

Remifentanil for Use During Conscious Sedation in Outpatient Oral Surgery

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Purpose: Remifentanil is a new, short-acting opioid that is similar pharmacodynamically to currently available opioids but differs in its pharmacokinetics. In the present study, we compared the use of remifentanil with the use of meperidine during intravenous conscious sedation for third molar surgery.

Patients and Methods: Forty patients who were scheduled for the removal of impacted third molars were randomly assigned to undergo 1 of 2 intravenous conscious sedation techniques. For both groups, 50:50 nitrous oxide oxygen were administered via nasal hood, and midazolam was titrated to Verrill's sign. Twenty patients each then received either remifentanil 0.05 $\mu\text{g}/\text{kg}/\text{min}$ or meperidine 50 mg. Both patients and surgeons were blinded to the narcotic that was used. Blood pressure, heart rate, and oxygen saturation were determined before sedation and every 5 minutes during surgery. Recovery was measured using serial Trieger tests every 5 minutes after surgery. Patient and surgeon satisfaction of the quality of sedation was measured with a visual analog scale.

Results: Peak heart rate (91 beats/min for remifentanil vs 107 beats/min for meperidine, $P < .01$) and peak systolic blood pressure (131 mm Hg for remifentanil vs 142 mm Hg for meperidine, $P < .05$) were significantly lower for the remifentanil group. Although there was a trend toward increased surgeon satisfaction with remifentanil (86 of 100 with remifentanil vs 73 of 100 with meperidine), it was not found to be statistically significant. Likewise, other physiologic parameters were not found to be statistically significant.

Conclusions: The lower peak heart rate and systolic blood pressure levels indicate that remifentanil may allow for less fluctuation in cardiovascular parameters. This could prove beneficial in patients with cardiovascular compromise.

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Remifentanil is a short-acting narcotic that is chemically related to the fentanyl family of phenyl-piperi-

dine derivatives. Remifentanil is unique among opioids, however, in its ester linkage, which renders it susceptible to plasma and tissue esterase degradation. This provides for rapid metabolism to essentially inactive metabolites ($t_{12\alpha}$ [drug redistribution] of 3 to 6 minutes, $t_{12\beta}$ [drug elimination] of 10 to 20 minutes), which is unchanged in the presence of hepatic and renal disease.¹⁻⁴ Remifentanil pharmacokinetics do not appear to be altered by pseudocholinesterase deficiency as well, implying that other nonspecific esterases are sufficient for remifentanil metabolism.⁵ Due to its rapid metabolism, remifentanil is typically administered via infusion using a computer-programmed intravenous infusion pump, which provides consistent and readily titratable opioid delivery.^{2,6}

Remifentanil is a μ -opioid receptor agonist and is reversible with naloxone. Due to its high lipid solubility, which provides the ability to rapidly cross the blood-brain barrier, it has an extremely rapid onset of action. Renal clearance is 3 to 4 L/min, with almost

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90% of the drug being recovered in urine as an inactive metabolite.^{2,3} Clearance is also independent of body weight, gender, or age.⁴ Its analgesic potency is similar to that of fentanyl.^{1,7} For example, a 100 μ g bolus of remifentanyl provides similar analgesic and respiratory depressant effects as 100 μ g of fentanyl. Remifentanyl provides consistent reductions in heart rate, blood pressure, and oxygen consumption, even in times of major surgical stress, and does not significantly increase intracranial pressure if respiration is artificially maintained.^{8,9}

Remifentanyl has side effects similar to those of fentanyl, including respiratory depression, bradycardia, and glottic/chest wall rigidity. The latter is typically seen in patients administered bolus doses and appears to be dose dependent.³ The incidence of these side effects appears to be greater with remifentanyl than with the commonly used fentanyl, owing to the more rapid uptake of remifentanyl into the central nervous system. Caution should be exercised whenever remifentanyl is administered via bolus technique. In addition, positive pressure oxygen and advanced airway management personnel and equipment, as well as succinylcholine, should be immediately available.

Clinical Studies in Remifentanyl Anesthesia

Numerous studies have investigated the use of remifentanyl in general anesthesia, deep and conscious sedation, and postoperative pain control. During total intravenous anesthesia, an infusion of propofol combined with an infusion of remifentanyl acts as a highly effective anesthetic technique for intubated general anesthesia cases, allowing for excellent hemodynamic control intraoperatively with rapid emergence.^{10,11} Fish et al,¹⁰ however, found that although this technique was highly effective, it provided no additional benefits regarding recovery time, postoperative nausea and vomiting, induction complications, or patient satisfaction compared with the use of sevoflurane and alfentanil for maintenance.⁵ In contrast, a separate study showed that an infusion of propofol plus remifentanyl caused less postoperative nausea and vomiting than did sevoflurane plus nitrous oxide for general anesthesia.¹² Using a different technique for comparison, Song and White¹³ found that when using desflurane/nitrous oxide for maintenance of general anesthesia, the addition of an infusion of remifentanyl decreased emergence time but did not decrease postoperative nausea and vomiting compared with the use of desflurane/nitrous oxide alone.²¹

Although remifentanyl is generally administered as an infusion, Monica et al¹⁶ compared infusion delivery

with intermittent bolus delivery during monitored anesthesia care. All patients were administered midazolam 2 mg intravenously and then were placed on a propofol infusion. Groups received remifentanyl via bolus only, via infusion only, or via infusion plus boluses, of which all were titrated to patient response to stimulation. The authors found that there was no difference in vital signs between groups despite previous reports of oxygen desaturation and thoracic rigidity with bolus doses.^{3,14} Bolus doses appear to be less likely to cause oxygen desaturation if administered slowly over 30 to 60 seconds.¹⁵ Although the bolus group required more interventions (additional boluses for complaints of pain), the infusion-only group received greater doses of remifentanyl. Patient satisfaction was equal among the 3 groups, likely due to acceptable amnesia for all participants, but the mean discharge time was shorter for the bolus group and pain scores were higher for the infusion-only group. The authors' consensus was that a continuous infusion plus boluses or boluses alone may be more effective than a variable-rate infusion.¹⁶ The surgical experience chosen for the study of Monica et al¹⁶ included those in whom adequate local anesthesia of the surgical site was not obtained, and this may have led to the authors' conclusion. In office-based oral surgery practice, there are rarely times of increased surgical stimulation due to the effectiveness of local anesthesia for oral procedures. A continuous infusion technique should provide good sedation/analgesia for most dentoalveolar procedures.

Other studies that used sedation techniques show a dose-dependent decrease in midazolam based on remifentanyl dosage, a decreased incidence of pain during nerve blocks when remifentanyl is used,¹⁵ and a 50% effective remifentanyl dosage of 0.043 μ g/kg/min when combined with regional anesthesia.¹⁷ Remifentanyl appears to be a poor sedative agent when used alone, resulting in a higher incidence of anxiety than when combined with a hypnotic agent.¹⁵ In an interesting study in children aged 2 to 12 years who were undergoing deep sedation during painful procedures (bone marrow aspiration, external fixator removal), Litman¹⁸ found a high rate of respiratory depression and treatment failures (requiring the use of a second anesthetic technique). He recommended avoidance of this technique in children younger than age 5 or in those with mental impairment.¹⁸ The manufacturer (GlaxoSmithKline, Research Triangle Park, NC) has no data on use in children younger than age 2. In children of ages 2 to 12 years, the pharmacokinetics have been found to be the same as those in adults, and dosage recommendations are the same.¹⁴

These results imply that remifentanyl would be an ideal narcotic for adult ambulatory surgery, especially for office-based oral and maxillofacial surgery, where

rapid recovery and return to street fitness are desired. The present study was designed to compare remifentanil with a more commonly used narcotic, meperidine. Meperidine, which is one of the most commonly used opioids in oral surgery practice, was chosen to provide an adequate duration of activity that would be comparable to the continuous analgesia of remifentanil.

Patients and Methods

PATIENT SELECTION

Forty patients undergoing oral and maxillofacial surgery on an outpatient basis who required the extraction of at least 3 impacted third molars were enrolled after informed consent was obtained to participate in this institutional review board-approved study. All patients were American Society of Anesthesiologists I or II and aged 18 to 40 years. Exclusionary criteria included current use of benzodiazepines, antidepressants, or long-term analgesics; presence of chronic renal or hepatic disease; or a documented history of coronary artery disease. Subjects had fasted for at least 8 hours.

Subjects were randomly assigned to 1 of 2 groups: group 1, which was the midazolam plus remifentanil sedation group (20 patients) or group 2, which was the midazolam plus meperidine sedation group (20 patients).

STUDY PROTOCOL

The surgeon was blinded as to the sedation technique and did not enter the surgical suite, which was fully equipped with all emergency drugs and equipment, including the ability to provide positive pressure oxygen and endotracheal intubation if needed, until the patient was sedated, as described later.

After participants verified that they had fasted for at least 8 hours, they were escorted to the surgical suite, where a noninvasive blood pressure monitor, pulse oximeter, and pretracheal stethoscope were applied. Blood pressure, heart rate, respiratory rate, and oxygen saturation were recorded every 5 minutes. A nasal hood was placed, delivering 6 L/min of 100% oxygen. This was gradually titrated to a 50:50 oxygen/nitrous oxide combination. Intravenous access was obtained, and a slow infusion of 0.9% normal saline was started. A memory card (a picture of animal with its name printed on the bottom of the card) was shown, and the Trieger test (to assess baseline psychomotor function) was administered. At this point, the participants were divided into 2 groups.

Group 1

A continuous infusion of remifentanil (GlaxoSmith-Kline) at 0.05 $\mu\text{g}/\text{kg}/\text{min}$ via an infusion pump set

was started at the most distal site on the intravenous extension set, very close to the intravenous catheter. This was immediately followed by a 50- $\mu\text{g}/\text{kg}$ bolus of midazolam (Roche Pharmaceuticals, Nutley, NJ). The patient was observed for Verril's sign after 3 minutes. Additional 1-mg increments of midazolam were administered if needed, and Verril's sign was rechecked. After 1 minute, a Trieger test and a memory card were administered. The surgeon then entered the surgical suite and administered local anesthetic agent (standard infiltration and nerve blocks with 2% lidocaine with 1:100,000 epinephrine). After 5 minutes, the surgeon assessed local anesthesia by placing a sharp explorer between the cuspid and first premolar. Additional local anesthetic agent was administered as necessary. The surgical procedure was then begun. When the last suture was placed, the remifentanil infusion was turned off, and a Trieger test and a memory card were administered. The patient was assessed every 5 minutes for 30 minutes thereafter with a Trieger test until he or she fulfilled standard discharge criteria. If at any time during the surgical procedure the respiratory rate dropped below 8 breaths per minute as monitored via the pretracheal stethoscope, the remifentanil infusion was decreased in 0.0125 $\mu\text{g}/\text{kg}/\text{min}$ increments until the respiratory rate increased to 8 or more breaths per minute.

Group 2

The protocol was like that for group 1 with the following changes. Instead of a remifentanil infusion, two 25-mg doses of meperidine (Abbott Laboratories, North Chicago, IL) were administered 3 minutes before surgery. This was followed immediately by midazolam as administered to group 1 patients. The intraoperative and postoperative protocols were the same as for group 1 patients. To blind the surgeon and patient, an infusion pump filled with 0.9% normal saline was begun before the surgeon entered the surgical suite.

Within 10 minutes of the conclusion of the operation, the surgeon rated the quality of sedation by placing a slash mark on a visual analog scale consisting of a 100-mm line labeled "Poor Sedation" at the left side (a value of 0 was assigned) and "Excellent Sedation" on the right side (a value of 100 was assigned). Just before discharge, the patient indicated the quality of sedation using a similar scale. When the patient met discharge criteria, he or she was discharged to home with his or her escort. The patient took home a questionnaire in a self-addressed stamped envelope to be filled out the morning after surgery. The questionnaire contained a compilation of the memory cards shown and other sham cards, and the patient was asked to identify the images that he or she remembered. The patient also filled out a

second visual analog scale indicating his or her satisfaction with the quality of sedation. The questionnaire contained the following questions: 1) Do you remember the intravenous line being started in your arm? 2) Do you remember the injections of local anesthetic agent being given in your mouth? 3) Do you remember any of your operation? 4) Did you feel that the effects of the sedative drugs lingered the rest of the day after you left the oral and maxillofacial surgery clinic? and 5) Did you feel that the effects of the sedative drugs had worn off when you woke up this morning?

ANALYSIS OF DATA

Sample size determination was based on what we considered to be 2 key variables in this study: peak heart rate and surgeon satisfaction. Peak heart rate was chosen because myocardial oxygen demand is most dependent on this variable and the goal of intravenous sedation frequently is to increase the safety of oral surgical procedures in the cardiovascularly compromised population. Surgeon satisfaction was selected for evaluation because many subjective criteria frequently enter into choice of sedation technique. With an α risk of .05 and 80% power, a sample size of 20 was required to demonstrate a difference of ± 16 beats/min for heart rate and ± 20 mm on the visual analog scale for surgeon satisfaction.

Differences between groups in reported quality of sedation, Trieger test scores, and the number of memory cards identified were analyzed nonparametrically using the Wilcoxon rank sum test. Patient questionnaire answers were assessed using the Fisher Exact test. Pretreatment variables (age, gender, weight, and midazolam dose) were evaluated using the independent *t* test. The maximum change from baseline in blood pressure, heart rate, and respiratory rate, as well as the means in each of these categories, were also assessed using the independent *t* test. Results were considered significant if $P < .05$.

Results

All differences between the groups in pretreatment variables of age, gender, weight, midazolam dose, and

surgical time proved to be nonsignificant (Table 1). Between-group differences in mean heart rate, mean blood pressure, patient and surgeon satisfaction, memory cards, recovery time (Trieger tests), and questionnaire results also were all nonsignificant (Table 2). Peak heart rate did prove to be significantly lower for remifentanyl (Table 2, Fig 1), as did peak systolic blood pressure (Table 2, Fig 2). There were no patients whose respiratory rate fell below 8 breaths per minute, and there were no changes in remifentanyl infusion parameters. Only 1 patient exhibited oxygen desaturation (lowest SpO₂ of 89%). All other patients maintained SpO₂ at 98% or higher. The patient, who was in the remifentanyl group, had a weight of 110 kg and an apparent respiratory rate of 12 at the time of desaturation. It was thought that partial airway obstruction rather than a decreased respiratory drive was responsible for desaturation in this obese individual. Stimulation and a change in head position resulted in a rapid increase in saturation. Respiratory effort was always maintained.

There were no significant between-group differences in the postoperative patient questionnaire (Table 3).

Discussion

The results of the present study indicate that remifentanyl is an excellent agent for use in conscious sedation during dentoalveolar surgery. The decreases in peak heart rate and systolic blood pressure in group 1 versus group 2 are consistent with the authors' observations that remifentanyl tended to provide less variability in vital signs and a subjectively smoother sedation compared with meperidine. It should be noted that meperidine may not have as prominent an effect on decreasing heart rate as other opioids and may have contributed to the apparent difference in peak heart rate demonstrated in this study. Meperidine was, however, chosen as a comparison agent due to its longer duration of action compared with other commonly used agents, such as fentanyl. This longer duration of action was thought to provide a more comparable sedation, because

Table 1. ANALYSIS OF PRETREATMENT VARIABLES

Variable	Meperidine Group			Remifentanyl Group			P
	n	Mean	SD	n	Mean	SD	
Age (yr)	20	23.6	3.6	20	22.3	3.1	.2348
Weight (lb)	20	68.0	14.2	20	71.3	16.1	.4891
Surgery time (min)	20	39.1	24.8	20	41.4	25.7	.7796
Recovery time (min)	20	8.8	4.6	20	7.9	2.9	.4623
Midazolam dose (mg)	20	5.5	1.8	20	6.7	2.0	.0637
Gender (M/F)	7/13			8/12			.7440

Table 2. ANALYSIS OF OUTCOME VARIABLES

Variable	Meperidine Group			Remifentanil Group			P
	n	Mean	SD	n	Mean	SD	
Mean heart rate (beats/min)	20	88.8	13.4	20	79.7	17.3	.0712
Mean systolic BP (mm Hg)	20	118.9	28.5	20	120.2	15.8	.8650
Mean diastolic BP (mm Hg)	20	70.1	8.5	20	66.4	9.5	.2035
Peak heart rate (beats/min)	20	106.7	17.8	20	90.7	17.3	.0063
Peak systolic BP (mm Hg)	20	142.3	16.9	20	130.7	17.5	.0397
Peak diastolic BP (mm Hg)	20	81.7	12.2	20	75.8	13.0	.1441
Surgeon satisfaction (mm)	20	73.1	27.0	20	85.8	12.9	.1592
Patient satisfaction immediate postsurgery (mm)	20	83.5	18.0	20	84.1	16.7	.8709
Patient satisfaction next day postsurgery (mm)	20	77.3	26.2	20	86.6	12.1	.8923
Memory cards recalled	20	1.5	0.7	20	1.5	0.5	.7955
Trieger test 1	20	5.9	7.1	20	7.2	6.5	.4532
Trieger test 2	1	53.0	NA	5	55.6	55.0	NA
Trieger test 3	20	30.6	35.0	20	25.5	17.9	.6165
Trieger test 4	18	22.9	23.7	20	17.7	14.4	.9883
Trieger test 5	7	23.7	15.3	6	11.3	9.1	.1336

Abbreviations: BP, blood pressure; NA, not applicable.

remifentanil was administered via continuous infusion for the entire procedure.

Given the rapid metabolism of remifentanil, it might be expected that patients in group 1 would have less postoperative nausea and vomiting, higher patient satisfaction scores, and faster recovery times. This was not the case in the present study and is likely due to a variety of factors. All patients received narcotic oral pain medication after surgery, which could have contributed to the postoperative questionnaire reports of dizziness, drowsiness, nausea, and vomiting by both groups. The administration of nitrous oxide also has been shown to increase the incidence of nausea and vomiting.¹⁹ None of the patients in this study reported immediate postoperative nausea. Most critically, patient satisfaction is probably highly dependent on the degree of amnesia of the surgical experience, which is in large part a function of the midazolam effect³ and independent of the narcotic used.

Recovery time to discharge is in large part dependent on drug redistribution ($t_{12\alpha}$) rather than on drug elimination ($t_{12\beta}$). The redistribution half-lives of the drugs used (midazolam, 16 minutes; meperidine, 7 to 17 minutes; remifentanil, 3 to 6 minutes) are all short enough to allow for significant redistribution (and for remifentanil, elimination as well) after the mean operation time in this study of approximately 40 minutes.^{7,14,20} In this regard, remifentanil may be more beneficial in reducing recovery time and providing consistent opioid delivery during longer outpatient operations, where additional, multiple boluses of opioids would be required. This is particularly true for patients in whom adequate local anesthesia cannot be obtained.

A potential disadvantage of the rapid metabolism of remifentanil is the lack of postoperative pain control. Schraag et al¹² investigated the potential for opioid tolerance when remifentanil was used

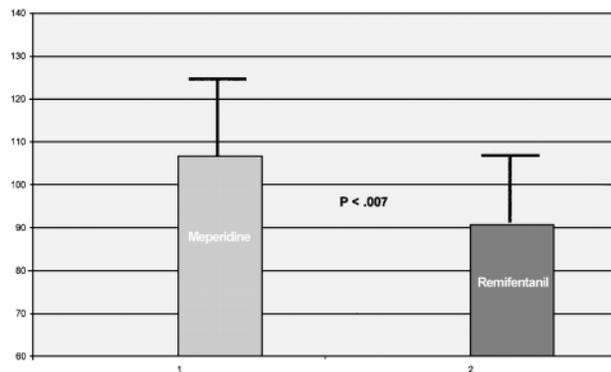


FIGURE 1. Peak heart rate (beats/min).

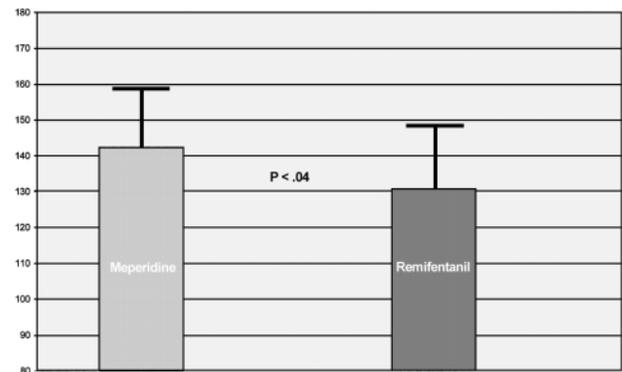


FIGURE 2. Peak systolic blood pressure (mm Hg).

Table 3. ANALYSIS OF POST-TREATMENT QUESTIONNAIRE

Question	Meperidine Group			Remifentanil Group		
	Response	n	%	n	%	P
Recall intravenous line started	Yes	20.0	100.0	19.0	95.0	1.0000
	No	0.0	0.0	1.0	5.0	
Recall local anesthetic injection	Yes	4.0	20.0	1.0	5.0	.3416
	No	16.0	80.0	19.0	95.0	
Recall surgery	Yes	17.0	85.0	14.0	70.0	.4506
	No	3.0	15.0	6.0	30.0	
Postoperative drug effects on day of surgery	Yes	11.0	55.0	7.0	35.0	.3406
	No	9.0	45.0	13.0	65.0	
Postoperative drug effects on day after surgery	Yes	18.0	90.0	17.0	85.0	1.0000
	No	2.0	10.0	3.0	15.0	

for patient-controlled analgesia in the inpatient setting. They found that tolerance did not develop in this group and that remifentanil was an effective agent for patient-controlled analgesia.¹⁹ Although this may be useful in the inpatient setting, it is obviously not practical for the patient population in the present study because the majority of dentoalveolar surgery is performed on an office-based outpatient basis. Fortunately, during dentoalveolar surgery, local anesthesia usually provides adequate pain control until oral pain medication can be administered.

Despite a reported higher incidence of bradycardia and glottic/chest wall rigidity with remifentanil, no episodes were noted in this small study.

Finally, the cost-effectiveness of remifentanil should be discussed. In the present study, the average cost per patient was \$2.70 for remifentanil and \$0.43 for meperidine. Unfortunately, remifentanil is available only as a lyophilized powder that must be reconstituted and used within 24 hours. Unless multiple cases are scheduled on the same day, there can be considerable drug waste. In addition, the initial cost of an infusion pump to deliver the remifentanil, additional syringes, and additional tubing contribute to the increased cost of remifentanil use.

Remifentanil is a highly effective narcotic that may be used in a variety of anesthetic techniques. It may provide a particular advantage during lengthy operations by providing consistent opioid delivery without concern over drug accumulation and prolonged recovery and when treating patients with cardiovascular disease such as coronary artery disease or angina, where unwanted heart rate increases or high peak systolic blood pressures are undesirable. Given its expense, however, it may not be cost-effective during routine dentoalveolar surgery compared with other available narcotics.

Conclusion

A sedation protocol consisting of midazolam plus remifentanil significantly reduced peak heart rate and peak systolic blood pressure compared with a protocol consisting of midazolam plus meperidine during conscious sedation in outpatient oral surgery.

References

1. Amin HM, Sopchak AM, Esposito BF, et al: Naloxone-induced and spontaneous reversal of depressed ventilatory responses to hypoxia during and after continuous infusion of remifentanil and alfentanil. *J Pharmacol Exp Ther* 274:34, 1995
2. Egan TD, Lemmens HJM, Fiset P, et al: The pharmacokinetics of the new short-acting opioid remifentanil (G187084B) in healthy adult male volunteers. *Anesthesiology* 79:881, 1993
3. Rosow C: Remifentanil: A unique opioid analgesic. *Anesthesiology* 79:875, 1993
4. Westmoreland CL, Hoke JF, Sebel PS, et al: Pharmacokinetics of remifentanil (G187084B) and its major metabolite (G190291) in patients undergoing elective inpatient surgery. *Anesthesiology* 79:893, 1993
5. Manullang J, Egan TD: Remifentanil's effect is not prolonged in a patient with pseudocholinesterase deficiency. *Anesth Analg* 89:529, 1999
6. Fragen RJ: Implications of the use of remifentanil on patient outcomes. *Eur J Anaesth* 12:75, 1995
7. Roche Pharmaceuticals: Product information, Versed injection USP. Nutley, NJ, Roche Pharmaceuticals, 1999
8. Minto CF, Schnider TW, Cohane RN, et al: The hemodynamic effects of remifentanil in volunteers over the age of 70. *Anesthesiology* 81:A11, 1994
9. Warner DS, Hindman BJ, Todd MM, et al: Intracranial pressure and hemodynamic effects of remifentanil versus alfentanil in patients undergoing supratentorial craniotomy. *Anesth Analg* 83:348, 1996
10. Fish WH, Hobbs AJ, Daniels MV: Comparison of sevoflurane and total intravenous anaesthesia for daycase urological surgery. *Anaesthesia* 54:1002, 1999
11. Hogue CW, Bowdle TA, O'Leary C, et al: A multicenter evaluation of total intravenous anesthesia with remifentanil and propofol for elective inpatient surgery. *Anesth Analg* 83:279, 1996
12. Schraag S, Checketts MR, Kenny GN: Lack of rapid development of opioid tolerance during alfentanil and remifentanil infusions for postoperative pain control. *Anesth Analg* 89:753, 1999

13. Song D, White PF: Remifentanil as an adjuvant during desflurane anesthesia facilitates early recovery after ambulatory surgery. *J Clin Anesth* 11:364, 1999
14. Product information, Ultiva for injection USP, Research Triangle Park, NC, Glaxo Wellcome Inc. 1996
15. Servin F, Desmots JM, Watkins WD: Remifentanil as an analgesic adjunct in local/regional anesthesia and in monitored anesthesia care. *Anesth Analg* 89:S28, 1999
16. Monica M, Rego S, Inagaki Y, et al: Remifentanil administration during monitored anesthesia care: Are intermittent boluses an effective alternative to a continuous infusion? *Anesth Analg* 88:518, 1999
17. Lauwers M, Camu F, Breivik H, et al: The safety and effectiveness of remifentanil as an adjunct sedative for regional anesthesia. *Anesth Analg* 88:134, 1999
18. Litman RS: Conscious sedation with remifentanil and midazolam during brief painful procedures in children. *Arch Pediatr Adolesc Med* 153:1085, 1999
19. Davison JK, Eckhardt WF, Perese DA: *Clinical Anesthesia Procedures of the Massachusetts General Hospital* (ed 4). Boston, MA, Little, Brown & Company, 1993, p 145
20. Product information, Demerol injection USP, Chicago, IL, Abbott Laboratories Inc, 1999