5 Guilleminault C. Benzodiazepines, breathing, and sleep. *Am J Med* 1990; 88: 25S-28S.
- 6 Sullivan CE, Issa FG, Berthon-Jones M, Eves L. Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. *Lancet* 1981; 1: 862-5.
- 7 Condos R, Norman RG, Krishnasamy I, Peduzzi N, Goldring RM, Rapoport DM. Flow limitation as a noninvasive assessment of residual upper-airway resistance during continuous positive airway pressure therapy of obstructive sleep apnea. *Am J Respir Crit Care Med* 1994; 150: 475-80.
- 8 Mihic DN, Abram SE. Optimal regional anaesthesia for abdominal hysterectomy: combined subarachnoid and epidural block compared with other regional techniques. *Eur J Anaesthesiol* 1993; 10: 297-301.
- 9 Chambers WA, Edstrom HH, Scott DB. Effect of baricity on spinal anaesthesia with bupivacaine. *Br J Anaesth* 1981; 53: 279-82.
- 10 Sinclair CJ, Scott DB, Edstrom HH. Effect of the Trendelenburg position on spinal anaesthesia with hyperbaric bupivacaine. *Br J Anaesth* 1982; 54: 497-500.
- 11 Isono S, Remmers JE. Anatomy and physiology of the upper airway obstruction. In: *Principles and Practice of*

- Sleep Medicine, 2nd ed. Philadelphia: WB Saunders Company, 1994; 642-56.
- 12 *Burger CD, Stanson AW, Sheedy PF II, Daniels BK, Shepard JW Jr.* Fast-computed tomography evaluation of age-related changes in upper airway structure and function in normal men. *Am Rev Respir Dis* 1992; 145: 846-52.
 - 13 *Nishino T, Shirahata M, Yonezawa T, Honda Y.* Comparison of changes in the hypoglossal and the phrenic nerve activity in response to increasing depth of anesthesia in cats. *Anesthesiology* 1984; 60: 19-24.
 - 14 *Bonara M, St. John WM, Bledsoe TA.* Differential elavation by protipityline and depression by diazepam of upper airway respiratory motor activity. *Am Rev Respir Dis* 1985; 131: 41-5.
 - 15 *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.
 - 16 *Dolly FR, Block AJ.* Effect of flurazepam on sleep-disordered breathing and nocturnal oxygen desaturation in asymptomatic subjects. *Am J Med* 1982; 73: 239-43.