Original Article

Risk Factors of Emergence Agitation in Adults Undergoing General Anesthesia for Nasal Surgery

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Objectives. To identify the incidence and the risk factors of emergence agitation in adults undergoing general anesthesia for nasal surgery.

Methods. We retrospectively examined 792 patients aged ≥18 years who underwent general anesthesia for elective nasal surgery between July 2012 and August 2013. Patients in the postanesthesia care unit with a Richmond Agitation Sedation Scale ≥+1 at any time were considered to have emergence agitation.

Results. The overall incidence of emergence agitation is 22.2%. From multivariate regression analysis, the following six variables were found to be significantly associated with emergence agitation ($P<0.05$): younger age, recent smoking, sevoflurane anesthesia, postoperative pain on the numerical rating scale (NRS) ≥5, presence of a tracheal tube, and presence of a urinary catheter. Presence of a tracheal tube was the greatest risk factor, increasing the risk of developing emergence agitation by approximately fivefold (odds ratio, 5.448; 95% confidence interval, 2.973 to 9.982). Younger age was also a strong risk factor (odds ratio, 0.975 for each 1-year increase; 95% confidence interval, 0.964 to 0.987). Current smoking, sevoflurane anesthesia, postoperative pain of NRS ≥5, and the presence of a urinary catheter nearly doubled the risk of emergence agitation.

Conclusion. Emergence agitation following general anesthesia is a common complication in adult nasal surgery patients. To reduce the occurrence and consequences of agitation episodes, elimination of the associated risk factors is necessary, especially in at-risk patients.

Keywords. *Anesthesia Recovery Period; Nasal Surgical Procedures; Psychomotor Agitation*

INTRODUCTION

Emergence agitation is a postanesthetic phenomenon that develops in the early phase of general anesthesia recovery, and is characterized by agitation, confusion, disorientation, and possible violent behavior [1]. Though agitation is observed more frequently in pediatric patients, the incidence in adults has been reported at 4.7% [2] or 21.3% [3]. Emergence agitation can lead to serious consequences such as self-extubation, removal of catheters, hem-

orrhage, and even severe injuries from falling out of the bed. Furthermore, it may increase the demand on human resources and cause medical staff injuries [4,5].

While its pathogenesis remains unclear, previous studies [3,6,7] reported that ENT (ear, nose, and throat) surgical procedures have a higher incidence of emergence agitation in both adults and children. Especially, it was our clinical impression that nasal surgical patients admitted to the postanesthesia care unit (PACU) have suffered emergence agitation more frequently than other surgical patients, possibly due to a sense of suffocation during emergence from anesthesia [7]. This phenomenon has been frequently studied in pediatric patients, but limited data for adults exists. Thus, we retrospectively investigated the incidence and associated risk factors for emergence agitation in adult patients who underwent general anesthesia for nasal surgery between July 2012 and August 2013 at Samsung Medical Center, a ter-

tiary hospital in Seoul, Republic of Korea.

MATERIALS AND METHODS

With the approval of Institutional Review Board of Samsung Medical Center (IRB No.: 2013-09-030, approval date: October 1, 2013), we retrospectively examined the records of 792 patients aged ≥18 years who underwent general anesthesia for elective nasal surgery from July 2012 to August 2013 at our institution. This study was registered with Clinical Research Information Service of Korean National Institute of Health (CRIS; http://cris.cdc.go.kr/cris/en/use_guide/cris_introduce.jsp) (ref: KCT 0000941).

To obtain a pure comparison regarding emergence agitation, patients who underwent concurrent surgeries other than nasal surgery (e.g., adenoidectomy or tonsillectomy) or closed reduction for nasal bone fracture were excluded from the study. Patients admitted directly to the intensive care unit (ICU) were also excluded.

In every patient admitted to the PACU following general anesthesia at our institution, a serial Richmond Agitation Sedation Scale (RASS) assessments [8] (on admission to the PACU and every 10 minutes thereafter) has been performed routinely since 2011. RASS is a 10-point scale with four levels of agitation, one level to denote a calm and alert state, and five levels of sedation (Table 1). Although RASS was originally created for ICU patients, it is also applicable in the PACU [9]. This clinical protocol encourages PACU nurses and physicians to target a RASS score of 0 ("alert and calm") in all patients. All newly hired PACU nurses

Table 1. Richmond Agitation Sedation Scale

Score	Term	Description
+4	Combative	Overtly combative, violent, immediate danger to staff
+3	Very agitated	Pulls or removes tube(s) or catheter(s); aggressive
+2	Agitated	Frequent nonpurposeful movement, fights ventilator
+1	Restless	Anxious but movements not aggressive or vigorous
0	Alert and calm	
−1	Drowsy	Not fully alert, but has sustained awakening (eye-opening/eye contact) to voice (>10 seconds)
−2	Light sedation	Briefly awakens with eye contact to voice (<10 seconds)
−3	Moderate sedation	Movement or eye opening to voice (but no eye contact)
−4	Deep sedation	No response to voice, but movement or eye opening to physical stimulation
−5	Unarousable	No response to voice or physical stimulation

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receive training in RASS assessments, followed by a competency assessment during the training period.

In all cases, anesthesia was induced by intravenous (IV) propofol or thiopental and rocuronium to provide neuromuscular blockade for endotracheal intubation. Anesthesia was maintained with total intravenous anesthesia (TIVA) using propofol and remifentanil or inhalational anesthesia with sevoflurane. Muscle relaxation was maintained by IV vecuronium (0.02 mg/kg) at regular intervals. IV opioids (meperidine or hydromorphone) or ketolorac is routinely given 30 minutes prior to the end of surgery for postoperative pain.

Three attending otolaryngologists performed the operations with residents assisting to their ability level. Upon surgery completion, the decision whether or not to perform nasal packing was made based on the surgeon's assessment of postoperative hemorrhage. For nasal packing, gauze or saline-soaked Merocel (Medtronic Xomed, Jacksonville, FL, USA) was applied and removed the following day. Merocel is composed of expandable hydroxylated polyvinyl acetate. The surgical procedures were grouped into four categories: septoplasty or/and rhinoplasty without osteotomies, septoplasty or/and rhinoplasty with osteotomies, endoscopic sinus surgery (ESS), and ESS with other nasal surgeries.

In the PACU, all patients were routinely managed using the following standardized postoperative protocol: (1) serial assessments of pain with an 11-point numerical rating scale (NRS), emergence agitation by RASS, and the presence of postnasal drip (PND, at admission, every 15 minutes thereafter, and at discharge from the PACU); (2) rescue analgesic administration of meperidine or hydromorphone in patients with a pain score≥5, and physical restraint or intermittent midazolam administration in severe cases of emergence agitation based on the decision of attending anesthesiologists; (3) antiemetic treatment with IV ramosetrone or granisetrone in patients with intolerable postoperative nausea and vomiting (PONV); and (4) PACU discharge criteria based on a modified Aldrete score (scores of 9 or greater were deemed appropriate for discharge).

Patients in the PACU with a RASS≥+1 at any time were considered to have emergence agitation. For patients with emergence agitation, we also noted the highest RASS score while in the PACU and whether of physical restraints or midazolam administration. For each patient, the following variables were noted: demographic data, American Society of Anesthesiologists (ASA) physical status (classification 1 vs. ≥2), current smokers (individuals having smoked at least 10 cigarettes per day for more than 1 year within at least 1 week before surgery), alcohol abuse (individuals having on average 3–4 drinks a day at least four or more times a week), surgery type and length, type of nasal packing (no packing, unilateral, or bilateral packing), premedication with midazolam, anesthesia type (sevoflurane anesthesia vs. TIVA) and length, analgesics used for postoperative pain (ketorolac, meperidine, or hydromorphone), presence of postoperative pain

(patients were considered to have pain if they had a NRS≥5 while in the PACU), presence of PONV requiring antiemetics, presence of PND, presence of a tracheal tube or urinary catheter on PACU admission, and length of stay in the PACU.

Statistical analyses were performed with PASW ver. 18.0 (SPSS Inc., Chicago, IL, USA). First, univariate characteristics between patients with and without emergence agitation were compared using unpaired *t* or chi-square tests. Second, a backward stepwise multivariate logistic regression analysis was conducted to identify independent risk factors for emergence agitation. Any variables that were significant at $P \leq 0.2$ in the univariate analysis were candidates for entry into the multivariate analysis. Model goodness-of-fit was evaluated using the Hosmer-Lemeshow test. Independent risk factors are expressed as odds ratio (OR) with 95% confidence interval (CI). In all analyses, $P < 0.05$ indicated statistical significance.

RESULTS

General description of the studied population
A total of 792 patients were included in the study. The mean age was 41.8 ± 16.2 years (range, 18 to 85 years); 26.9% of patients

(n=213) were females. Emergence agitation occurred in 176 patients (22.2%) in the PACU. In agitated patients, eight patients needed physical restraint, and of these, two received benzodiazepines to control agitation. All patients regained normal cognitive status before discharge from the PACU. In agitated patients, the RASS level of agitation was: 3.4% combative agitated patients (n=6), 9.1% very agitated patients (n=16), and 87.5% restless or agitated patients (n=154).

Univariate and multivariate analyses between agitated and nonagitated patients
The incidence of emergence agitation did not differ depending on the presence of nasal packing ($P=0.193$) (Table 2). Further subgroup analysis showed that, in both unilateral and bilateral packing groups, type of packing material (gauze vs. merocel) was not associated with the incidence of emergence agitation ($P=0.812$ and $P=0.102$, respectively).

In univariate analyses, significant differences were observed between nonagitated and agitated patients when considering gender, age, smoking habits, ASA physical status, type of anesthesia, premedication with midazolam, presence of a tracheal tube, presence of a urinary catheter, postoperative pain, and PONV requiring antiemetic treatment ($P<0.05$) (Table 2).

Table 2. Univariate analyses: risk factors for emergence agitation after nasal surgery

Variable	Nonagitated (n=616)	Agitated (n=176)	*P*-value
Gender, male/female	437/179	142/34	0.013*
Age (year)	43.1±16.5	36.7±15.0	<0.001*
Current smokers/ex- or nonsmokers	109/507	51/125	0.001*
Alcohol abuse, yes/no	66/550	15/161	0.481
Body mass index (kg/m²)	24.1±3.4	24.0±3.3	0.651
ASA physical status, 1/≥2	386/230	128/48	0.017*
Premedication with midazolam, yes/no	542/74	136/40	0.001*
Duration of surgery (minute)	93.0±44.1	102.5±44.9	0.562
Duration of anesthesia (minute)	142.6±47.2	150.7±47.8	0.642
Type of anesthesia, TIVA/sevoflurane anesthesia	561/55	141/35	<0.001*
Type of surgery			0.220
Septoplasty or/and rhinoplasty without osteotomies	51	20	
Septoplasty or/and rhinoplasty with osteotomies	171	55	
ESS only	163	41	
ESS with other nasal surgeries	231	60	
Nasal packing, none/unilateral/bilateral	180/50/386	43/10/123	0.193
Analgesics used for postoperative pain, ketolorac/meperidine/hydromorphone	19/377/220	5/122/49	0.132
Presence of tracheal tube, yes/no	442/174	163/13	<0.001*
Presence of urinary catheter, yes/no	21/595	14/162	0.017*
Postoperative pain, NRS≥5/NRS<5	377/239	130/46	0.003*
PONV requiring antiemetics, yes/no	12/604	9/167	0.041*
Core temperature, <36.0°C/36.0°C–37.5°C/>37.5°C	33/570/13	7/166/3	0.800
Presence of postnasal drip, yes/no	21/595	6/170	1.000
PACU stay time (minute)	68.6±13.9	69.2±17.7	0.529

Values are presented as number or mean±SD.
ASA, American Society of Anesthesiologists; TIVA, total intravenous anesthesia; ESS, endoscopic sinus surgery; NRS, numerical rating scale; PONV, postanesthesia nausea and vomiting; PACU, postanesthesia care unit.
*$P<0.05$, statistically significant difference.

Table 3. Multivariate logistic regression analysis: independent risk factors for emergence agitation

Variable	Odds ratio (95% CI)	*P*-value
Age (year)	0.975 (0.964–0.987)	<0.001
Recent smoking	2.038 (1.350–3.075)	0.001
Type of anesthesia, sevoflurane anesthesia vs. TIVA	2.320 (1.414–3.807)	0.001
Postoperative pain, NRS≥5 vs. NRS<5	1.813 (1.222–2.691)	0.003
Presence of a tracheal tube	5.448 (2.973–9.982)	<0.001
Presence of a urinary catheter	2.416 (1.222–2.691)	0.023

CI, confidence interval; TIVA, total intravenous anesthesia; NRS, numerical rating scale.

In addition to these 10 variables, two variables associated with emergence agitation (*P*≤0.2) in the univariate analysis (type of nasal packing and analgesic treatment of postoperative pain) were entered into multivariate logistic regression analysis. Male gender, ASA physical status classification≥2, no premedication with midazolam, and PONV requiring antiemetics were significantly associated with emergence agitation in the univariate analyses (*P*<0.05) (Table 2), but their independence was not confirmed in the multivariate logistic regression analysis. The following six variables were found to be significantly associated with emergence agitation: younger age, recent smoking, sevoflurane anesthesia, postoperative pain with NRS≥5, presence of a tracheal tube, and presence of a urinary catheter (Table 3).

Presence of a tracheal tube was the greatest risk factor, increasing the risk of developing emergence agitation by about five times (OR, 5.448; 95% CI, 2.973 to 9.982; *P*<0.001). By using age as a continuous variable, younger age was also a strong risk factor (OR, 0.975 for each 1-year increase; 95% CI, 0.964 to 0.987; *P*<0.001). Current smoking, sevoflurane anesthesia, postoperative pain with NRS≥5, and presence of a urinary catheter nearly doubled the risk of emergence agitation (Table 3).

Mean length of stay in the PACU was similar between those who experienced emergence agitation and those who did not (69.2±17.7 minutes vs. 68.6±13.9 minutes) (Table 2).

DISCUSSION

The present study showed that emergence agitation was a common phenomenon occurring in 22.2% in adult patients undergoing general anesthesia for nasal surgery. Severe agitation necessitating use of sedatives or physical restraint was present in only 4.5% of those with agitation (1.0% of all patients). The overall incidence of emergence agitation in the present study is relatively low compared to the 52.0%–55.4% in the similar surgical cohorts of previous studies [3,10]. This is attributed to the somewhat different study cohorts (nasal surgical patients vs. ENT surgical patients) [3,10] and the different anesthetic techniques (primary use of TIVA vs. primary [3] or absolute [10] use of inhala-

tional anesthetics). Operations involving the oral cavity and inhalational anesthesia are well-established risk factors for emergence agitation [3,6].

In the present study, six independent risk factors (younger age, recent smoking, sevoflurane anesthesia, postoperative pain of NRS≥5, presence of a tracheal tube, and presence of a urinary catheter) were identified. The most surprising finding of the present study is that nasal packing was not a risk for emergence agitation. Although the necessity for nasal packing following nasal surgeries is still a matter of debate, many surgeons prefer to use nasal packing to prevent synechiae, hematoma formation, and lateralization of the middle turbinate [11,12]. Intuitively, we hypothesized that patients undergoing nasal surgery might have a higher risk of emergence agitation because of a sense of suffocation due to nasal packing. However, both the unilateral and bilateral nasal packing groups did not have a significant difference in emergence agitation compared to the no packing group. It is clear that patients with nasal packing feel a more uncomfortable sense of nasal fullness than those without nasal packing, especially as nasal secretions accumulate or swelling at the operation sites increases [13].

The most likely explanation for this unexpected result is that nasal packing could cause significant breathing difficulty on emergence from anesthesia in our patients. Because approximately one half of the respiratory airway resistance to airflow is provided by the nasal airway [14], nasal packing inevitably causes acute breathing difficulty in healthy adults. Most patients in our study cohort are likely chronic mouth breathers with a considerable degree of nasal obstruction. Nasal obstruction is a dominant symptom associated with all types of rhinosinusitis including nasal septal deviation, nasal polyps, and inferior turbinate hypertrophy. Thus, obstructing the nasal airway by nasal packing has little impact on breathing difficulty for these patients, and did not cause agitation. Similarly, nasal packing after nasal surgery was found to increase an objective index of respiratory distress in patients with mild obstructive sleep apnea (OSA), but not in obligatory mouth breathing patients with moderate/severe OSA [15].

Another possible explanation is that either unilateral or bilateral nasal packing did not obstruct the corresponding nasal airway completely while in the PACU. In the present study, gauze (squeezed tightly after saline-soaking) or saline-soaked merocel was used as packing material. In the immediate postoperative period, nasal obstruction due to nasal packing may not be marked, although it becomes severe as the operation site swelling increases and nasal secretions accumulate over time. This assumption is supported by the previous study [16] in which subjective nasal fullness was compared by an 11-point visual analogue scale at 1, 6, and 24 hours after septoplasty. In that study, nasal fullness scores at postoperative 1 hour were significantly lower than those at postoperative 6 and 24 hours (1–2 vs. 5–7), regardless of the packing material.

In the present study, sevoflurane anesthesia, postoperative pain of NRS≥5, presence of a tracheal tube, and presence of a urinary catheter were identified as independent risk factors of

emergence agitation. These variables were repeatedly suggested as risk factors in previous studies for emergence agitation after general anesthesia for procedures other than nasal surgery [1-3,6,9]. The presence of a tracheal tube on emergence is a main cause of agitation in our study cohort. Similarly, Lepouse et al. [2] evaluated the most probable causes in the agitated patients and found that the most common cause of emergence agitation was the presence of a tracheal tube (53.1%, 34/64). When considering that nonuniform recovery of different parts of the central nervous system is suggested as the main mechanism of emergence agitation [1,3], a tracheal tube can be distressing in partially awake (i.e., somewhat dissociated) patients. Such a situation can be more stressing in our patients because they are likely chronic mouth breathers.

For the first time, our study demonstrated that younger age and current smoking were associated with a higher incidence of emergence agitation. Radtke et al. [9] suggested that patient age influenced the occurrence of emergence agitation. Unlike our study, they arbitrarily classified the study cohort into three age groups (18–39, 40–64, and ≥65 years) and found that older patients as well as younger patients showed a risk for emergence agitation. Contrarily, other studies [2,3] failed to demonstrate patient age as an independent risk factor with age examined as a continuous variable as in the present study. A prospective randomized controlled study design will be required to clarify this issue by elimination of potential selection bias.

Our results suggest that current smoking nearly doubles the risk of emergence agitation. To date, only one study [9] has evaluated this issue and found a negative relationship between smoking and emergence agitation. However, several studies regarding postoperative delirium have noted an increased risk for postoperative delirium in smokers [17,18]. Our findings may reflect either a withdrawal agitation due to the sudden cease of nicotine consumption or a direct neurotoxic effect of tobacco in the brain that produces a diminished adaptive function to stressful situations. As smoking is suggested to worsen surgical outcomes following nasal surgery [19], our finding is an additional reason to stop smoking prior to surgery.

There were several limitations to the present study. First, as the subjective or objective preoperative data on patients' nasal obstruction were absent, the impact of different nasal packing types on breathing difficulty could not be individually evaluated. Second, although two commonly used nasal packing materials were applied, many different commercially available packing materials are used with different degrees of nasal obstruction. An additional source of confounding may have been introduced through the inclusion of three surgeons in the study, although there is no difference in the occurrence of emergence agitation depending on the surgeon (*P*=0.321). Lastly, there are inherent limitations of a retrospective study design. However, as the study was performed in a relatively large study cohort with standardized management protocol for emergence agitation, the overall results may be less influenced by occasional errors and more representative of routine clinical practice.

The present study describes a high incidence (22.2%) of emergence agitation in adult patients undergoing general anesthesia for nasal surgery, and identifies younger age, current smoking, sevoflurane anesthesia, postoperative pain of NRS≥5, presence of a tracheal tube, and presence of a urinary catheter as risk factors. The mainstay for management of emergence agitation is elimination of preventable causes, especially in at-risk patients. The following are the main strategies to reduce the occurrence and consequences of emergence agitation episodes: encouraging patients to quit smoking at least 1 week before surgery, selecting a TIVA rather than sevoflurane anesthesia, providing adequate postoperative analgesia, removing tracheal tubes and urinary catheters as early as possible following surgery, and more vigilant monitoring for emergence agitation in younger patients.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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