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Effects of fentanyl on emergence characteristics from anesthesia in adult cervical spine surgery: a comparison of fentanyl-based and sevoflurane-based anesthesia

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Abstract
Purpose. To evaluate the effects of different anesthesia regimens on bucking, awareness, and pain during the emergence from anesthesia, which may affect neck stabilization and neurological assessment immediately after cervical spine surgery.
Methods. Patients scheduled to undergo cervical spine surgery were assigned randomly into one of three groups: maintenance of anesthesia with fentanyl and propofol TCI (group FP, $n = 25$); maintenance with fentanyl and supplementation with less than 1% sevoflurane (group Fs, $n = 25$); and maintenance solely with sevoflurane (group S, $n = 25$). The severity of bucking, extent of awareness during neurological examination, and perception of pain during the emergence phase were assessed using predetermined scoring scales by a nurse blinded to the method of anesthesia.
Results. The bucking score and pain score were significantly better in group FP and group Fs than in the group S, whereas there was no significant difference between the data of group FP and group Fs.
Conclusion. The quality of emergence from anesthesia in patients with cervical spine surgery is improved with fentanyl-based anesthesia, but there is no difference between the use of propofol TCI and less than 1% sevoflurane as a concomitant sedative agent with fentanyl.

Key words Quality of emergence · Cervical spine surgery · Fentanyl · Anesthesia regimen

Introduction

Smooth emergence from anesthesia without hazardous coughing/bucking is ideal in terms of neck stabilization in patients undergoing cervical spine surgery. Moreover, rapid transition to consciousness without agitation is also desirable because it facilitates neurological examination immediately after operation to exclude surgical failure or possible hematoma formation.

Sevoflurane is employed in a wide range of clinical practice, because its low blood-gas partition coefficient facilitates rapid emergence from anesthesia. However, rapid recovery from sevoflurane is sometimes associated with a greater incidence of emergence agitation or excitatory behavior [1,2], which may entail risks of unexpected events for the cervical spine and could disturb subsequent postoperative neurological examinations. Several studies have suggested that postoperative restlessness and agitation are mainly caused by pain during the emergence period [3,4], and that the concomitant use of an opioid provides smoother anesthetic management.

On the other hand, an intravenous anesthetic propofol might allow anesthesiologists to achieve a smoother recovery profile by reducing coughing/bucking or excitatory behavior [5]. The target controlled infusion (TCI) system was recently introduced in clinical practice [6,7]. This technique facilitates easy titration of the depth of anesthesia with propofol and has therefore become an attractive option as an anesthesia regimen [8] that might improve the quality of emergence from anesthesia.

The present randomized prospective study was designed to evaluate the properties of sevoflurane-based and fentanyl-based anesthesia regimens, in combination with supplemental hypnotic propofol or a low-concentration sevoflurane, with respect to the quality of emergence from anesthesia, which is especially of clinical importance in cervical spine surgery in adult patients.

Materials and methods

After obtaining institutional review board approval, 75 patients with American Society of Anesthesiologists

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Table 1. Type of cervical spine disease and performed operation

Preoperative diagnosis	
Cervical spine trauma	10
Cervical spondylotic myelopathy	37
Ossification of the cervical posterior longitudinal ligament	11
Cervical soft disk hernia	4
Atlantoaxial subluxation	5
Syringomyelia	5
Cervical spondylotic radiculopathy	3
Performed operation	
Anterior approach	31
Posterior approach	40
One-stage anterior and posterior approach	4

Data are numbers of patients

physical status 1 or 2 who were scheduled to undergo cervical spine surgery were enrolled in this study. Written informed consent was obtained from all subjects before commencement of the study. Preoperative diagnoses and operations performed are listed in Table 1. Patients were randomly assigned into one of three groups: (i) maintenance of anesthesia with fentanyl and propofol TCI (group FP, $n = 25$); (ii) maintenance mainly with fentanyl with supplementary sevoflurane (group Fs, $n = 25$); and (iii) maintenance solely with sevoflurane (group S, $n = 25$). Patients in all three groups were premedicated with 25 mg hydroxyzine and 0.5 mg atropine sulfate intramuscularly 30 min before arriving to the operating room.

For patients assigned to the group FP, both intermittent fentanyl 50-μg boluses and propofol TCI (typically 1.5–3.5 μg/ml) using the Terfusion TCI pump (TE-371; Terumo, Tokyo, Japan) were titrated against clinical signs in induction and maintenance of anesthesia. Patients assigned to the group Fs were induced with 100 μg fentanyl and propofol 1–2 mg/kg intravenously. Anesthesia was maintained with incremental intermittent fentanyl 50-μg boluses in combination with supplemental inhaled sevoflurane at less than 1% (0.5%–1.0% end-tidal). Patients assigned to the group S were induced with 100 μg fentanyl and propofol 1–2 mg/kg intravenously. Anesthesia was maintained solely with sevoflurane (typically 1.5%–2.5%, end-tidal).

In all groups, vecuronium was administered to facilitate tracheal intubation, and incremental doses were subsequently added according to the surgical requirement. Nitrous oxide 60% in 40% oxygen was also administered during maintenance of anesthesia. Standard respiratory and cardiovascular monitoring consisted of continuous ECG, pulse oximetry, end-tidal CO_2, and intermittent (2.5-min interval) noninvasive blood pressure measurement. A certified anesthesiologist (Y.I.) was in charge of anesthetic management in all patients, and anesthetic depth was titrated mainly with blood pressure and heart rate according to the anesthesia protocol regimens.

At the completion of dressing of the surgical field, anesthetic agents were discontinued and the patients were returned to a spine-neutral position. When sufficient spontaneous respiration, bucking, or involuntary movement emerged without any stimulations or drugs for reversal, and the patients were deemed ready for extubation by the investigator, they were encouraged by a verbal command to squeeze their fingers and wiggle their feet as neurological examinations. At that time, the severity of bucking and the extent of awareness and readiness for the neurological examination were assessed using a predetermined scoring scale by a nurse observer blinded to the method of anesthesia. The scores were three-point scales as follows: bucking score: 1 = no bucking, 2 = controllable with light restraint, 3 = uncontrollable without heavy restraint; and awareness score: 1 = able to respond smoothly, 2 = unable to respond without a disturbing loud verbal command and mild prodding, 3 = unable to respond to a loud verbal command and mild prodding.

Subsequently, tracheal extubation was performed and the perception of pain was assessed when the patient became alert by the same interviewing nurse using a five-point verbal descriptor score: 1 = no pain, 2 = weak pain, 3 = tolerable moderate pain, 4 = intolerable strong pain, 5 = very strong pain with agitation. Administration of 50 mg flurbiprofen axetil intravenously and 50 μg fentanyl intramuscularly was considered immediately after the evaluation as rescue analgesics. The time to extubation, defined as the duration between the completion of dressing of the surgical field and tracheal extubation, was recorded.

Postoperative assessment by patient interview, including nausea and vomiting during the first 24-h postoperative period and amnesia in the operating room, was performed on postoperative day 1.

Demographic continuous data were expressed as mean ± SD, and the data were analyzed using one-factor analysis of variance for three group-data sets, or the unpaired Student's t test for two group-data sets. Nominal data were analyzed using the χ^2 contingency table. The time to extubation, bucking scores, awareness scores, and pain scores were analyzed using the Mann–Whitney's U tests with Bonferroni's correction. $P < 0.05$ was considered statistically significant.

Results

There were no differences among FP, Fs, and S groups with respect to age, gender, weight, and duration of surgery. The total amount of fentanyl used in the FP and Fs groups was similar (Table 2).

Table 2. Patient demographics

	Group FP ($n = 25$)	Group Fs ($n = 25$)	Group S ($n = 25$)
Gender (M/F)	18 / 7	16 / 9	19 / 6
Age (years)	55 ± 18	60 ± 16	59 ± 13
Body weight (kg)	62 ± 12	57 ± 11	63 ± 10
Duration of surgery (min)	114 ± 57	127 ± 58	112 ± 62
Total dose of fentanyl (μg)	276 ± 88	280 ± 92	100 ± 0

Data are mean ± SD or numbers of patients
FP, anesthesia with fentanyl and propofol; Fs, fentanyl supplemented with less than 1% sevoflurane; S, sevoflurane only

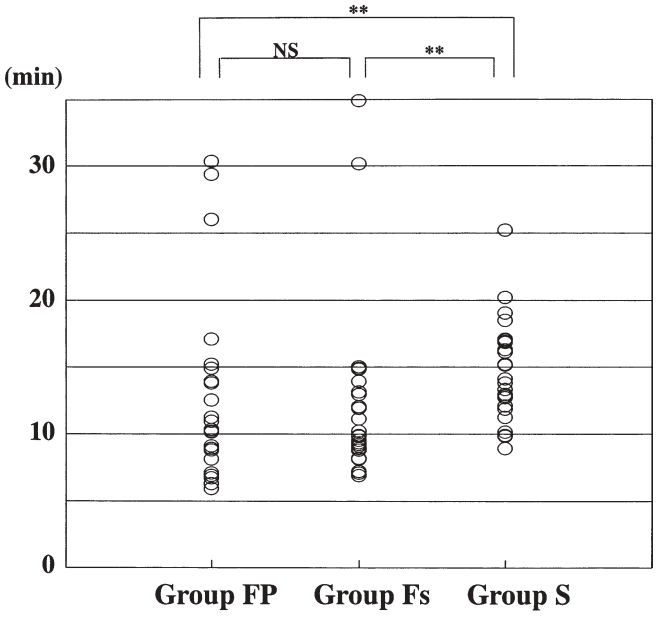

Fig. 1. Time to extubation. The mean time to extubation was longer in group S (sevoflurane only) compared with that in groups FP (fentanyl and propofol) and Fs (supplementary sevoflurane) (**$P < 0.01$), whereas it tended to be more variable in groups FP and Fs. *NS*, not significant

The median time to extubation was longer in group S than in groups FP and Fs ($P < 0.01$). However, five patients in group FP and Fs needed more than 25 min before extubation (Fig. 1). The bucking score was better in the groups FP and Fs than the group S ($P < 0.05$) (Fig. 2). The awareness score for neurological examination was similar in all three groups. More than 60% of patients in each group responded smoothly to a verbal command for neurological examination, and one and two patients of groups S and Fs, respectively, could not be assessed neurologically due to insufficient level of consciousness or agitation. The pain score was better in the groups FP and Fs than the group S ($P < 0.01$) (Fig. 3).

All 15 patients in whom the pain score was 4 or 5 were treated with 50 mg flurbiprofen axetil intravenously, and in 9 of these 15 patients, an additional 50 μg fentanyl was injected intramuscularly as rescue analgesic in the operating room.

There were no light anesthesia responses such as hazardous involuntary movements, bucking, or awareness during surgery.

The reported incidence of nausea and vomiting during the first 24-h postoperative period was 24%, 36%, and 28% in groups FP, Fs, and S, respectively, which was not significantly different between the groups.

Discussion

We demonstrated in the present study that the bucking scores and pain scores were better in groups FP and Fs than group S, but not different between groups FP and Fs. These findings imply that the quality of emergence from anesthesia after cervical spine surgery was improved with fentanyl-based anesthesia and that there was no difference between propofol TCI and less than 1% sevoflurane as an adjunct sedative agent with fentanyl.

Many of the previous studies that reported the profile of emergence from anesthesia were designed to compare the preference for ambulatory surgery [9–12] or agitation in pediatric patients [3,4]. In contrast, in our study, we focused as an endpoint on the emergence period from anesthesia to specifically delineate the profile in cervical spine surgery that facilitates cervical stability and swift neurological examination to exclude surgical failure or potential dangerous hematoma formation.

Several studies have reported that postoperative restlessness and agitation could be effectively treated with analgesics [3,4]. Our data also strongly support that opioids presumably play an important role in ensuring smooth emergence from anesthesia. As opioids block noxious stimuli not only from the surgical field [13] but also from the tracheal tube, we consider that appropriate intraoperative use of fentanyl could improve both the pain score and the bucking score in the FP and Fs groups.

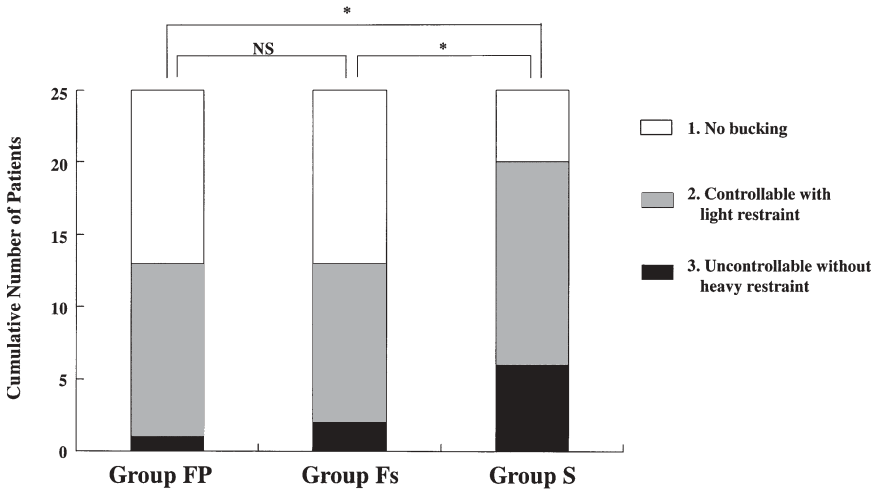

Fig. 2. Bucking score. The bucking score was better (lower) in group FP and group Fs compared with that in group S (*$P <$ 0.05)

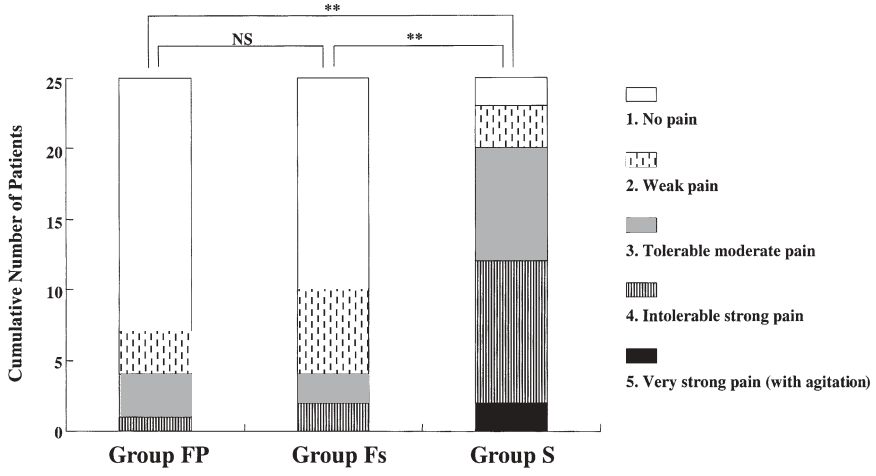

Fig. 3. Pain score. The pain score was superior (lower) in group FP and group Fs compared with that in group S (**$P <$ 0.01)

We retrospectively calculated the effective site concentrations of fentanyl with a three-compartment model using the computer program Palmakokinetics (http://homepage1.nifty.com/o-uchida/palmacokinetics/index-j.htm). Fentanyl concentrations at the end of surgery were 0.90 ± 0.35 and 0.89 ± 0.31 ng/ml in group FP and group Fs, respectively. Although the level of concomitant hypnotic agent might affect intraoperative fentanyl requirements [14], our findings suggest that these dosages and concentrations of fentanyl are recommended to improve emergence characteristics in cervical spine surgery.

With respect to postoperative nausea and vomiting, our data did not demonstrate a significant difference among the three groups. A power analysis indicated that 228 patients in each group would be required to detect a difference at $\alpha = 0.05$ and $\beta = 0.20$ (power = 0.80). In our cases, administration of additional opioid for pain management during the postoperative period was routinely considered, which might have partially affected the data. Our clinical impression was that intraoperative opioid administration is advantageous with respect to the emergence profile, despite being a possible causative factor for postoperative nausea and vomiting, which may interfere with cervical stability, and the antiemetic effect of intraoperative use of propofol [15] is not reliable in the postoperative period.

The affordability of anesthetic agents may influence their usage. Remifentanil and an α_2-agonist (e.g., dexmedetomidine) would be expected to produce a more ideal profile for the emergence period of anesthesia with their reported attractive characteristics [16–18]. However, remifentanil is not yet commercially available and dexmedetomidine is not approved for intraoperative use in Japan. Future studies are expected to reveal the usefulness of these drugs in cervical spine surgery.

In conclusion, for optimal emergence phase in adult cervical spine surgery, a fentanyl-based anesthesia regimen with propofol or sevoflurane appears to be advantageous over sevoflurane-based anesthesia. Our results

indicated no difference between propofol and sevoflurane as hypnotic adjuncts to fentanyl.

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