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Comparative study of emergence agitation between isoflurane and propofol anesthesia in adults after closed reduction of distal radius fracture

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ABSTRACT. Distal radius fracture is a common wound. It is reduced by surgery under anesthesia. Emergence agitation can often occur after anesthesia. It is associated with increased morbidity and hospital costs. However, there have been almost no reports in the medical literature on the occurrence of emergence agitation in adults. This study aimed to compare emergence agitation between isoflurane and propofol anesthesia in adults after closed reduction of distal radius fracture. Forty adults (ASA I-II) undergoing closed reduction of distal radius fracture were randomly assigned to either the isoflurane or propofol group and anesthesia was maintained with isoflurane or propofol. The bispectral index was monitored and maintained within 40-60. After reduction of fracture and fixation with plaster, patients were transported to the post-anesthetic care unit (PACU) and agitation state scale was checked by Aono's four-point scale (AFPS). AFPS score of 3 or 4 was considered to be emergence agitation. Pain scores were measured by the numeric rating scale (NRS) on arrival and at peak value at PACU. Eight

(40.0%) patients in the isoflurane group and 2 (10.0%) patients in the propofol group developed emergence agitation (P = 0.031). There was no correlation between peak NRS and AFPS. Propofol may decrease the incidence of emergence agitation compared to isoflurane in adults undergoing closed reduction of distal radius fracture.

Key words: Adult; Emergence agitation; Propofol; Isoflurane

INTRODUCTION

Closed reduction of distal radius fracture, which can cause intense pain, is performed under general anesthesia, despite it being a short surgery. Due to the short surgery time, it is preferable to use an anesthetic with rapid emergence. Isoflurane is a kind of inhaled anesthesia drug that produces rapid anesthesia and emergence from general anesthesia, and it has a slight muscle relaxing action. Thus, it is often used in short surgeries, and pediatric patients are particularly known to have a higher incidence of emergence agitation (Singh et al., 2012). Propofol also has rapid anesthesia induction and emergence from general anesthesia. Moreover, it causes a lower incidence of emergence agitation when anesthesia is maintained through intravenous administration compared to other inhaled anesthesia (Uezono et al., 2000).

Emergence agitation can often occur after anesthesia and can increase the risk of falling, bleeding, self-extubation, and removal of endotracheal tubes, and there is the need for continuous monitoring of patients by recovery room staffs and treatments such as drug administration or physical restraint of the patient (Lepouse et al., 2006). However, there are little data on these patients. Therefore, in adult patients scheduled for closed reduction of distal radius fracture, with the most common general anesthesia, we compared the incidence and degree of emergence agitation with isoflurane and propofol in this study.

MATERIAL AND METHODS

This study was approved by the Institutional Review Board of the hospital, and the purpose and method were explained to the patient and guardian prior to surgery to obtain informed consent. The study was conducted on 40 adult patients aged 25-65 years in American Society of Anesthesiologists (ASA) class I or II who were scheduled for closed reduction of distal radius fracture. Patients with signs or symptoms of heart diseases, open fracture of wrist, local infection of wrist, and administered medication for psychiatric diseases were excluded from the study. Using the table of random sampling numbers, the patients were randomly assigned to receive isoflurane (group I) or propofol (group P). A medical attendant was unaware of the grouping of the patients and evaluated each patient's response in recovering from anesthesia in the recovery room.

All patients were transported to the operating room before reduction and they were reminded that there would be discomfort from reduction. All patients had the following monitoring devices attached: electrocardiography, noninvasive blood pressure, pulse oximetry monitor, and bispectral index (BIS). While patients were being administered 100% oxygen through a face mask, they received fentanyl 1 μg/kg by *iv* injection. For the purpose of group comparison, patients in group I received thiopental 5 mg/kg by *iv* injection and group P received propofol 2 mg/kg by *iv* injection. Both groups of patients received succinylcholine 1

mg/kg by *iv* injection. After fasciculation had passed, manual ventilation was continued. At start, inhalation isoflurane concentration was 0.5 vol%. After 7 to 10 min, patients were in a general anesthesia state, which was maintained by increasing isoflurane concentration to 1.5 vol% or by continuous injection of propofol at 200 $\mu g \cdot kg^{-1} \cdot min^{-1}$, according to group until the BIS level reached 60. After BIS reached 60, endotracheal intubation was performed, and anesthesia was then maintained by controlling the concentration of sevoflurane and the injection speed of propofol, so the BIS value remained 40-60. Respiration rate and tidal volume were controlled so end-tidal CO_2 concentration was maintained at 30-34 mmHg, and 2 L/min nitrous oxide and oxygen was administered in a 1:1 ratio as inhalation gas. Additional opioids were not used during surgery in any of the patients, and when blood pressure showed a difference of more than ±20% from baseline levels, labetalol or ephedrine was injected *iv* for adjustment. All patients underwent closed reduction and fixation with plaster. After the completion of surgery when the operating surgeon attached plaster, all anesthesia was ceased and 100% oxygen was administered to all patients. An anesthesiologist was assigned to observe each patient, and found that spontaneous respiration and muscle strength of the patient recovered sufficiently to answer questions and that the patient's eyes had opened. The endotracheal tube was then removed and the patient was transported to the recovery room.

When the patients were able to describe their feelings, the medical attendant carefully recorded the patients' state. The degree of emergence agitation of the patient was measured using Aono's four-point scale (AFPS; Table 1). The degree of pain was determined by a numeric rating scale (NRS) (0 = no pain, 10 = unimaginably severe pain). The measurements aimed to obtain the peak of NRS and AFPS scores. Furthermore, the exposure time to anesthetics, surgery time, time from end of surgery to extubation, and duration of emergence agitation were investigated. When patients' NRS score was higher than 3, 25 µg fentanyl was administered *iv*, recording the total amount. When emergence agitation continued for more than 3 min, the patient received 10 mg nalbuphine *iv*. When emergence agitation continued for more than 1 min after drug administration, patients received 10 mg nalbuphine injected *iv*, repeatedly.

Table 1. Aono's four-point scale.

Calm	1
Not calm, but could be easily calmed	2
Moderately agitated or restless	3
Combative, excited, disoriented	4

Occurrence of complications or side effects was monitored during recovery, for example, nausea, vomiting, tremors, hypersalivation, and malignant fever. Once finding symptoms of nausea or vomiting, the patient received ramosetron 0.3 mg *iv*; pethidine 25 mg was administered *iv* to patients if they experienced tremors. Emergence agitation was defined as an AFPS score of 3 or higher (Aono et al., 1997). When the patient was hemodynamically stable, with autonomous respiration and maintained oxygen saturation greater than 95%, the patient was transported to the ward, and the duration of stay in the recovery room was recorded.

Data are reported as means ± standard deviation, and SPSS version 12.0 was used for statistical analysis. The *t*-test was used in the analysis of parametric data between the 2 groups, and the Mann-Whitney U-test was used for non-parametric data. In the case of categorical

data, the chi-square test was used, and the Fisher exact test was used when necessary. Spearman correlation was used to analyze the correlation between patient's pain and emergence agitation. Findings were considered to be statistically significant when $P < 0.05$.

RESULTS

There were no statistically significant differences in the demographic and perioperative data of the 2 groups. NRS scores in the recovery room and the administered amount of fentanyl showed no statistically significant differences between the 2 groups (Table 2).

Table 2. Demographic and perioperative data.

	Group I (N = 20)	Group P (N = 20)
Age (years)	50.00 ± 2.28	50.50 ± 2.40
Gender (male/female)	4/16	5/15
Height (cm)	160.03 ± 1.63	159.95 ± 1.84
Weight (kg)	68.60 ± 1.47	67.93 ± 1.81
Duration of surgery (min)	10.28 ± 1.57	10.24 ± 1.19
Duration of anesthetic exposure (min)	16.85 ± 1.64	16.25 ± 1.31
Time from end of surgery to extubation (min)	10.21 ± 1.07	10.35 ± 1.12
Time to discharge from PACU (min)	22.00 ± 2.22	23.30 ± 1.58
Duration of agitation (min)	0.98 ± 0.25	0.85 ± 0.36
Peak NRS	4.10 ± 0.38	4.70 ± 0.43
Total amount of fentanyl in the PACU (μg)	25.00 ± 6.54	32.95 ± 6.90

Data are reported as means ± SD. Group I = isoflurane group; Group P = propofol group; PACU = post-anesthetic care unit; NRS = numeric rating scale: 0 (no pain) to 10 (unimaginably severe pain).

Emergence agitation occurred in 8 patients in group I (40.0%), and 2 patients in group P (10.0%), so the incidence of emergence agitation was higher in group I ($P = 0.031$) (Table 3).

Table 3. Postoperative Aono's four-point scale, agitation.

	Group I (N = 20)	Group P (N = 20)
Aono's four-point scale		
1	1 (5.0%)	14 (70.0%)
2	11 (55.0%)	4 (20.0%)
3	6 (30%)	2 (10.0%)
4	2 (10.0%)	0 (0.0%)
Emergence agitation		
3 + 4	8 (40.0%)*	2 (10.0%)

Values are number of patients. Aono's four-point scale 3 or 4 are considered as emergence agitation. Group I = isoflurane group; Group P = propofol group; *$P < 0.05$ compared with group P.

There were no differences observed in the incidence of severe emergence agitation, defined as an AFPS score of 4. There was no correlation between peak NRS and AFPS score, and there was one patient who displayed vomiting in group P. There were two patients who felt sick and one patient displayed tremors in group I (Table 4).

Table 4. Postoperative complication and side effects.

	Group I (N = 20)	Group P (N = 20)
Vomit	0	1
Nausea	2	0
Tremors	1	0
Hypersalivation	0	0
Malignant fever	0	0

Group I = isoflurane group; Group P = propofol group.

DISCUSSION

Emergence agitation often occurs temporarily in the process of emerging from anesthesia. The incidence of emergence agitation in adults is lower than in pediatric patients, so little research has been done on adults. However, the occurrence of emergence agitation in adults results in a greater possibility of injury, and medical staff may not be able to restrain the agitation. Thus, the study was conducted since problems can arise in the safety of both the patient and the medical staff.

The incidence of emergence agitation in adults differs according to the investigator. Yu et al. (2010) reported 21.3% and Radtke et al. (2010), 5%, whereas in our study, it was 20%. The difference in incidence of emergence agitation according to investigator is considered to be due to differences in criteria or differences in the standards used to define emergence agitation, where AFPS, Riker Sedation-Agitation Scale, Richmond Agitation-Sedation Scale, or personally categorized criteria have been used. Yu et al. (2010) found that the incidence of emergence agitation was lower in the group that received *iv* anesthetics than the group that received sevoflurane. In our study, the propofol group had a lower incidence of emergence agitation compared to the sevoflurane group.

Isoflurane is a widely used drug because it has low blood-gas solubility, fast inducement of and recovery from anesthesia, and a pleasant smell. In addition, it shows high cardiovascular stability. However, there are reports demonstrating that isoflurane has a higher rate of emergence agitation compared to other anesthetics (Mendel et al., 1995; Jindal et al., 2012). In our study, group I also exhibited a higher incidence of emergence agitation. There were two mechanisms accounting for the emergence agitation in patients who had undergone anesthesia with isoflurane. The first theory is that emergence agitation occurs due to the changes and relationship of gamma-aminobutyric acid A receptors in the central nervous system, and in the model of Sachedev and Kruck, the mechanism of excitement is explained as resulting from decreased inhibitory signals from the globus pallidus interna and substantia nigra, and the inability to suppress thalamocortical neurons and brain stem neurons due to disorder in the nervous system (Lindenmayer, 2000). Another explanation proposed by Meyer et al. (2007) is that the cause of emergence agitation results from the difference in recovery speed within the nervous system, increasing the sensitivity to stimulation from the surrounding environment and creating a state of functional dissociation.

Propofol is another drug with a rapid recovery time from general anesthesia as the patient emerges when the blood concentration decreases to less than 50% and it is an *iv* anesthetic with rapid excretion through the kidneys. It results in a smooth recovery (Huddy, 2010) with a remaining sedative effect in the early stages of emergence and euphoria caused by the drug (Parbrook et al., 1989). Thus, in contrast to isoflurane, propofol does not have a

high incidence of emergence agitation in pediatric patients (Meyer et al., 2007). Compared to inhalation anesthetics, propofol has a decreased occurrence of nausea and vomiting, and characteristically has a lower occurrence of hangover. This is considered to be related to the reduction in occurrence of emergence agitation.

Some studies have suggested that postoperative pain can be a risk factor related to emergence agitation (Yu et al., 2010), and there are also numerous reports suggesting that there is no relationship between pain control and emergence agitation (Zhao et al., 2012). Our study confirmed the latter, as there was no correlation between the patient's NRS score and AFPS score and no significant difference in the amount of fentanyl administered between the 2 groups.

Previous studies have reported methods to prevent emergence agitation, such as administration of propofol, ketamine or dexmedetomidine. Besides, there are reports showing that fentanyl, nalbuphine, midazolam, and lidocaine are effective in reducing emergence agitation (Galinkin et al., 2000; Cohen et al., 2001; Dalens et al., 2006; Kim et al., 2011; Seo et al., 2011). In our study, nalbuphine 10 mg was to be administered *iv* when a state of emergence agitation continued for more than 3 min, which if necessary, could be used again after 3 h. However, the state of emergence agitation in both groups only lasted about 1 min, so additional administration of medication was unnecessary. A total of 24 patients reported an NRS score of 3 or higher; in these cases, fentanyl was administered *iv* to the patients.

A limitation of this study is that we did not measure the patient's degree of anxiety before surgery. Lepouse et al. (2006) reported that preoperative anxiety was a risk factor for emergence agitation, and in the research of Kain et al. (2004), preoperative anxiety was related to delirium or changes in behavior after surgery.

In conclusion, the incidence of emergence agitation in adult patients who underwent closed reduction of distal radius fracture was lower in the group that had general anesthesia using propofol than in the group that received isoflurane. There was no correlation between postoperative pain and severity of emergence agitation. However, there is the need for further research on patients undergoing other surgeries to confirm whether propofol can reduce the incidence of emergence agitation in adult patients.

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