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ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

Influence of sevoflurane on hemodynamic parameters in low flow anesthesia applied without nitrous oxide

Azotprotoksitsiz uygulanan düşük akımlı anestezide sevofluranın hemodinamik parametreler üzerine etkisi

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ABSTRACT

Objective: In this study, it was aimed to investigate the hemodynamic effects of sevoflurane in low flow anesthesia (LFA) without nitrous oxide.

Methods: A total of 40 ASA I-II patients aged between 18-70 years were included in this study. Patients were randomly allocated to two groups. Group 1 (LFA with nitrous oxide) was applied preoxygenation with 10 L/min 100% O_2 for 2 min. After preoxygenation, 4-7 mg/kg pentothal, 0.1 mg/kg vecuronium bromide and 1 µg/kg fentanyl were applied respectively via intravenous route. Endotracheal intubation was applied 3 min later after induction. 4 L/min (50% O_2-50% N_2O) normal flow had been applied within the first 10 min of the operation following intubation, it was switched to 1 L/min (50% O_2-50% N_2O) low flow. Sevoflurane concentration was set as 0.8-1 MAK so as to keep mean blood pressure (MBP) within ± 20% limits. In Group 2 (LFA without nitrous oxide) all procedure was the same with Group I except that air was used instead of N_2O. Heart rate (HR), MAP, SPO_2 and $ETCO_2$ values were recorded just after intubation and following 15, 30, 45 and 60. min and switched to 4 L/min of normal flow 15 min before termination of the operation.

Results: There were no significant differences between the groups from measurement after induction to 60 min measurement in terms of systolic blood pressure (SBP) and $ETCO_2$. Values in Group I were found greater than those in Group II at 15 min measurement in terms of diastolic blood pressure (DBP), MAP and HR ($p<0,05$). No complications were encountered in patients.

Conclusion: We concluded that preferring LFA techniques applied without N_2O, with sevoflurane is beneficial if proper conditions are provided. *J Clin Exp Invest 2014; 5 (1): 12-17*

Key words: Low flow anesthesia, nitrous oxide, sevoflurane, hemodynamic parameters

ÖZET

Amaç: Bu çalışmada azotprotoksitsiz (N_2O) düşük akımlı anestezide (DAA) sevofluranın hemodinamik açıdan etkilerini araştırılması amaçlandı.

Yöntemler: Bu çalışmaya ASA I-II, 18-70 yaş arası 40 hasta dahil edildi. Hastalar rastgele iki gruba ayrıldı. Grup I'e (Azotprotoksitli DAA) 10 L/dk %100 O_2 ile 2 dk preoksijenizasyon uygulandı. Preoksijenizasyon sonrası, intravenöz yoldan sırası ile 4-7 mg/kg pentotal, 0,1 mg/kg veküronyum ve 1 µg/kg fentanil uygulandı. 3 dk sonra endotrakeal entübasyon uygulandı. Entübasyonu takiben operasyonun ilk 10 dakikasında, 4 L/dk (%50 O_2-%50 N_2O) normal akım uygulandıktan sonra, 1 L/dk (%50 O_2-%50 N_2O) düşük akıma geçildi. Sevofluran konsantrasyonu, 0,8-1 MAK olarak preoperatif ortalama kan basıncı (OKB) ± %20 sınırlarında tutacak şekilde ayarlandı. Grup 2 (Azotprotoksitsiz DAA) ile Grup I arasında yapılan tüm işlemler, Grup 2'de N_2O yerine hava kullanılması dışında aynı idi. Entübasyondan hemen sonra ve takip eden 15, 30, 45. ve 60. dakikalarda, hastaların kalp atım hızı (KAH), OKB, SpO_2 ve $EtCO_2$ değerleri kaydedilerek operasyonun bitimine 15 dakika kala tekrar 4 L/dk normal akıma geçildi.

Bulgular: Sistolik kan basıncı (SKB) ve $EtCO_2$ değerleri bakımından; indüksiyon sonrası ölçümünden 60. dk. ölçüme kadar gruplar arasında anlamlı farklılık bulunamadı. Diyastolik kan basıncı (DKB), OKB ve KAH değerleri bakımından; 15. dk ölçümünde Grup 1'deki değerler Grup 2'ye göre daha yüksek bulundu ($p<0,05$). Hastalarda herhangi bir komplikasyona rastlanmadı.

Sonuç: Uygun koşullar sağlanmak kaydıyla sevofluran ile uygulanan N_2O'siz DAA tekniklerinin anestezi uygulamalarında tercih edilmesinin yararlı olduğu kanısına vardık.

Anahtar kelimeler: Düşük akım anestezi, azotprotoksit, sevofluran, hemodinamik parametreler

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INTRODUCTION

The term 'low flow anesthesia (LFA)' is to give at least 50% of fresh oxygen flow to the patient together with sufficient amount of volatile anesthetics to meet the need of the body after CO_2 is removed from the gas mixture expired from the patient and it is a method applied with a semi-closed system reusing expiration air [1,2].

High standards of anesthesia machines, presence of monitores which continuously analyze the anesthetic gas content in detail, accumulating data about pharmacokinetics and pharmacodynamics of inhalation anesthetics have largely facilitated the safely use of low flow anesthesia [3].

Nitrous oxide (N_2O) has been used together with volatile anesthetics in general anesthesia for more than 150 years. Use of N_2O which has been accepted as the ideal anesthetic for long years is gradually been questioned today. Mainstays of this include drawbacks from the known side effects, introduction of new proper agents and to be able to apply low flow anesthesia easier and safely [4,5].

Effects of N_2O in recovery period has been mainly addressed in postoperative nausea-vomiting axis. No comprehensive studies investigating its effect on hemodynamic parameters have been encountered.

In our study, we aimed to investigate the hemodynamic effects of sevoflurane in LFA without N_2O.

METHODS

This prospective randomized double-blind study was conducted in Department of Anesthesiology and Reanimation, Eskişehir Osmangazi University Medical Faculty after ethics committee approval (11-06-2009 / 248) and written informed consent of the patients had been obtained. This study was conducted on forty healthy patients. İnclusion criteria were American Society of Anesthesiologists (ASA) class I-II, age 18 to 70 years, scheduled elective ear-nose-throat operations under general anesthesia with an expected duration of 60 min. Patients who had cardiovascular, renal, hepatic and pulmonary problems, history of chronic analgesic use, obesity, alcohol and opioid addiction, allergy and who underwent emergent surgery were excluded from the study.

After the patients who were not applied premedication had been taken to operating table, soda lime of the Dräger brand of Primus anesthesia machine was renewed. Leak control of anesthesia machines and calibration of gas monitors were done. Appropriate fluid replacement was done for the patients. Preoperative electrocardiography (ECG), heart rate (HR), sytolic blood pressure (SBP), mean arterial pressure (MAP), diastolic blood pressure (DBP) and peripheral oxygen saturation (SPO_2) values of the patients were recorded. After preoxygenation with 10 L/min 100% O_2 for 2 min, 4-7 mg/kg pentothal, 0.1 mg/kg vecuronium bromide and 1 µg/kg fentanyl were applied respectively via intravenous route. Bispectral index (BIS) monitorization (The Aspect Medical Systems A-2000™ BIS® Monitor) was used to measure the depth of anesthesia for all patients. Endotracheal intubation was applied 3 min later after induction. Patients were randomly divided by using concelead envelopes to two groups as Group 1 (LFA with nitrous oxide) and Group 2 (LFA without nitrous oxide) with 20 patients in each. After the intubation, it was switched to 1 L/min low flow anesthesia (50% O_2-50% N_2O) after 4 L/min of normal flow (50% O_2-50% N_2O) had been applied within the first 10 min of the operation in Group I. Sevoflurane concentration was set at 0.8-1 MAC so as to keep MAP within ± 20% limits. In both groups fentanyl was given as loading dose in induction (1 µg/kg). Between the groups, the only difference is; in Group 2, air was used instead of N_2O. During anesthesia, the concentration of level of sevoflurane has been adjusted according to BIS value 40-60. In both groups, HR, MAP, SpO_2, end tidal carbon dioxide ($EtCO_2$) values of the patients were recorded. 4 L/min of normal flow was started again 15 min before the end of the operation and the patient was ventilated. At the end of the operation, anesthetic gases were discontinued, fresh gas flow was done 6 L/min 100% O_2 and patients were extubated. Patients were evaluated in terms of parameters like spontaneous respiration, eye opening, response to verbal orders, airway sensitivity, cough reflex and possible side effects and sent to recovery room.

Recovery in term of orientation was assessed in the recovery room using a modified Aldrete scoring system (Level of Consciousness; Fully awake, orientated in place and time scored 2, Rousable on calling name scored 1 Not responding scored 0. Activity; Moving all four limbs on command scored 2, Moving two limbs spontaneously scored 1, Not moving at all scored 0. Respiration; Breathes and coughs well scored 2, Dyspnea or tachypnea scored 1, Apnea scored 0. Circulation; BP +/- 20% of pre-anesthetic value scored 2, BP +/- 20 – 49% of pre-anesthetic value scored 1, BP +/- 50% of pre-anesthetic value scored 0. Saturation; SpO_2 > 92% on room air scored 2, O_2 required to keep SpO_2 at 90% scored 1, SpO_2 < 90% with O_2 scored 0). Patients were evaluated at 10 minute intervals in re-

covery room by an observer blinded from the anesthetic used until the patients were transferred to the clinics. Nurses and patients were also blinded to the modified Aldrete score (MAS). When patients have score 9 of Modified Aldrete Scoring they have been considered to be able to leave the recovery unit.

Statistical Analysis

Data analysis was done with SPSS (Statistical Package for Social Sciences) for Windows 15.0 program. All values were expressed as mean ± standard deviation (SD). In presence of two groups in comparison of quantitative data, independent samples t-test was used for inter-group comparison of normally distributed parameters and Mann-Whitney U test was used for inter-group comparison of parameters not showing normal distribution. The power of the study was performed using by G power package program and found 0.87 (n1= 20, n2= 20, effect size (d)= 1, α = 0.05, Power (1-β)= 0,87). P<0.05 value was considered to be statistically significant.

RESULTS

A significant difference was not found between groups in terms of demographic data (p>0.05) however anesthesia and operative time were found significantly longer in Group 1 than the Group 2 (p<0.05) (Table 1).

A significant difference was not found between groups in terms of SBP from control measurement to post-extubation measurement (p<0.05) (Table 2).

DBP, MAP and HR values in Group 1 were found greater than those in Group 2 for 15 min measurement (p<0.05). There was not a difference between groups in terms of other measurements (p>0.05) (Table 3, Figure 1).

SpO_2 values were found lower in Group 1 compared to Group 2 at control measurement (p<0.05). There was not a difference between groups in terms of other measurements (p>0.05) (Table 4).

A difference was not found between groups in terms of $EtCO_2$ values from post-induction measurement to 60 min measurement (p>0.05) (Table 5).

In Group 1 and Group 2, MAS 40 min. values are ≥ 9. There were not a significant differences between the groups in term of MAS values.

Side effects were encountered in no patients. In addition, no patients reported remembering the events during the operation, being aware or dreaming.

Table 1. Demographic data (mean±SD)

	Group 1 (n=20)		Group 2 (n=20)		p
	Mean ±	SD	Mean ±	SD	
Age (year)	40.6 ±	15.2	38.8 ±	14.0	0.820
Kilogram(kg)	72.5 ±	10.1	75.7 ±	9.3	0.341
ASA	17/3		18/2		0.500
Duration of anesthesia (min)	104 ±	27.7	86.2 ±	29.1	0.011
Duran of surgery (min)	95.2 ±	25.2	79.8 ±	27.1	0.010

Table 2. Sytolic blood pressure values (mmHg) (mean±SD)

SBP	Group 1 (n=20)		Group 2 (n=20)		p
	Mean ±	SD	Mean ±	SD	
Control	131.25 ±	16.27	135.65 ±	13.10	0.273
Post induction	120.05 ±	16.94	122.05 ±	19.93	0.490
Post entubation	143.20 ±	17.08	140.95 ±	28.93	0.978
15. min.	119.95 ±	19.39	108.50 ±	22.33	0.058
30. min.	123.85 ±	18.11	111.85 ±	21.09	0.074
45. min.	113.35 ±	17.39	111.45 ±	18.28	0.787
60. min.	107.40 ±	16.52	109.75 ±	20.91	0.675
Post extubation	130.45 ±	20.76	132.60 ±	18.41	0.787

Table 3. Mean arterial pressure values (mmHg) (mean±SD)

MAP	Group 1 (n=20)		Group 2 (n=20)		p
	Mean ±	SD	Mean ±	SD	
Control	94.45±	12.79	98.00±	12.74	0.329
Post induction	89.90±	15.63	88.25±	19.36	0.860
Post entubation	108.50±	15.43	109.7±	25.90	0.665
15. min.	89.25±	15.83	77.90±	16.96	0.031*
30. min.	96.55±	17.81	84.75±	20.80	0.058
45. min.	88.90±	18.24	82.75±	15.10	0.364
60. min.	81.75±	14.99	78.15±	18.17	0.626
Post extubation	98.55±	18.43	95.20±	14.82	0.507

* p< 0.05, MAP: mean arterial pressure

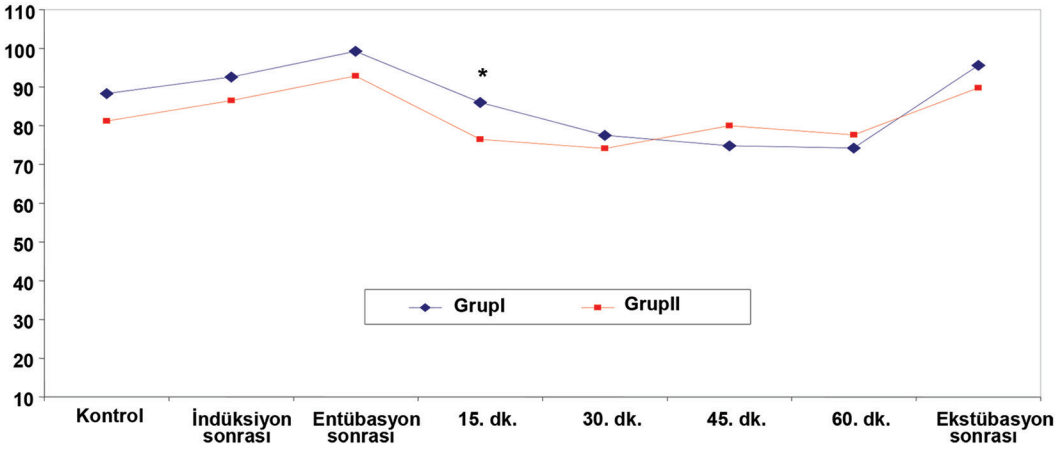

Figure 1. Heart rate values (beat/min)

Table 4. Peripheral oxygen saturation values (%) (mean±SD)

(SPO_2)	Group 1 (n=20) (mean± SD)	Group 2 (n=20) (mean± SD)	p
Control	98.60 ± 1.50	99.50 ± 1.19	0.018*
Post induction	99.20 ± 1.24	99.70 ± 0.73	0.095
Post entubation	99.05 ± 1.19	99.00 ± 1.08	0.772
15. min.	98.95 ± 1.10	98.75 ± 1.12	0.572
30. min.	99.10 ± 1.21	98.70 ± 1.49	0.371
45. min.	98.95 ± 1.43	98.25 ± 1.52	0.097
60. min.	98.85 ± 1.46	98.15 ± 1.53	0.112
Post extubation	99.10 ± 1.37	98.20 ± 3.62	0.381

* p< 0.05

Table 5. $EtCO_2$ values (mmHg) (mean±SD)

$EtCO_2$	Group 1 (n=20)		Group 2 (n=20)		p
	Mean ±	SD	Mean ±	SD	
Post induction	27.50 ±	4.10	26.60 ±	3.94	0.328
Post entubation	32.60 ±	4.19	33.05 ±	4.85	0.606
15. min.	31.60 ±	4.31	33.60 ±	3.72	0.145
30. min.	31.85 ±	3.67	33.45 ±	3.85	0.144
45. min.	31.15 ±	4.44	33.15 ±	3.80	0.158
60. min.	30.80 ±	4.94	31.90 ±	5.04	0.350

DISCUSSION

Development of modern anesthesia devices, presence of detailed gas monitorization, increased environmental sensitivity, introduction of novel beneficial but expensive inhalation anesthetics and limited economic sources for medical care have led to a tendency to low flow anesthesia techniques during the recent 20 years and this tendency should be encouraged [6].

Continuous monitorization of airway pressure, expired gas volume, carbondioxide concentration and oxygen saturation is mandatory according to European standards. A safe anesthesia is possible through these monitorizations during application of low flow anesthesia techniques [7]. Tokgöz et al reported that low-flow anaesthesia, accompanied by close monitoring of blood gases and lactate levels and the use of appropriate techniques and devices, can be applied safely in children [8]. In our study, we also considered that LFA technique is a hemodynamically safe and stable method. In inter-group comparison, while a significant difference was not seen in SBP, SpO_2 and $EtCO_2$ values, although significant differences are seen in 15 min values of DBP, MAP and HR compared to pre-induction period in Group II, this difference was in clinically normal ranges.

Removal of nitrogen begins with its replacement with N_2O-O_2 mixture [9]. Therefore, high flow should be applied for a certain time at the beginning although low flow anesthesia technique is preferred. High flow was applied for the first 10 min in LFA applied groups also in our study. Physico-chemical properties of the inhalation agent also gain importance at this stage [10]. The most important factor for us to prefer sevoflurane in our study is its physico-chemical superiorities arising from its low solubility in the blood.

In low flow anesthesia, the main factor, which leads the anesthetists to avoid from routine use of LFA is the fear for hypoxia beside the worries about adequate administration of inhalation agent and hemodynamic stability. In LFA application, inspired O_2 concentration should certainly be reduced

when flow is reduced without fresh gas mixture is changed. When the flow is reduced, ratio of O_2 concentration in fresh gas content should be increased in order to maintain adequate O_2 concentration in inspired gas [11].

According to Baum et al. [12], O_2 flow is recommended as 1.4 L/min and N_2O flow 3 L/min in high fresh gas flow period during the beginning phase which takes approximately 10-15 min. In most patients, this fresh gas composition warrants at least 30% O_2 in inspired air. Re-ventilation significantly increases with reduced flow. Inspiration gas also includes expiration air, which has a low O_2 concentration. Low O_2 ratio in gas mixture is compensated by increasing fresh gas O_2 concentration and this should certainly be done when flow is being reduced. According to this, fresh gas O_2 concentration should be elevated to 50% (min 40%) in LFA for a safe oxygenation.

In our study, fractioned oxygen (FiO_2) concentration was kept at 50% during high flow and following low flow periods. Anesthesia was applied so as to keep safety alarm systems of anesthesia machine. According to our data, hypoxia was encountered in no patients with pulse oxymeter monitorization which we applied routinely in both groups. Minimum SpO_2 value was seen to be 94% during follow up times of all patient groups. In addition, $EtCO_2$ monitorization was also done for all patient groups during anesthesia and no difference was seen in in-group and inter-group comparisons. Similarly to our study, Gedik et al. [13] reported that SpO_2 value reduced below 98% in no groups in LFA methods in which sevoflurane was applied with N_2O:O_2 mixture and the method was reported to be safely. Kupisiak et al also concluded that the use of both low-flow and high-flow rate general anesthesia provided appropriate oxygenation of the central nervous system and hemodynamic stability in patients undergoing laparoscopic cholecystectomy [14].

Most anesthetists believe that N_2O is a main factor as it has a quite potent analgesic effect and shows a moderate but significant hypnotic effect together with other inhalation anesthetics, its use may reduce the doses of other anesthetics and opioids, it is rapidly removed from the system, it accelerates recovery with its dose-reducing effect, it prevents awareness during the operation and it suppresses spinal reflex movements due to severe surgical stimulation [15].

However the common opinion that this gas can be used completely unproblematically has begun to be questioned. Diffusion of N_2O into gas-containing areas in long-standing abdominal operations may lead to intestinal distention, significant reduction of myocardial contractility in patients with impaired coronary perfusion, myeloneuropathy in patients with vitamin B12 deficiency and it is contraindicated in pregnant women in the first two trimeters due to proven harmful effects on DNA synthesis. In addition, N_2O is not ecologically inert; it is known to give significant harm to atmosphere [15]. Ryan and Nielsen applied mathematical projections and calculated global warming potential (GWP) for the drugs by using the infrared absorption of the inhaled agents. Highest GWP was recorded with Nitrous oxide but desflurane was the culprit of the inhaled agents [16]. Anesthesiologists should benefit from actual technology in order to minimize unnecessary use of N_2O [15].

Eger et al. and von Tramer et al. considered that not using N_2O could increase the risk of awareness during the operation [17,18]. Baum et al. emphasized based on their clinical experience of inhalation anesthesia without N_2O with more than 2700 cases that they did not see even one patient reporting awareness [19]. In our study, none of the patients reported remembering the operation, awareness or dreaming.

The study of Barçın et al revealed that patients had desired MAP levels, hemodynamic stability and safe inspiration parametres by using dexmedetomidine instead of nitrous oxide in LFA. They concluded that dexmedetomidine infusion with medical air-oxygen as a carrier gas represents an alternative anesthetic technique [20].

Effects of re-ventilation are also important. Cost is certainly important in health care, particularly in this era of weak economies and limited resources. It is known that use of low and minimal fresh gas flow results in lower cost [21]. According to the studies of Odin, it was detected that 1% of all hospital expenditures come from anesthesia department, anesthetic drugs consist 5.7% of total consumption of drug storage of the hospital and volatile anesthetics consist 20% of this [22]. So the most important factor for determination of the cost of inhalation anesthetic is the control of the anesthetist and consumption may be reduced as fresh gas flow is reduced [23].

In anesthesia application of Yıldırım et al. in Turkey, it was determined that 312 mL isoflurane, 574 mL sevoflurane, 1130 mL desflurane was used in LFA in which fresh gas flow applied for 8061 min was 1 L/min. 889 mL isoflurane, 1697 mL sevoflurane, 3320 mL desflurane was consumed when flow rate was 4 L/min [24]. Isoflurane consumption may decrease 65%, sevoflurane 67%, desflurane 66% when gas flow reduces from 4 L/min to 1 lt/min.

Hönemann et al presented that LFA techniques improve pulmonary dynamics of the anesthetic gases, increase mucocilliary clearance, maintain body temperature and reduce fluid loss [25]. Reduction of anaesthesia gas consumption provides lower impact on the ozone layer and decrease of greenhouse gas emissions.

In our study, not to be able to determine a valid indication for N_2O use beside its known many side effects has led us to suspect. We also concluded that not using N_2O did not differ from using it in terms of hemodynamic parameters, and provided economic and ecologic advantages. We determined that LFA applications are hemodynamically safe when required technical conditions are provided, and it reduced volatile anesthetic consumption.

In conclusion, we considered that preferring LFA techniques applied without N_2O, with sevoflurane is beneficial if proper conditions are provided.

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