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The Effects of Fresh Gas Flow on Emergence Agitation for Gynecologic Surgery: A Clinical Study

Jinekolojik Cerrahide Taze Gaz Akımının Derlenme Ajitasyonu Üzerine Etkileri: Klinik Bir Çalışma

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ABSTRACT

Objective: This prospective study aimed to determine whether low flow anesthesia (LFA) has an effect on emergence agitation in women who underwent laparotomic gynecologic surgeries.

Method: Sixty four female patients were enrolled in this prospective randomized study. The patients were randomly allocated into two groups: Group 2 and Group 0.5. The fresh gas flow (FGF) rate was set at 4 L min^{-1} in both groups, initially. When all patients reached 1 minimum alveolar concentration of sevoflurane, the FGF rate was reduced to 2 L min^{-1} in Group 2 and 0.5 L min^{-1} in Group 0.5. For Group 0.5, vapor was closed 15 minutes before the end of surgery, while it was closed at the end of the operation for Group 2. At the end of the surgery, the FGF rate was increased to 4 L min^{-1}. Emergence agitation was assessed using the Riker Sedation Agitation Scale (SAS) in the post-anesthesia care unit at 5, 10, 20 and 30th minutes.

Results: Emergence agitation was observed in 5 patients, no significant difference was found between two groups. For all evaluation times, number of patients with SAS=4 was significantly higher in Group 0.5, while the number of patients with SAS<4 was significantly higher in Group 2 ($p<0.05$).

Conclusion: The number of patients who are calm and cooperative was higher in LFA.

Keywords: Emergence agitation, general anesthesia, fresh gas flow

ÖZ

Amaç: Bu prospektif çalışma laparotomik jinekolojik cerrahi geçiren hastalarda düşük akımlı anestezinin (DAA) derlenme ajitasyonu üzerine etkisi olup olmadığını tespit etmeyi amaçlamaktadır.

Yöntem: Bu prospektif randomize çalışmaya 64 hasta dahil edildi. Hastalar rastgele iki gruba ayrıldı: Grup 2 ve Grup 0,5. Taze gaz akımı (TGA) başlangıçta her iki grupta da 4 L dk^{-1} olarak ayarlandı. Tüm hastalarda sevofluran 1 minimum alveolar konsantrasyona ulaştığında TGA Grup 2 için 2 L dk^{-1} ve Grup 0,5 için 0,5 L dk^{-1}'ye düşürüldü. Vaporizatör Grup 2'de cerrahi bitiminde kapatılırken, Grup 0,5'te cerrahi bitmeden 15 dakika önce kapatıldı. Cerrahi bittiğinde TGA 4 L dk^{-1}'ye yükseltildi. Derlenme ajitasyonu post-anestezi bakım ünitesinde 5, 10, 20 ve 30. dakikalarda Riker sedasyon ajitasyon skalası (SAS) kullanılarak değerlendirildi.

Bulgular: Beş hastada derlenme ajitasyonu gözlendi ve gruplar arasında istatistiksel olarak derlenme ajitasyonu açısından anlamlı fark saptanmadı. Tüm değerlendirme sürelerinde SAS=4 olan hasta sayısı Grup 0,5'te anlamlı olarak daha fazla iken SAS<4 olan hasta sayısı Grup 2'de anlamlı olarak daha fazla idi ($p<0,05$).

Sonuç: Sakin ve koopere olan hasta sayısı DAA uygulanan hastalarda daha fazlaydı.

Anahtar sözcükler: Derlenme ajitasyonu, genel anestezi, taze gaz akımı

INTRODUCTION

Emergence agitation (EA) is also referred as emergence delirium develops in the early phase following general anesthesia during recovery, and involves excitation, confusion, disorientation, and possible violent behavior (1). Although most studies on EA have been performed in pediatric patients, it is also an important issue for adults, and little data about this issue exist (2,3).

Low flow anesthesia (LFA) is an inhalation anesthetic technique in which the rebreathing fraction reaches 50% at least, thus 50% of the exhaled gas mixture is returned to the patient after CO_2 is removed in the next inspiration (4). In 1974, Vir-

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tue described a technique using a fresh gas flow (FGF) rate of 0.5 L min^{-1}, which was named "minimal flow anesthesia" (5). In 1994, the FGF rate used in anesthetic practice was classified as medium (1–2 L min^{-1}), low (500–1000 mL min^{-1}), minimal (250–500 mL min^{-1}), and metabolic flow (250 mL min^{-1}) by Baker (6). The benefits of LFA include reduction of consumption of inhaled agents, improved body temperature, lowered loss of heat and moisture, and reduced environmental pollution (7).

In our clinical practice while we used 0.5 L min^{-1} of FGF rate, it was observed that patients recovered more calmly and comfortably from anesthesia. When we looked at the literature, we could not find a study investigating the relationship between LFA and EA in adults. Hence, we aimed to evaluate the effects of FGF on EA who received laparotomic gynecologic surgery in adults under sevoflurane anesthesia in this prospective, double-blind, randomized study.

MATERIAL and METHODS

Study Design

After approval from the Institutional Ethics Committee of the Sakarya University (25.05.2018, No:98), this study was registered at ClinicalTrials.gov with the unique registration number NCT03862391. All patients provided written informed consent before the surgery. Sixty four female patients who were between 18 and 65 years, who had an American Society of Anesthesiologists (ASA) physical status classification of I–II, and who were scheduled for elective laparotomic gynecologic surgery requiring general anesthesia were enrolled. The patients who were pregnant, had an ASA classification of III and above, were <18 or >65 ages, had a body mass index (BMI)>30 kg m^{-2}, had a preoperative hematocrit <25%, had significant cardiac, pulmonary, renal and liver disease, and had any psychiatric disease that interfered with the patient's decision were excluded.

Management of General Anesthesia and Recovery

All patients were premedicated with 0.02 mg kg^{-1} midazolam before the procedure and standard monitoring (electrocardiogram, noninvasive blood pressure, pulse oximetry) was applied. The level of neuromuscular blockade was monitored by acceleromyograph with train-of-four (TOF) (TOF-Watch SX, Schering-Plough, Dublin, Ireland). Prior to induction, the epidural catheter was inserted through the T8–T10 intervertebral space via an 18-gauge Tuohy needle with the loss of resistance technique in the sitting position. After a negative test dose of 3 mL of 2% lignocaine with 1:200,000 adrenalin for blood and cerebrospinal fluid, an initial bolus of 10 mL of 0.125% bupivacaine and 50 µg fentanyl was administered before the surgery. Subsequent top-up doses were given according to intraoperative requirements.

The patients were allocated randomly assigned to two groups, Group 2 (n=32) and Group 0.5 (n=32), using a computer-generated random number assignment. After preoxygenation, anesthesia induction was performed by 1 µg kg^{-1} of fentanyl, 1 mg kg^{-1} of lidocaine, 2 mg kg^{-1} of propofol, and 0.6 mg kg^{-1} of rocuronium. At the beginning of anesthesia, FGF rate was set at 4 L min^{-1} in both groups, and ventilation was started with an 8 mL kg^{-1} tidal volume and a respiratory rate of 12 using a 40% oxygen-in-air mixture. When all patients reached 1 MAC of sevoflurane, the FGF rate was reduced to 2 L min^{-1} in Group 2 and 0.5 L min^{-1} in Group 0.5. Throughout the procedure, the sevoflurane concentration was adjusted to maintain 1 MAC, and the tidal volume and respiratory rate were adjusted to maintain $EtCO_2$ at 35–40 mmHg. The lower alarm of the inspiratory oxygen concentration was set at 30%.

In Group 0.5, vapor was closed 15 minutes before the end of the operation, while it was closed at the end of the operation in Group 2, and in both groups, the FGF rate was increased to 4 L min^{-1}, and FiO_2 was increased to 80. All patients received epidural analgesics 20 minutes before the end of the operation. Additionally, the residual effects of rocuronium were antagonized by 2 mg kg^{-1} of sugammadex. After the operation, the patients were observed in the recovery room.

Patients were extubated when the TOF ratio was >90%.

Measurement of Emergence Agitation, Postoperative Pain and Postoperative Nausea and Vomiting

The anesthesiologist who blinded to FGF rate during anesthesia assessed EA in the recovery room by the Riker sedation-agitation scale (SAS; Table I) (8). Emergence Agitation was defined as a Riker SAS score ≥5 at any time in the recovery room.

Postoperative pain was assessed using the visual analogue scale (VAS, 0–10, 0=no pain, 10=worst imaginable pain). When the VAS was found to be ≥4, a 50 mg dexketoprofen trometamol was given.

Postoperative nausea and vomiting (PONV) were evaluated as: 0, no nausea; 1, mild nausea, duration ≤15 minutes; 2, nausea ≥15 minutes; 3, retching or vomiting. When the PONV score was ≥2, a 4 mg ondansetron was given.

For each patient age, height, weight, BMI, ASA, duration of anesthesia, duration of surgery, and adverse effects were recorded at 5, 10, 20 and 30th minutes in the recovery room.

Statistical Analysis

The primary outcome of this study was the incidence of EA under different FGF regimens. Based on another study reporting an EA incidence rate of 55.4% following general anesthesia in adult patients, the sample size of 32 patients

Table I. Riker Sedation-Agitation Scale (8)

7	Dangerous Agitation	Pulling at endotracheal tube, trying to remove catheters, climbing over bed rail, striking at staff, thrashing side to side
6	Very Agitated	Does not calm, despite frequent verbal reminding of limits; requires physical restraints, biting ET tube
5	Agitated	Anxious or mildly agitated, attempting to sit up, calms down to verbal instructions
4	Non-agitated Calm-cooperative	Calm, awakens easily, follows commands
3	Sedated	Difficult to arouse, awakens to verbal stimuli or gentle shaking but drifts off again, follows simple commands
2	Very sedated	Arouses to physical stimuli but does not communicate or follow commands may move spontaneously
1	Unrousable	Minimal or no response to noxious stimuli, does not communicate or follow commands

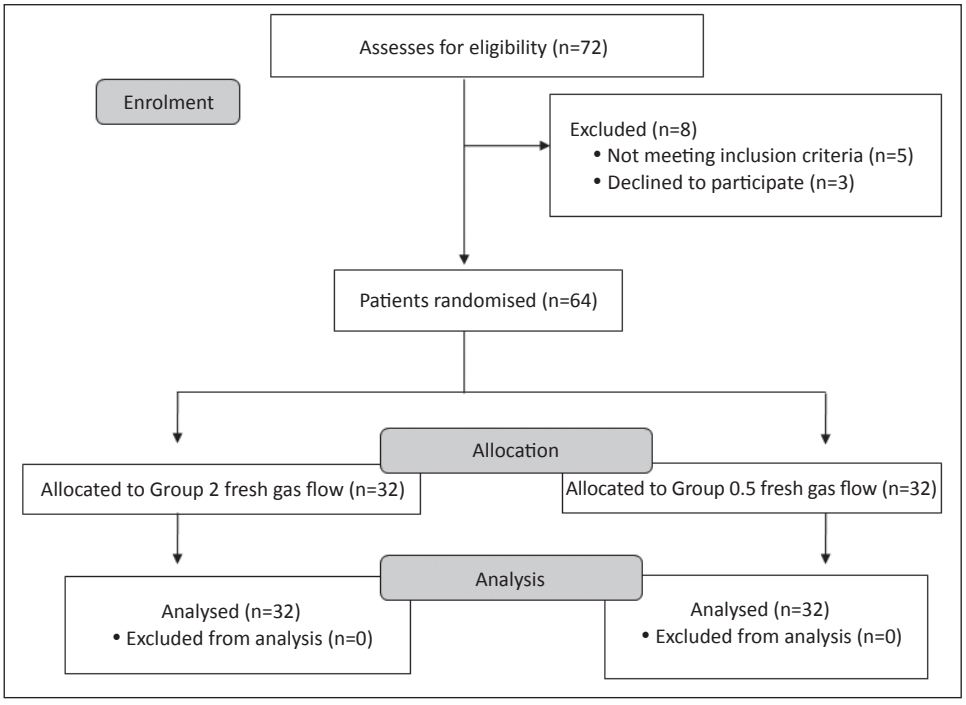

Figure 1. Flow chart illustrating patient recruitment into the study.

in each group was calculated to detect a 50% reduction in EA incidence with power analysis (a=0.05 [2-sided], power = 0.80) (2).

Data were expressed as mean±SD, percentages, and median. To compare perioperative data and VAS scores between the groups two-tailed t test, Pierson chi-square test and Mann-Whitney U tests were used. For all analyses, IBM SPSS version 21.0 was used and the statistical significance was set at $p<0.05$.

RESULTS

Of the 72 patients assessed for eligibility, 5 were excluded for failure to meet inclusion criteria and 3 declined to participate (Figure 1). This study enrolled 64 patients.

There were no significant differences in the age, height, weight, BMI, ASA, or duration of anesthesia (Table II). Emergence agitation (SAS score≥5) was observed in 5 patients (7.81%) in the recovery room at 5th minute, and 2 of them (3.1%; 1 from each group) were very agitated and received benzodiazepines to control agitation. The number of patients with SAS score=4 (i.e., calm and cooperative) were higher in Group 0.5, Group 0.5 (Figure 2).

As shown in Table III, the VAS scores were comparable at all-time intervals. None of the patients in either group had hypotension, bradycardia, or respiratory depression. Only 1 patient from Group 2 whose PONV score was 2 required an antiemetic agent.

Table II. Demographic Data and Duration of Anesthesia

	Group 0.5 (n=32)	Group 2 (n=32)	p
Age (years)	50.1 ± 13.4	49.1 ± 9.5	0.732[a]
Height (cm)	165.1 ± 4.1	166.6 ± 5.4	0.231[a]
Weight (kg)	78.6 ± 16.2	78.5 ± 6.3	0.976[a]
BMI	28.8 ± 5.9	28.4 ± 3.4	0.733[a]
ASA, n (%)			
I	16 (50)	19 (59.4)	0.451[ł]
II	16 (50)	13 (40.6)	
Duration of Anesthesia (min)	150 (120-192)	142 (121-188)	0.914*

ASA: American Society of Anesthesiologist, **BMI:** Body mass index, **min:** minutes
[a]Two-tailed t-test (mean±SD); [ł] Pearson chi-square; *Mann-Whitney U[median (IQR)]

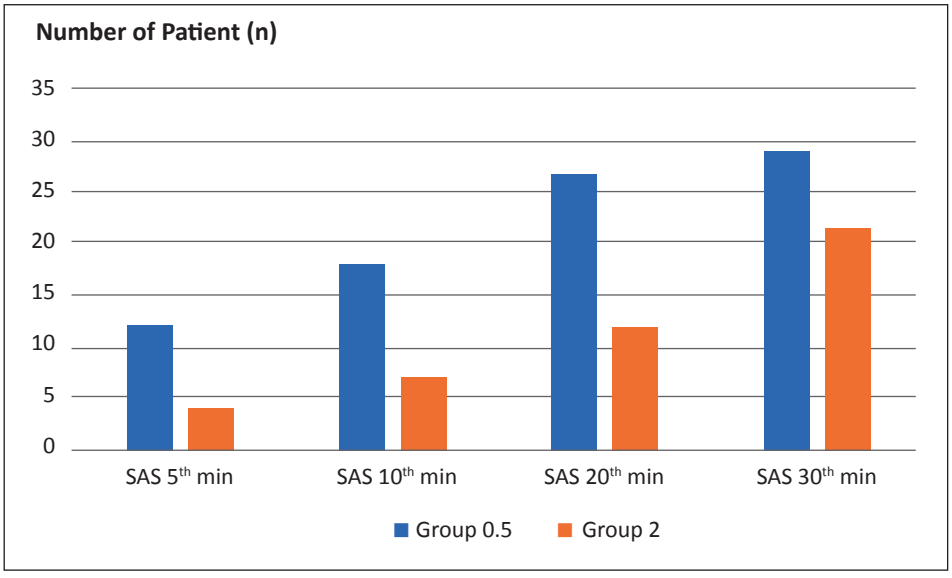

Figure 2. The number of patients with Riker Sedation-Agitation Scale 4 (calm and co-operative).
SAS: Sedation-Agitation Scale

DISCUSSION

Although a difference was not found between two FGFs in terms of EA, this study observed that the number of patients who were calm and cooperative was higher in patients who received LFA.

Emergence agitation is a temporary mental anxiety that occurs during recovery from general anesthesia. In studies, the frequency of adult EA was reported to 4.1%. The risk factors of EA in adult patients are the presence of pain (Numeric Rating Scale score ≥5), gastric tube, urinary catheter, or tracheal tube, and sevoflurane anesthesia (2,3). In the present study, we prevented pain that causes EA with thoracic epidural anesthesia providing effective perioperative analgesia. Additionally, all patients underwent urinary catheterization, had the same surgical and anesthetic procedure. These applications attempted to keep the risk factors for EA formation similar for both FGFs. Thus, the study was able to determine whether the amount of FGF applied to the patient had an effect on the development of EA.

Inhalation agents have been shown to be a risk factor developing of EA (9). In studies investigating the EA development rates for inhalation anesthetics in pediatric patients, sevoflurane appeared to have the highest propensity for causing EA (9,10). Similarly, the risk of developing EA was reported to be 22.5% (95% CI, 7.3–37.7) higher in adult patients with sevoflurane (11,12). Therefore, sevoflurane may be a major contributor for EA. We used sevoflurane during general anesthesia so that more patients would develop EA and the effects of FGF on EA could be more clearly understood. However, in our study there was no difference in the incidence of EA, so we couldn't say that high FGF rates lead to higher incidence for EA in adults.

Sevoflurane is a commonly used halogenated volatile anesthetic agent with a low blood-gas partition ratio, and its rapid

Table III. Visual Analogue Scale Scores of Patients at Postoperative Unit

	Group 0.5 (n=32)	Group 2 (n=32)	p*
VAS 5th minute	0 (0-4)	0 (0-4.7)	0.797
VAS 10th minute	0 (0-3.7)	2.5 (0-5)	0.331
VAS 20th minute	2.5 (0-4)	3 (0-5)	0.295
VAS 30th minute	2.5 (0-4)	3 (0-4.7)	0.245

* Mann-Whitney U-test [median (IQR)], **VAS:** Visual Analogue Scale

removal from the brain may cause EA in patients (13). It was reported that the possible mechanism of EA in patients who received sevoflurane anesthesia was the difference in rapid neurological recovery (3). Using a high FGF rate during sevoflurane anesthesia has been shown to increase the incidence of EA children (14). However there was no difference in adult women patients in our study.

Our anesthesia machines could be able to predict the estimated anesthetic agent concentrations for the next 20 minutes following the closure of the anesthetic agent. To ensure a slow sevoflurane excretion, the sevoflurane was closed 15 minutes before the end of the operation in LFA. It was reported that anesthetic gas concentration decreased slowly during LFA (15). We found that there were higher number of patients who were calm and cooperative in patients in LFA group. This could be associated with longer wash-out period of sevoflurane and slower excretion of sevoflurane might have a positive effect on recovery.

One of the limitations of our study is the small sample size. If the number of patients were large, there might be a difference in EA between LFA and HFA. Secondly, extubation times, verbal response times and eye opening times were not evaluated.

CONCLUSION

The results from this study clearly indicated that LFA with a 0.5 L min^{-1} FGF was not associated with decreasing EA in adult women patients under sevoflurane anesthesia. Slower and longer clearance from the brain during LFA compared to HFA may be the cause of these patients' elevated levels of awareness because the inhale anesthetic is ceased earlier during LFA.

AUTHOR CONTRIBUTIONS

Conception or design of the work: ATT, AFE

Data collection: GD

Data analysis and interpretation: HK

Drafting the article: ATT

Critical revision of the article: ATT

Other (study supervision, fundings, materials, etc): AFE

All authors (ATT, GD, HK, AFE) reviewed the results and approved the final version of the manuscript.

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