

Even Lower is Possible: Impact of Flow Rate on Safety Issues in Low Flow Anaesthesia

Daha Azı Da Mümkün: Düşük Akımlı Anestezide Akım Hızlarının Güvenlik Sonuçları Üzerine Etkisi

 Ali Bestami Kepekçi¹,  Derya Özden Omaygenç²,  İbrahim Oğuz Karaca³,  Serkan Telli⁴,
 Serkan Yücepur⁵,  Ecder Özenç⁶

¹Yeni Yüzyıl University, Gaziosmanpaşa Hospital, Vocational School of Health Services, Clinic of Anesthesia, İstanbul, Turkey

²Yedikule Chest Diseases and Chest Surgery Training and Research Hospital, Clinic of Anesthesiology, İstanbul, Turkey

³İstanbul Medipol University Hospital, Clinic of Cardiology, İstanbul, Turkey

⁴Atatürk University Research Hospital, Clinic of Anesthesiology and Reanimation, İstanbul, Turkey

⁵Amasya Suluova State Hospital, Clinic of Anesthesiology and Reanimation, İstanbul, Turkey

⁶University of Health Sciences, Haseki Training and Research Hospital, Clinic of Anesthesiology and Reanimation, İstanbul, Turkey

ABSTRACT

Objective: Although various issues about low flow anaesthesia had been investigated previously, impact of different flow rates on perioperative follow-up and safety outcomes were not well-addressed. Here, we aimed to assess the influence of different flow rates of low flow fresh gas mixtures on hemodynamic state, gas exchange parameters and recovery time during general anaesthesia of urogenital system operations in a single tertiary centre.

Materials and Methods: Sixty-two patients (American Society of Anaesthesiologists score I or II) to whom low flow anaesthesia with sevoflurane had been administered were subsequently gathered in three distinct -A, moderate flow (2 L/minimum), B, low flow (1 L/minimum), C, minimal flow (0.5 L/minimum) -groups. Hemodynamic data before and during anaesthesia, additionally, gas exchange and blood gas analysis parameters at 30th minute and before cessation of anaesthesia were recorded. Recovery period was observed by a second physician and times of interest were noted.

Results: Demographic characteristics were similar among study groups. Most of the data regarding vital signs, gas exchange and blood gas analysis at the 30th minute and prior to cessation of anaesthesia were comparable. During operation, inspiratory sevoflurane levels were significantly higher in group A (1.7±0.6 vs 1.3±0.3 vs 1.3±0.3, p=0.043). There were no significant differences between the groups in terms of recovery data [time to spontaneous breathing (p=0.21), time to extubation (p=0.113), time to eye opening (p=0.5), time to verbal response (p=0.518) and time to reach a Modified Aldrete score of 9 or 10 (minimum, 13.7±6.8 vs 13.6±5.2 vs 14.8±4, p=0.717)].

Conclusion: Limiting the flow rate of gas mixture to 0.5 L/minutes in low flow anaesthesia maintenance may facilitate reduced utilization of volatile anaesthetics without a compromise in hemodynamic status and recovery process.

Keywords: Anesthesia, inhalation, recovery period, sevoflurane

ÖZ

Amaç: Düşük akımlı anesteziyle ilişkili birçok araştırma yapılmış olsa da, operasyon sırasında takip verileri ve güvenlik sonuçları üzerine farklı akım hızlarının etkileri net olarak bilinmemektedir. Üçüncü basamak bir merkezde ürogenital sistem operasyonları sırasında uygulanan genel anestezi için düşük akımlı taze gaz karışımlarının farklı akım hızlarında kullanıldığı bu çalışmada, hemodinami, gaz değişim verileri ve derlenme zamanlarının gruplar arasında farklılık arz edip etmediği araştırılmıştır.

Gereç ve Yöntemler: Sevofluran ile düşük akımlı anestezi uygulanan ardışık altmış iki hasta (Amerikan Anestezistler Derneği skoru I veya II) üç grupta toplandı: A, orta akım (2 L/dk), B, düşük akım (1 L/dk), C, minimal akım (0,5 L/dk). Operasyon öncesinde ve sırasında kaydedilen hemodinamik verilere ek olarak, 30. dakika ve anestezi sonlandırılmadan hemen önceki gaz değişim ve arter kan gazı değerleri incelendi. Derlenme ikinci bir hekim tarafından gözlendi ve gerekli süreler not edildi.

Bulgular: Çalışma grupları arasında demografik özellikler benzerdi. Otuzuncu dakika ve anestezi sonlanımı öncesi vital bulgular, gaz değişim ve arter kan gazı analiz sonuçlarının çoğunluğu karşılaştırılabilir düzeydeydi. Operasyon sırasında, inspiratuvar sevofluran düzeyleri grup A'da anlamlı olarak daha yüksekti (% 1,7±0,6 ve 1,3±0,3 ve 1,3±0,3, p=0,043). Derlenme zamanları açısından gruplar arasında fark tespit edilmedi [spontan soluma zamanı (p=0,21), ekstübasyon zamanı (p=0,113), göz açma zamanı (p=0,5), sözel yanıt zamanı (p=0,518) ve Modifiye Aldrete skoru 9 veya 10'a ulaşmaya kadar geçen süre (dk, 13,7±6,8 ve 13,6±5,2 ve 14,8±4, p=0,717)].

Sonuç: Düşük akımlı anestezi idamesinde gaz karışımının akım hızını 0,5 L/dk'ya kadar düşürmek, hemodinamik istikrar ve derlenme sürecine ilişkin herhangi bir taviz vermeden volatil anestetik ajanların tüketiminin azaltılmasına yardımcı olabilir.

Anahtar kelimeler: Anestezi, inhalasyon, derlenme dönemi, sevofluran

Received/Geliş tarihi: 5.10.2017 | Accepted/Kabul tarihi: 29.12.2017

Address for Correspondence/Yazışma Adresi: Derya Özden Omaygenç, Yedikule Chest Diseases and Chest Surgery Training and Research Hospital, Clinic of Anesthesiology, İstanbul, Turkey

Phone/Telefon: +90 505 442 47 19 **E-mail/E-posta:** drderyaozden@yahoo.com **ORCID-ID:** orcid.org/0000-0003-1037-8915

Citation/Atıf: Kepekçi AB, Omaygenç DÖ, Karaca İO, Telli S, Yücepur S, Özenç E. Even Lower is Possible: Impact of Flow Rate on Safety Issues in Low Flow Anaesthesia. Bakırköy Tıp Dergisi 2019;15:15-23. <https://doi.org/10.4274/BTDMJB.galenos.2017.20171005064643>



INTRODUCTION

Low flow anesthesia, recently and repetitively drew interest in clinical practice thanks to constantly innovating anaesthetic techniques and monitoring devices. The method relies upon reinhalation at least 50% of a fresh gas mixture comprising volatile anaesthetics and oxygen sufficient, for providing metabolic demands which is obtained from expired gases after removal of CO₂ (1,2). Reduced costs, prevention of air pollution, and preserved body heat and moisture might be considered as main advantages of low flow anaesthesia (3,4). Moreover, anesthesia with low fresh gas flow improves the flow dynamics of the inhaled air and increase mucociliary clearance (5,6). From the financial point of view, routine administration of low flow anaesthesia can result in up to 75% reduction of expenditures (7). Along with the benefit of minimizing the emission of nitrous oxide -one of the major human derived ozone-depleting and heat-trapping gases-, global gas exposure of operation room personnel is decreased as well (4). Finally, risk of hypoventilation due to potential leaks, extensive system volume, the discrepancy between the delivered fraction and the inspired fraction of inhaled gases and the risk of accumulation of toxic compounds can be counted as main hazards (8).

Although these abovementioned issues about low flow anaesthesia had been investigated previously in general terms, safety of extremely low flow rates (namely 0.5 L/minutes for maintenance in our study) as compared to conventional rates were not specifically addressed. Regarding the rationale of establishing the lowest possible flow rate that may not jeopardize patients' well-being, we analysed the data (including hemodynamic state, gas exchange parameters and recovery time) of a sample population who underwent various urogenital system operations under inhalation anesthesia with different flow rates in a single tertiary centre.

MATERIALS AND METHODS

American Society of Anesthesiologists (ASA) score of I or II patients scheduled for elective urogenital operations under general anesthesia were enrolled for evaluation. Patient inclusion and randomization were carried out between February 2013 and October 2013 in a single tertiary health center and the study was approved by local Ethics Committee. Oral and written informed consent was obtained from all participants. 152 patients were evaluated

for eligibility to be involved in study population and 90 of them were excluded mainly because of not meeting the criteria about age limits and procedure times. Eventually 62 patients were found to be suitable and assembled in three distinct groups. The age of sample population ranged between 18-70 years old. In general anaesthesia volatile anaesthetic agents -sevoflurane and nitrous oxide- were invariably utilized. Individuals with ischemic heart disease and severely reduced contractile function -left ventricular ejection fraction <35%-, significant anemia, chronic obstructive lung disease, uncontrolled diabetes mellitus and arterial hypertension, morbid obesity, hepatic or renal failure were excluded. Besides extremes of age, drug or alcohol abusers, pregnant or lactating women, patients with a history of malignant hyperthermia and those with excessive procedure times ->4 hours- were postulated as unsuitable for investigation and had not been involved.

Patients were assigned to three groups according to flow rates by simple randomization with random digits. Sample size was determined in accordance with available resources and mid-term analysis results.

Features of the Operation Room and Anaesthetic Technique

The whole study population was premedicated with 1 mg midazolam thirty minutes before entering the room. A specific attention was paid to keep the room at a constant temperature of 21-22° C during the entire procedure. Before induction, rhythm with D2 derivation on electrocardiogram, non-invasive blood pressure and pulse oxymeter monitorizations were performed. MS13466E539D (Infinity® Delta, Dräger Medical Inc. Telford, USA) was used for continuous monitoring of hemodynamic and gas exchange parameters.

Potential leakages from anaesthesia circuits were checked and gas exchange monitors were calibrated before each procedure. The circuits and anti-bacterial filters were disposable. Inspiratory carbon dioxide (CO₂) level was strictly followed and as soon as the level reached to 1, soda-lime was immediately replaced.

All patients were oxygenized for 2 minutes with a flow rate of 4 L/minutes before induction. Fentanyl (1 mcg/kg), thiopental (6 mg/kg) and rocuronium (0.6 mg/kg) were given by intravenous route for induction. After administration of thiopental, patients had been ventilated manually with 100% O₂ until endotracheal intubation was performed.

Ventilation in volume control mode was provided by Dräger Primus® (Dräger Medizintechnik, Lübeck, Germany) anaesthesia system with a tidal volume of 7 mg/kg, respiration frequency of 12 breaths/minutes and positive end-expiratory pressure of 5 cm H₂O thereafter.

Anaesthesia maintenance was performed by inhalation of low flow fresh gas mixtures including sevoflurane, nitrous oxide and O₂. Content of gas mixture was set in pre-defined ratios regarding to the flow rate and taking this fact into account, entire population was gathered in three distinct groups.

In groups A, B and C, 40% O₂, 60% nitrous oxide and 2% sevoflurane mixture was administered with a flow rate of 4 L/minutes for 10 minutes. Then, flow rate of fresh gas mixture was reduced to 2 L/minutes and 1 L/minutes in group A and B, respectively. Sevoflurane concentration was kept between 1-2% during the rest of anaesthesia for these groups. Although flow rate of 2 L/minutes is accepted as upper limit of low flow anaesthesia, in our study design this group was named as moderate flow group. Group B, was defined as low flow group, instead. In group C, flow rate was reduced to 0.5 L/minutes after 10 minutes of initial high flow anaesthesia and unlike other groups, 60% O₂, 40% N₂O, 1-2% sevoflurane mixture was used for maintenance. This group was defined as minimal flow group.

Inhalation anaesthesia was ceased 10 minutes before termination of the procedure and at the end of operation, patients were ventilated with 100% O₂ at a flow rate of 6 L/minutes. When recovery of spontaneous breathing was observed, atropin (0.01 mg/kg) and neostigmin (0.02 mg/kg) were administered for decurarization.

Data Collection

Demographic characteristics including age, gender, body mass index, ASA score, surgical positions, and procedure times were noted for the study population. Blood pressure, oxygen saturation and heart rates of the patients were continuously monitorized and preprocedural, 30th minute and postprocedural values were recorded. Following intubation, via gas samples collected from Y connection, inspired and expired O₂, volatile agent concentrations; on vaporizer, percentage of administered inhalation anaesthesia and end-tidal CO₂ (ETCO₂); and on ventilator, age adjusted minimum alveolar concentration (MAC) values were monitorized and regularly recorded. Blood

samples were drawn for arterial blood gas analysis at the 30th minute and before cessation of anaesthesia.

Postoperative recovery process was observed and relevant data were collected by a second physician. Time to spontaneous breathing, time to extubation, time to eye opening, time to verbal response and time to reach a Modified Aldrete score of 9 or 10 were accepted as major determinants of recovery.

Statistical analysis

Statistical analyses were conducted using SPSS (version 17.0, SPSS Inc., Chicago, IL, USA). Data were expressed as mean ± standard deviation for continuous variables and percentage for categorical variables. Normal distribution of the data was tested by the Shapiro-Wilk test. Student's t-test was used for comparing the means of the numeric variables that showed normal distribution, while the Mann-Whitney U test was used for non-normally distributed samples. Associations of the categorical variables between groups were tested using chi-square test. For comparison of more than 2 groups, equality of the mean values was tested by One-Way ANOVA test. Statistical significance was defined as a p value <0.05 for all comparisons.

RESULTS

Sixty-two patients were assembled in three groups according to the flow rate of gas mixture. Demographic characteristics including age, gender, body mass index, ASA score, and procedure related factors like surgical position and operation time were similar among groups (Table 1). Moreover, preoperative hemodynamic parameters were comparable (Table 2).

Similarity of vital monitorization parameters of study groups persisted at 30th minute of operation. While ETCO₂ values were not different, inspiratory sevoflurane concentration and MAC of sevoflurane were significantly higher in group A. As expected partial oxygen pressure and oxygen saturation were higher in minimal flow group due to increased ratio of oxygen in gas mixture. In blood gas analysis apart from oxygenation parameters, all but lactate levels were similar. Lactate levels were higher in low flow and minimal flow groups (Table 3).

Hemodynamic and respiratory monitorization data were recorded again just before cessation of inhalation anaesthesia and blood gas parameters were re-assessed as well. These data were displayed in Table 4.

Table 1: Demographic characteristics of study groups

	Group A (n=21)	Group B (n=20)	Group C (n=21)	p value
Gender (male), n (%)	15 (71.4)	12 (60)	17 (80.9)	0.335
Age, years	51.0±12.7	49.4±12.6	55.9±15.8	0.296
BMI, kg/m²	27.1±5.3	29.5±6.0	26.3±3.8	0.133
ASA score, n (%)				
1	6 (28.5)	7 (35)	9 (42.8)	0.619
2	15 (71.4)	13 (65)	12 (57.1)	
Surgical position, n (%)				
Lateral	4 (19)	3 (15)	3 (14)	0.851
Supine	9 (42)	9 (45)	8 (38)	
Lithotomy	8 (38)	8 (40)	10 (47)	
Operation time, minutes	145.9±65.1	122.1±55.0	100.4±46.6	0,102

BMI: Body mass index, ASA: American Society of Anesthesiologists

Table 2: Preoperative hemodynamic data

	Group A (n=21)	Group B (n=20)	Group C (n=21)	p value
Systolic BP, mmHg	146.6±20.7	153.4±19.3	149.5±20.6	0.569
Diastolic BP, mmHg	87.9±15.6	94.2±17.7	88.3±11.7	0.336
Mean BP, mmHg	112.9±18.4	116.1±17.4	115.4±16.7	0.825
Pulse rate, bpm	78.5±12.3	81.3±15.3	76.0±11.8	0.142
SaO₂, %	98.2±1.9	97.7±1.4	97.9±1.2	0.253

BP: Blood pressure, SaO₂: Oxygen saturation**Table 3:** Hemodynamic parameters, respiratory monitorization and blood gas analysis data obtained at 30th minute of operation

	Group A (n=21)	Group B (n=20)	Group C (n=21)	p value
Mean BP, mmHg	89.1±15.9	92.6±13.7	94.5±20.1	0.575
Pulse rate, bpm	72.2±15.7	78.7±17.3	69.5±11.2	0.140
ETCO₂, mmHg	31.3±2.9	31.9±2.5	31.7±3.0	0.853
InsO₂, mmHg	39.6±1.3	39.1±1.6	52.7±4.3	<0.001*
Ins sevo, %	1.7±0.6	1.3±0.3	1.3±0.3	0.043*
MAC	1.3±0.3	1.1±0.1	0.9±0.2	<0.001*
pH	7.39±0.06	7.39±0.04	7.40±0.03	0.714
pO₂, mmHg	168.6±43.9	165.4±39.9	245.5±51.5	<0.001*
pCO₂, mmHg	38.5±3.0	37.4±3.7	38.9±4.2	0.434
SaO₂, %	168.6±43.9	165.4±39.9	245.5±51.5	<0,001*
Lactate, mmol/L	1.04±0.56	1.29±0.49	1.33±0.46	0.038*
Base excess	-2.06±3.48	-2.64±1.96	-1.03±2.18	0.186
COHb, %	1.33±0.46	1.27±0.32	1.39±0.52	0.967

BP: Blood pressure, ETCO₂: end-tidal carbon dioxide pressure, InsO₂: Inspiratory oxygen pressure, Ins sevo: Inspiratory sevoflurane concentration, MAC: Minimum alveolar concentration, pH: Power of hydrogen, pO₂: Partial pressure of oxygen, pCO₂: Partial pressure of carbon dioxide, SaO₂: Oxygen saturation, COHb: Carboxyhemoglobin

Table 4: Hemodynamic parameters, respiratory monitorization and blood gas analysis data obtained prior to cessation of anaesthesia

	Group A (n=21)	Group B (n=20)	Group C (n=21)	p value
Mean BP, mmHg	89.8±19.6	95.7±20.3	95.4±16.3	0.529
Pulse rate, bpm	71.5±18.4	72.5±12.9	68.8±12.8	0.657
ETCO ₂ , mmHg	31.9±3.2	32.6±3.4	31.9±3.1	0.275
InsO ₂ , mmHg	38.4±1.5*	35.0±2.0*	52.1±3.6	<0.001*
Ins sevo, %	1.6±0.5	1.3±0.4	1.3±0.3	0.180
MAC	1.3±0.3	1.2±0.2	1.0±0.2	0.001*
pH	7.38±0.07	7.38±0.05	7.39±0.03	0.599
pO ₂ , mmHg	165.6±41.8	152.7±64.3	227.9±46.7	<0.001*
pCO ₂ , mmHg	37.3±4.3	38.1±3.9	39.3±4.9	0.328
SaO ₂ , %	98.08±1.42	98.06±2.11	98.81±1.08	0.028*
Lactate, mmol/L	1.08±0.48	1.27±0.58	1.22±0.52	0.623
Base excess	-3.12±3.65	-3.82±2.21	-1.65±2.74	0.087
COHb, %	1.36±0.50	1.32±0.33	1.33±0.4	0.767

BP: Blood pressure, ETCO₂: End-tidal carbon dioxide pressure, InsO₂: Inspiratory oxygen pressure, Ins sevo: Inspiratory sevoflurane concentration, MAC sevo: Minimum alveolar concentration of sevoflurane, pH: Power of hydrogen, pO₂: Partial pressure of oxygen, pCO₂: Partial pressure of carbon dioxide, SaO₂: Oxygen saturation, COHb: Carboxyhemoglobin

Table 5: Recovery times of patients

	Group A (n=21)	Group B (n=20)	Group C (n=21)	p value
Time to spontaneous breathing, minutes	0.8±1.2	1.2±1.7	1.4±1.5	0.210
Time to extubation, minutes	3±2.4	4.1±2.5	4.9±3.7	0.113
Time to eye opening, minutes	6.8±4.5	7.3±3.6	8.2±3.5	0.500
Time to verbal response, minutes	9±5.5	8.8±3.9	10±3.8	0.518
Time to reach a Modified Aldrete score of 9 or 10, minutes	13.7±6.8	13.6±5.2	14.8±4	0.717

Values regarding oxygenation were still higher in group C at the end of operation. Not inspiratory concentration but MAC of sevoflurane was lower in this group. Difference at lactate levels favoring group A at 30th minute was eventually diminished and lost statistical significance.

Time to spontaneous breathing, time to extubation, time to eye opening, time to verbal response and time to reach a Modified Aldrete score of 9 or 10 were determined as indicators of recovery. And there were no statistically significant differences among groups regarding these data (Table 5).

DISCUSSION

Main goals of anaesthesia practice are appropriate induction phase without causing hemodynamic deterioration, maintenance of perioperative stability, rapid recovery free of side effects and early mobilization (9).

Low flow anaesthesia had been authenticated for meeting these properties in addition to various advantages like reduced gas consumption which leads to reduced costs, less personnel exposure and less pollution, preserved heat and humidity of respiratory system and improved flow dynamics (2,4).

In conventional low flow anaesthesia, inhalation agents such as sevoflurane, isoflurane and desflurane are widely used (10,11). Sevoflurane is one of the safest volatile anesthetic agents with the desirable properties of rapid uptake and elimination due to its low blood/gas solubility which makes it favorable for this technique (12,13).

Increased health expenditures and air pollution are two major entities that accentuated the usage of low flow technique. Approximately 80% of volatile anaesthetics are eliminated without utilization in high flow anaesthesia. Not only the ozone layer but also the operation room staff is directly influenced from this adversity (14).

Aside from these facts, preserving the heat and moisture of gas mixtures is another advantage of low flow technique. Modulating the gas climate via this method improves the functionality of ciliary epithelium and mucus clearance. Keeping the heat is also crucial for avoiding postoperative hypothermia (15).

Another keypoint of proper anaesthetic management in low flow systems is maintenance of humidity in absorbent agent to keep CO production in clinically insignificant levels (15). In response to superiority of wet absorbents over dry agents on anaesthetic gas degradation properties which favor their utilization in low flow systems, these systems help keeping humidity by increasing generation of additional water during re-breathing phase (16). Fang et al. encouraged utilization of fresh gas flow below 2-3 L/minutes to prevent the absorbent from accidentally drying process (17). A randomised investigation on 1258 subjects supported this finding and reducing the flow rate down to 0.5 L/minutes after induction resulted in COHb levels of 1.22 ± 0.98 % at 30th minute and this endpoint had not been altered by the time passed since absorbent had been replaced even if the replacement had been constantly executed once a week (18). Moreover, in a different investigation usage of extremely low gas flow rates and once a week replacement of absorbent did not yield a significant or critical rise at COHb levels (19). We preferred to change soda lime when CO₂ level at inspiratory gas mixture (FiCO₂) reached 1 with the advantage of CO₂ monitoring ability of devices. COHb levels were similar among groups and none of them was above the limits.

Risk of hypoxia should also be concerned in low flow anaesthesia. According to Brody's equation oxygen consumption of an unanaesthetized healthy individual weighing 70 kg is 250 mL/minutes (20). Spiess investigated the effect of depth of anaesthesia and certain agents on oxygen consumption in low flow anaesthesia and declared that during minimal flow anaesthesia oxygen consumption was reduced to 165 mL/minutes at 1 MAC (21). As gas flow rate decreases, gradient between oxygen content and inspired oxygen concentration gradually increases. To avoid hypoxemia precisely and to maintain a constant oxygen supply FiO₂ should be kept over 30% at least (22). Grote denoted the necessity of increasing the O₂ flow to 0.6 L/minutes when total gas flow was 1 L/minutes particularly for the operations lasting more than an hour.

Besides, they did not recommend routine monitorization of oxygenation in low flow anaesthesia if FiO₂ levels had been set in pre-defined rates (23). In 1998, Frink and Kharash also mentioned about the risk of hypoxia when low flow anaesthesia with sevoflurane mixture was administered (24). In our study design, to consider this issue, in moderate and low flow groups FiO₂ was kept at 40% and in minimal flow group it was 60%. We preferred to monitorize FiO₂ levels and other oxygenation parameters and observed that in minimal flow group these were significantly higher than others. Regarding these findings, if gas flow rate will be reduced to 1 L/minutes, we recommend setting the initial gas fractions as 50% O₂ and 50% N₂O for operations over 1 hour, especially when FiO₂ monitorization is not available.

Depth of anaesthesia is another key parameter to compare during general anaesthesia with different flow rates of fresh gas mixtures. Depth is clinically assessed by sympathetic and somatic response to painful stimuli. Indicators of sympathetic stimulation are gradual increase in systolic arterial pressure and heart rate, diaphoresis and alterations of pupil diameter. Sustained utilization of neuromuscular blocking agents suppress somatic response and narcotic analgesics alter pupillary response, thus precludes accurate evaluation. Particularly in low flow anaesthesia, regarding the fact that inspired and expired gases are constantly merged, inspired gas concentration is not precisely concordant with vaporizer settings. As a result, modulating anaesthesia depth is troublesome unless continuous gas monitorization is available (25-27). We evaluated the depth of anaesthesia by following heart rate and arterial blood pressure along with inspiratory sevoflurane monitorization. No statistically significant difference was reached among study groups according to hemodynamic data. Although inspiratory sevoflurane concentration was higher in moderate flow group at 30th minute, this gap was reduced and lost statistical significance at the end of anaesthesia. Several other studies investigating the effect of low flow desflurane anaesthesia on perioperative blood pressure and heart rate measurements in pediatric and adult population exist in the literature. They did not report a marked diversity either, even when low flow technique was used (28,29).

Tokgoz et al. stated in their trial comparing high flow and low flow anaesthesia that lactate values at blood gas analysis were apparently higher in low flow group (30). In

our study, similar findings were attained. Although there was a statistical significance favoring moderate flow at the early phase of operation, before cessation of anaesthesia lactate levels were only tended to be lower in this group. Fortunately, all these values were in normal ranges and we reached a decision that this distinction had not indicated an evident deprivation in tissue oxygenation especially when similarities between oxygen transportation parameters among groups were considered.

For terminating anaesthesia, infusion of volatile anaesthetic agents to fresh gas mixture might be halted 15-30 minutes prior to cessation of surgical intervention by turning the vaporizer off while preserving the total fresh gas volume. This situation is based on extent of time constant. Thereby, the slower gas flows, the slower inhaled agent concentration reduces. After these arrangements at the very end of the procedure, adjustable pressure limiting valve is opened and O₂ flow rate is enhanced to 4-6 L/minutes to eliminate anaesthetic gases and get prepared for recovery (15).

Recovery in inhalation anaesthesia is associated with multiple factors like liposolubility, concentration, utilization period of the agent and individual alveolar ventilation rate. Early recovery occurs approximately in 15 minutes after inhalation anaesthesia of 2 hours duration (31,32). It is crucial to denote that inhaled agents constitute a certain part of balanced general anaesthesia, thus several other entities play role in recovery process (32,33). Hence for research purposes, merely following a fixed inhalation anaesthesia protocol as well as standardizing opioid and neuromuscular blocking agent amounts can provide a self-directed recovery to some extent.

Lastly, one of the main goals of our investigation was to determine whether gradual decrease in gas flow rate had deleterious effects on recovery status. Time consumed for various recovery indicators like time to extubation, time to eye opening and time to orientation -namely modified Aldrete score of 9 or 10- were used for assessment. Recovery times in all study groups were comparable with previous similar studies performed with conventional flow rates of gas mixtures (>3 L/minutes) involving sevoflurane (26,34,35).

Limited numbers of studies utilizing low flow gas mixtures and considering recovery as an endpoint exist in the literature. Elmicioğlu et al. stated that low flow anaesthesia

utilizing desflurane might be safely administered to patients with ASA score I or II. They also emphasized that low flow anaesthesia had no adverse effect on hemodynamic stability and recovery phase irrespective of the flow rates (0.5, 1 and 2 L/minutes) and could be an alternative to conventional inhalation anaesthesia (29). Okada et al. reported the safety of 3% sevoflurane, 50% nitrous oxide and 50% O₂ mixture administered at a flow rate of 600 mL/minutes without the risk of hypoxia and retarded recovery (36). Our research verified the fact that reducing the flow rate even to 0.5 L/minutes did not elicit a significantly prolonged recovery phase for low flow anaesthesia utilizing sevoflurane.

Study Limitations

Relatively small study population should be considered as main limitation of the study. Randomizing the individuals from a specific surgical procedure, brief randomization interval and strict exclusion criteria led to this situation. But it was mandatory to minimize the variables that may alter the results about such a multifactorial process. Apart from that anaesthesia depth was evaluated with indirect parameters instead of Bispectral Index monitorization due to unavailability of the device. Finally, oxygen concentration of the gas mixture could be set to a value lower than %60 for minimal flow group. Concerns about the risk of hypoxia in this group led to iatrogenic hyperoxia during anaesthesia.

CONCLUSION

Widespread utilization of low flow anaesthesia is a cornerstone for the evolution of inhalation anaesthesia regarding the cost reduction efforts of public health policies and conservation of the personnel's health and air purity. From this point of view, it is reasonable to suggest that less is better. Usage of semi-closed breathing systems, proper selection of cuffed endotracheal tubes and paying special attention on leakages may substantially decrease gas exposure during low flow anaesthesia. Here we report the safety -by means of avoiding hypoxia, acidosis, hemodynamic disturbance and retarded recovery phase- of administering gas mixtures with sevoflurane even at very low flow rates which meet the needs of modern inhalation anaesthesia. Obviously, verification with larger study populations is required to express more precise statements.

Etik**Etik Kurul Onayı:** Haseki EAH etik kurulu, No:56**Hasta Onayı:** Alındı.**Çıkar Çatışması:** Yok**Finansal Destek:** Yok**REFERENCES**

- Eger EI II. Uptake and distribution. In: Miller RD (Ed.) Anesthesia. 6th ed. Philadelphia: Elsevier Churchill Livingstone; 2005:131-53.
- Baum JA, Aitkenhead AR. Low-flow anaesthesia. *Anaesthesia* 1995;50:37-44.
- Nunn G. Low-flow anaesthesia. *Contin Educ Anaesth Crit Care Pain* 2008;8:1-4.
- Baum JA. Low-flow anaesthesia: Theory, practice, technical preconditions, advantages, and foreign gas accumulation. *J Anesth* 1999;13:166-74.
- Aldrete JA, Cubillos P, Sherrill D. Humidity and temperature changes during low flow and closed system anaesthesia. *Acta Anaesthesiol Scand* 1981;25:312-4.
- Kleemann PP. Humidity of anaesthetic gases with respect to low flow anaesthesia. *Anaesth Intensive Care* 1994;22:396-408.
- Suttner S, Boldt J. Low-flow anaesthesia. Does it have potential pharmacoeconomic consequences? *Pharmacoeconomics* 2000;17:585-90.
- Tempia A, Olivei MC, Calza E, Lambert H, Scotti L, Orlando E, et al. The anesthetic conserving device compared with conventional circle system used under different flow conditions for inhaled anaesthesia. *Anesth Analg*. 2003;96:1056-61.
- Ceylan A, Kirdemir P, Kabalak A, Aksu C, Baydar M, Gögüs N. Comparison of arterial carboxyhemoglobin, hemodynamic and recovery characteristics of low flow desflurane and sevoflurane anaesthesia. *Gulhane Medical Journal* 2004;46:294.
- Kharasch, ED, Thummel KE. Identification of cytochrome P450 2E1 as the predominant enzyme catalyzing human liver microsomal defluorination of sevoflurane. *Anaesthesiology* 1993;79:795-807.
- Eger, EI 2nd. New drugs in anaesthesia. *Int Anesthesiol Clin* 1995;33:61-80.
- Bito H, Ikeda K. Renal and hepatic function in surgical patients after low-flow sevoflurane or isoflurane anaesthesia. *Anesth Analg* 1996;82:173-6.
- Philip BK, Kallar SK, Bogetz MS, Scheller MS, Wetchler BV. A multicenter comparison of maintenance and recovery with sevoflurane or isoflurane for adult ambulatory anaesthesia. *Anesth Analg* 1996;83:314-9.
- Baum JA. What are the ecological benefits of low flow anaesthesia? In: Baum JA (Ed). *Low-Flow Anaesthesia with Dräger Machines*, 2nd Ed. Drägerwerk AG, Lübeck, 1993:52.
- Baum JA. Low Flow Anaesthesia: The Theory and Practice of Low Flow, Minimal Flow and Closed System Anaesthesia, 4th ed. Oxford: Butterworth-Heinemann; 2001.
- Eger EI II, Ionescu P, Gong D. Circuit absorption of halothane, isoflurane and sevoflurane. *Anesth Analg* 1998;86:1070-4.
- Fang ZX, Eger EI II, Laster MJ, Chortkoff BS, Kandel L, Ionescu P. Carbon monoxide production from degradation of desflurane, enflurane, isoflurane, halothane, and sevoflurane by soda-lime and baralyme. *Anesth Analg* 1995;80:1187-93.
- Baum J, Sachs G, vd Driesch C, Stanke HG. Carbon monoxide generation in carbon dioxide absorbents. *Anaesth Analg* 1995;81:144-6.
- Morita S. Inspired gas contamination by non anaesthetic gases during closed circuit anaesthesia. *Circular* 1985;2:24-5.
- Brody S. *Bioenergetics and Growth*. New York: Reinhold Publishing Corp; 1945.
- Spieß W. Oxygen consumption and intake of nitrous oxide and volatile anaesthetics. In: Lavin P, H von Aken, U Schneider, *Alternative methoden der anaesthesia* Theime Stuttgart: INA-Schriftenreihe Bd.; 1985:8-18.
- Hendrickx JFA, Cooman DS, Vandepuot DM, et al. Air-oxygen mixtures in circle systems. *Journal of Clinical Anesthesia* 2001;13:461-4.
- Grote B. Principles of the closed system inhalation anaesthesia. In: Hossli G, Frey P, Kreienbühl G(Ed.) *ZAK Zurich, Band II*. Zurich: Springer Verlag; 1983:137-42
- Frink EJ, Kharash E. Sevoflurane in low flow anaesthesia. In: *Low flow anaesthesia and the role of sevoflurane: A contemporary clinical perspective*, Adis International Inc. 1998:25-40.
- Gögüş D, Göksu S, Öner Ü, Altıntaş F. Administration of low flow anaesthesia. *Klinik Gelişim* 1999;12:813-16.
- Gowrhe-Mohan S, Chakrabarti MK, Lockwood GG. The estimation of inspired isoflurone concentration in a low flow system. *Anaesthesia* 1995;50:706-8.
- Christina MB. Clinical comparison of sevoflurane and isoflurane when administered with nitrous oxide for surgical procedures of intermediate duration. *Can J Anaesth* 1995;42:1991-5.
- Yıldız TŞ, Baykara N, Bozkurt N, Oysu DA, Solak M, Tokar K. Impact of clonidine on tremor in low-flow desflurane anaesthesia, *Türk Anest Rean Der Dergisi* 2005;33:29-35.
- Elmacioğlu MA, Göksu S, Koçoğlu H, Öner U. Effect of flow rate on hemodynamic parameters and agent consumption in low-flow desflurane anaesthesia: An open labels prospective study in 90 patients. *Current Therapeutic Research* 2005;66:4-12.
- Tokgöz N, Ayhan B, Sarıcaoğlu F, Akıncı SB, Aypar U. Comparison of low and high flow desflurane anaesthesia in pediatric population. *Türk J Anaesth Reanim* 2012;40:303-9.
- Xie G, Jiang H. Clinical study of desflurane on low flow anaesthesia compared with sevoflurane and enflurane. *Chin Med* 1997;110:707-10.
- Aitkenhead AR, Smith G. *Textbook of Anesthesia*, 6th ed. London: Churchill Livingstone; 2013.

33. Tarazi, EM, Philip BK. A Comparison of recovery after sevoflurane or desflurane in ambulatory anesthesia. *J Clin Anesth* 1998;10:272-7.
34. Nathanson MH, Fredman B, Smith I, Whie PF. Sevoflurane versus desflurane for outpatient anesthesia. A comparison of maintenance and recovery profiles. *Anesth Analg* 1995;81:1186-90.
35. Philip BK. Multicenter Comparison of Maintenance and Recovery with Sevoflurane or Isoflurane for Adult Ambulatory Anesthesia. *Anesth Analg* 1996;83:314-9.
36. Okada K, Asano N, Kimura O, Okada H, Nishio S, Wakusawa R. Low flow anesthesia using a fresh gas flow of 600 mL.min⁻¹ for 5 hours. *Masui* 1997;46:1321-8.