Comparison of three anesthetic techniques on emetic symptoms using sufentanil for outpatient surgery

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With the increase in surgery done in an ambulatory surgical setting, anesthetic techniques must be evolved whereby patients awaken quickly with minimal side effects and are released home with no fear of recurring anesthetic problems. An experimental study using sufentanil in three combinations of anesthetic agents in a balanced anesthetic technique is presented. Patients (N = 60) scheduled to undergo surgery in an ambulatory surgical setting were induced with sufentanil, thiobarbiturates and atracurium. They were randomly assigned to one of three groups for anesthetic maintenance: Group I (N = 18) - 67% N₂O and 33% O₂; Group II (N = 21) - 67% N₂O, 33% O₂ and droperidol 0.015 mg/kg; Group III (N = 21) - 0.7% isoflurane and 100% O₂. Advantages and disadvantages experienced with each group are discussed with special emphasis on time to awakening, time to orientation and incidence of emetic symptoms.

Because of the rising cost of health care, more surgery is being done in an ambulatory surgical setting. It is, therefore, important to have an effective anesthetic that enables quick awakening with minimal side effects. Sufentanil seems to be such an agent.

Sufentanil, a derivative of fentanyl, was first described in 1976. Its potency is five to ten times that of fentanyl, while its termination elimination half-life is shorter. Additionally, sufentanil has a faster onset of action, a shorter duration of postoperative recovery and less tendency to accumulate after repeated doses.¹

When compared to fentanyl-nitrous anesthesia during general surgery² and isoflurane - nitrous anesthesia for total hip replacement³, sufentanil was found to produce more profound postoperative analgesia and less respiratory depression.

Since its introduction, clinical trials have been done to evaluate sufentanil’s potential as a primary agent for major surgery. No published, controlled study to date has evaluated its potential as a primary agent for short surgical procedures in an ambulatory surgical setting.

One study by Williams, Weis, Adragna and Nohejl did report the use of sufentanil with nitrous oxide for short surgical procedures in a one-day surgery unit. Although sufentanil did prove to be an effective anesthetic in terms of providing a smooth induction and a rapid time to awakening, there was a high incidence of nausea and vomiting associated with its use.⁴

Nausea and vomiting are the most common reasons for delay in discharging clients from an ambulatory surgical setting. If a technique could be developed to limit the incidence of postoperative nausea and vomiting associated with sufentanil,
the new opioid could be used for varying ASA class patients while maximizing patient comfort and minimizing delay in recovery from anesthesia.

The purpose of this study is to evaluate the incidence of nausea, vomiting and retching (NVR), time to awakening and time to orientation, when sufentanil is used with particular combinations of drugs, specifically nitrous oxide, droperidol, and isoflurane.

**Methods**

This study was approved by the Research and Human Subjects Review Committee, State University of New York at Buffalo, and the Institutional Review Board, Erie County Medical Center. Subjects were selected from a convenient sample of patients scheduled for elective surgery in a one-day surgery unit at Erie County Medical Center. Only ASA Class I and II adults between the ages of 17 and 59 who were not presently taking medications known to affect nausea and vomiting were allowed to participate. Types of elective procedures were limited to arthroscopy, dental extractions and/or restorations and laparoscopy for diagnostic evaluation or tubal ligation.

Patients were questioned as to their past history of NVR associated with anesthesia and their expectation of whether they thought they would be nauseated after anesthesia. Positive responses to these questions did not prevent them from participating in the study. Subjects also were questioned about the presence of a cold or ear infection or a history of ear surgery. They were excluded from the study if their responses to these questions were positive.

After obtaining written informed consent, 60 subjects were assigned randomly to one of three groups: Group I (N=18) - 67% nitrous oxide and 33% oxygen; Group II (N=21) - 67% nitrous oxide, 33% oxygen and droperidol 0.015 mg/kg; Group III (N=21) - 0.7% isoflurane and 100% oxygen. An intravenous (IV) line with 5% dextrose in lactated Ringer's solution was started, and 500 cc were infused prior to induction.

Patients were instructed to take three maximal inspirations while 100% oxygen was delivered by mask. Sufentanil 0.0004 mg/kg, atracurium 0.4 mg/kg and thiopental or thiamylal 4.0 mg/kg were given IV in that order. Neuromuscular blockade was monitored by peripheral nerve stimulator (Ministim, model MS-1, Professional Instruments Company, Houston, TX). Inspired concentration of oxygen was monitored by an in-line oxygen monitor (Oxycheck, Model 2000, Critikon, Inc.).

Blood pressure was measured by aneroid sphygmomanometer every 30 seconds during induction and at least once every 5 minutes during surgery.

Upon loss of lid reflex, a train-of-four (T4) stimulus was elicited with the peripheral nerve stimulator and used as a baseline measurement of neuromuscular blockade. Respirations were assisted and then controlled by mask ventilation with 100% oxygen.

Once T4 was 80% depressed, the patient was intubated, and respirations were controlled by mechanical ventilator. Inhalation agents were administered according to group assignment.

Group II subjects received the calculated dose of droperidol during the surgical procedure. The concentrations of the inhalation agents, isoflurane and nitrous oxide, were chosen because they are thought to be equipotent in terms of their ability to produce analgesia and amnesia. The concentration of isoflurane is well above that believed to produce amnesia.

Anesthesia was supplemented with sufentanil 0.0001 mg/kg, if the blood pressure or pulse exceeded 20% of the baseline level. Baseline blood pressure and pulse values were defined as those taken in the preoperative holding area. Additional muscle relaxation was given in a dose of 0.1 mg/kg, if T4 exceeded 80% of control or the patient moved.

If intraoperative hypertension occurred despite supplemental narcotic administration, subjects were supplemented with isoflurane in concentrations necessary to control blood pressure.

Upon completion of surgery, muscle relaxation was reversed with edrophonium 10-50 mg and atropine 0.4-1.8 mg until T4 returned to control levels or the patient could sustain a head lift for five seconds. Once the patient was awake and breathing adequately, the trachea was extubated and the oral airway was removed.

All patients were awakened in the operating room prior to transport to the recovery room. Each patient was then transported to the recovery room and monitored according to the usual postoperative routine. Subjects were monitored continuously for postoperative emetic symptoms until the time of discharge.

Subjects were contacted by telephone 24 to 72 hours postoperatively and questioned about any NVR they may have experienced during the postoperative period. The variability in postoperative followup telephone contact was secondary to the availability of the subject at the time the investigator attempted contact. The maximum score at
any time from the time to awakening through the postoperative followup telephone call was recorded as the emetic score.

Emetic symptoms were scored using a method similar to that described by Bellville in 1959:6

0 = no nausea, retching/gagging or vomiting from the time of awakening until the time of followup telephone contact.

1 = nausea only, from the time of awakening until the time of followup telephone contact.

2 = nausea and retching/gagging from the time of awakening until the time of followup telephone contact.

3 = vomiting with or without nausea from the time of awakening until the time of followup telephone contact.

The Statistical Package for the Social Sciences was used in analyzing data.7 One-way analysis of variance (ANOVA) was used to test the significance of variance between the three groups in terms of emetic score, time to awakening and time to orientation. If a significant difference among the three groups was found with respect to the three dependent variables, the Tukey Honestly Significant Difference (HSD) procedure was used to specify the difference between group means.

Results

ANOVA showed that the three groups did not differ in terms of sex, age, number of fasting hours, percentage of ideal body weight and dose of atropine received at the end of the case.

Time to awakening. ANOVA demonstrated a significant difference in mean time to awakening among the three groups (Table I). The Tukey HSD procedure showed a significant difference in mean time to awakening in Group III, when compared to Group I and Group II. While mean time to awakening was significantly shorter in Group I when compared to Group III, it was not shorter in Group I, when compared to Group II. Mean time to awakening was significantly longer in Group III, but only 5.5 minutes from the time the isoflurane was discontinued.

Emetic score. Variance in emetic score was shown to be significant with respect to Group I, when compared to Group II and Group III. The incidence of NVR was greater in Group I (66.7%), when compared to Group II (28.6%) or Group III (9.6%) (Table 2).

One assumption of the emetic scale used is that vomiting is less desirable than nausea, gagging or retching; this is not necessarily so. If subjects were given the choice of experiencing one episode of vomiting rather than 12 hours of nausea, undoubtedly the former would be chosen. For this

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( ) = percentage of population in each group

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<td>Frequency distribution: Modified emetic score by group</td>
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( ) = percentage of population in each group
reason, the emetic symptoms were equal to a score of 1 and no emetic symptoms were equal to 0.

ANOVA was used to test variance of mean scores. The results of the modified score were the same as the original method of scoring; a significant difference was found only with respect to Group I, when compared with Group II and Group III. The frequency distributions of emetic scores and incidence of emetic symptoms, using both the original and the modified scoring methods, are shown in Tables II and III, respectively.

Discussion

Emetic symptoms. This study evaluated the incidence of emetic symptoms, time to awakening and time to orientation when sufentanil was used with three different combinations of adjunctive agents in a balanced anesthetic technique.

The results of this study concur with those found by Williams et al. in terms of a higher incidence of emetic symptoms associated with sufentanil when used with nitrous oxide, oxygen and a muscle relaxant. In that study, investigators found a 54% incidence of nausea and a 44% incidence of vomiting when sufentanil was used with the above combination of adjunctive agents.

While the emetic symptoms were not evaluated identically, this study showed emetic symptoms occurring in 66.7% of subjects using the identical combination of agents (Group I). The high incidence of emetic symptoms was significantly lowered by the use of either low-dose droperidol (0.015 mg/kg) or the elimination of nitrous oxide.

In a study designed to demonstrate the role of nitrous oxide in postoperative emetic symptoms, Alexander, Skupski and Brown found a threefold increase in the incidence of nausea and vomiting (61%) in a group maintained with nitrous oxide and fentanyl, compared to a group maintained with isoflurane and fentanyl. It should be noted, however, that in this study the group with the highest incidence of nausea and vomiting had nearly twice as many subjects as the other groups.

In a study measuring middle ear pressure during nitrous oxide-oxygen anesthesia, Perreault et al. showed increases in middle ear pressure 30 minutes following induction with 66%, nitrous oxide and 33% oxygen. Alexander postulates that this may explain the high incidence of emetic symptoms associated with the use of nitrous oxide.

The incidence of NVR was greatest in Group I. While there was no significant difference in mean emetic scores between Group II and Group III, this sample may have been to small for it to be evidenced.

In Groups I and II, two subjects were asymptomatic throughout the hospitalized postoperative period but vomited while traveling home. In Group III, the only subject experiencing vomiting did so only once while getting up to the bathroom. There were no further emetic symptoms. This seems to support Bellville's postulate that opiates sensitize the vestibular apparatus causing postoperative movements to have an important influence on the frequency of opiate-induced emesis. No attempt was made to control for patient movement in this study.

Five subjects in Group III who had a prior history of NVR associated with anesthesia were asymptomatic during their postoperative course. This also was true for two subjects in each of the other two groups.

Time to awakening and orientation. In order to control postoperative emetic symptoms associated with the use of perioperative opiates, it has become practice to combine the narcotic with a long-acting antiemetic. The use of the butyrophenone droperidol as such a prophylactic agent has been widely investigated and reported. One concern with the use of the drug is its effect on postoperative recovery time. In a double-blind study, O'Donovan and Shaw showed ultra-low-dose droperidol (0.25 mg) to be an effective antinauseant that did not prolong recovery time. Interestingly, in the same study they found a larger dose of droperidol (1.25 mg) to be less effective as an antinauseant and to produce a slight delay in recovery time.

Wetchler, Collins and Jacob found a statistically significant reduction in postoperative emetic symptoms in patients given 0.625-1.25 mg of droperidol intra-anesthetically or 0.625 mg given at the onset of symptoms, when compared to a control group. Additionally, recovery time was not prolonged in either group receiving droperidol; recovery time was prolonged for those experiencing emetic symptoms.

Korntila, Kauste and Auvinen found droperidol 1.25 mg, administered intra-anesthetically to be more effective than domperidone or metoclopramide; time to eye opening was delayed in the droperidol group.

In this study, time to awakening was defined as the amount of time from discontinuation of the inhalation agent to the time the patient opened his/her eyes in response to verbal or auditory stimulation. Time to orientation was defined as the amount of time from discontinuation of the inhalation agent to the time the patient could state his/her environment correctly. Both time to awak-
ening and time to orientation were shortest in the group receiving an intra-anesthetic dose of droperidol (Group II).

Although time to ambulation and discharge were not measured in this study, it would be interesting to see these parameters measured in a future, similarly designed study. Clinically, there was no delay in ambulation or readiness for discharge in Group III compared with Groups I or II.

Other clinical observations. The most common postoperative symptoms elicited by subjects who received intra-anesthetic droperidol (Group II) were dizziness (N=4) and drowsiness (N=3). Subjects in Group II appeared more drowsy in the postoperative hospitalized period than subjects in either of the other two groups. Followup contact with subjects in Group II revealed most continued to sleep well into the postoperative period at home.

No subject in either Group I or Group III complained of postoperative drowsiness or dizziness.

Summary
There was a statistically significant high incidence of NVR when sufentanil was used in combination with nitrous oxide and muscle relaxant in a balanced anesthetic technique. This incidence was significantly lowered either by use of low-dose droperidol or by eliminating nitrous oxide and using isoflurane for amnesia and analgesia.

While there is a slower time to awakening and orientation when isoflurane is used instead of low-dose droperidol, the authors do not feel this was clinically significant in terms of patients' readiness for discharge. Since the termination of this study, Group III protocol has become essentially standard procedure for outpatient anesthesia by the authors.

REFERENCES

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