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Evaluation of Low and High Flow Anesthesia Methods Effects on Perioperative Hemodynamics, Depth of Anesthesia and Postoperative Recovery in Patients Undergoing Abdominal Surgery

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Abstract:
Objective: The safe implementation of low-flow anesthesia has greatly facilitated, because of the anesthesia machines monitors that analyze the anesthetic gas composition detailed way, increase the knowledge of anesthetics. In this research; we aimed to compare the effects of high and low-flow general anesthesia methods on the peroperative hemodynamics, anesthesia depth and postoperative recovery time in patients with abdominal surgery in the presence of bispectral index monitoring.
Methods: ASA I-II, 40 patients; 18 - 75 ages, who will have abdominal surgery were randomly divided into two groups, after the approval of the ethics committee (2016 - 06/02) and the patients. Anesthesia induction was performed with 6 mg/kg thiopental sodyum, 1 μg/kg remifentanil and 0.5 - 20 μg/kg/min remifentanil infusion, 4 - 6% desflurane after routine ECG, blood pressure, SpO_2 and BIS monitorization to all patients. In the low-flow group after the first 10 min 4 lt/min fresh flow, the flow was reduced to 1 lt/min. Values of the heart rate, MBP, SpO_2, FiO_2, BIS, tympanic temperature at before induction and after intubation and the minutes of 15th, 30th, 45th, 60th, 90th,120th are recorded. Lactate and COHb values were measured in blood gas analyzes performed at 30th and 90th minutes.
Results: When SpO_2 and FiO_2 values measured in different time periods of the individuals in both two groups were compared, differences between the minutes of 30th, 45th, 60th, 90th, 120th were significant.
Conclusion: In this research; it is revealed that low-flow anesthesia which has advantages in many aspects can be used safely like high flow anesthesia when applied with adequate information equipment, appropriate anesthesia devices and necessary monitorizations.

Keywords: Low flow anesthesia; Bispectral index; Desflurane

Introduction

Anesthesia using low fresh gas flow is defined as; re-administering at least 50% of fresh oxygen flow with the adequate amount of volatile anesthetics which meets the metabolic requirement of the body, after removing carbondioxide from patients' exhaled gas mixture with the help of an anesthesia system that has a re-ventilation feature. Interest in anesthesia methods with the low fresh gas flow has been increasing in recent years[1,2].

When low fresh gas flow anesthesia is applied; cost reduction and prevention of environmental pollution is achieved, as well as the humidity levels of the gases reach higher values than the high fresh gas flow techniques and heat loss is minimized. Thus, the physiology of the trachea and bronchial environments is better preserved and it is useful in preventing postoperative hypothermia[2,3]. Another important advantage of low fresh gas flow anesthesia is that: complications that may occur during anesthesia applications can be detected sooner, and therefore patient safety is increased due to the necessity of monitoring the patient more closely[2,4].

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Bispectral index (BIS) is a special Electroencephalography (EEG) parameter that can quantitatively evaluate the sedative and hypnotic effects of anesthetic drugs and is used in the follow-up to reduce the use of these agents. It detects EEG signals through electrodes placed in the forehead and temporal region. The BIS index refers to values ranging from 0 to 100. BIS values at 100 indicate that the patient is awake, while 0 indicates isoelectric activity. Studies have reported that maintaining BIS index values between 40 and 60 during general anesthesia provides sufficient hypnotic effect[2].

Carbon monoxide (CO) has high affinity to hemoglobin. However concentration can reach clinically significant levels in; excessive smokers, hemolysis, porphyria and especially smoking donor-sourced blood transfusion etc. In some studies; low flow anesthesia techniques have been implicated to not have a unique increase in the risk of carbon monoxide poisoning as the use of constantly low fresh gas flows are a fundamental measure to prevent the formation of carbon monoxide[2].

The purpose of this study was to compare the effects of low and high flow general anesthesia methods, in combination with desflurane inhalation anesthesia and standardized anesthesia depth via BIS, on perioperative hemodynamics, parameters of arterial blood gas parameters (lactate, carboxyhemoglobin) routinely performed, and postoperative recovery time in adult abdominal surgeries lasting 2 hours and more.

Materials and Methods

After approval of the ethics committee (2016 - 06/02); 40 ASA I-II patients between the ages of 18 and 75 were informed about all the details of the study, their informed consent forms were taken and they were randomized into 2 groups. Among the criteria for exclusion from the study were; malignant hyperthermia history, the presence of significant anemia clinic, morbid obesity, alcohol or drug dependence, COPD, excessive smoking history, decompensated diabetes mellitus, kidney and liver failure, previous history of ischemic cerebrovascular disease, pregnancy and lactating women, patients with opioid susceptibility.

Two of the 42 patients meeting the study criteria were excluded due to the need for blood transfusions and transitioning from low flow to high flow. Patients in both groups were fasted for 8 hours before surgery and received crystalloids from 2 ml kg^{-1} per hour.

Before each patient, the anesthesia circuits were checked for leakage, the gas monitors were calibrated, and alarm limits were checked; a disposable anesthetic cycle and a bacterial filter were used, the soda lime was changed at the end of the day.

In addition to routine monitoring including ECG, non-invasive blood pressure, $EtCO_2$, SpO_2; tympanic thermometer on the tympanic membrane and BIS monitorization were performed. After the BIS instrument calibration and contact testing of the electrodes were completed, the measured BIS and other values were recorded in the case follow-up form.

In all patients; heart rate, mean blood pressures, SpO_2, $EtCO_2$, inspired oxygen concentration (FiO_2), BIS, tympanic temperature measurements were recorded preop (5 min before induction), after intubation (0 min) and at 15 min, 30 min, 45 min, 60 min, 90 min, 120 min. In addition, lactate and COHb levels were recorded in blood gas analyzes routinely performed at 30 min and 90 min after intubation.

Intravenous midazolam (IV) was administered at 0.02 - 0.03 mg kg^{-1} to all patients 30 minutes before the procedure. Peripheral vascular access was established with 18 - 20 gauge cannula and initiation of crystalloid infusion at maintenance dose was begun. All patients received induction of anesthesia with 7 mg kg^{-1} thiopental sodium, 1 µg kg^{-1} remifentanil followed by µg kg^{-1} per min IV infusion, muscle relaxation with 0.6 mg kg^{-1} rocuronium bromide. After 5 minutes of mask preoxygenation with 100% oxygen and endotracheal intubation, all patients were ventilated with tidal volume 7 ml kg^{-1} and respiration rate 12 min^{-1} by (Drager-Primus) anesthesia device. 4 - 6% desflurane was used in anesthesia maintenance. In the first 10 min, 4 lt min^{-1} of high flow was applied to patients.

After intubation, desflurane was applied at 6% concentration in 4 lt min^{-1} O_2 in both groups for 10 min. Subsequently, Group I transitioned to low flow (1 lt min^{-1}). In Group II, high flow (4 lt min^{-1}) continued. The desflurane level was adjusted to be BIS 40 - 60. BIS values over 60 were accepted as superficial and values under 40 were accepted as deep anesthesia, and control of the depth of anesthesia was aimed to be achieved with changes of 1 - 2% in concentration of desflurane in the vaporizer. In Group I, 10 minutes before the anesthesia was terminated, high fresh gas flow anesthesia was applied again (4 lt min^{-1}) to ensure rapid elimination of anesthetic gases and vapors from the lungs.

When the final skin suture started, the anesthetics were stopped and the patient was manually ventilated with 100% O_2 until spontaneous respiration started. At the onset of spontaneous breathing, the muscle relaxant was decurarized with 0.04 mg kg^{-1} neostigmine and 0.01 mg kg^{-1} atropine. Extubation was performed when sufficient spontaneous respiration occurred and the BIS value reached 80% and above. The time between stopping volatile agents and extubation was considered as extubation time, the time between stopping volatile agents and tongue removal was considered as tongue removal time, and an Aldrete score of 9 was considered as full recovery. All patients' times and scores were recorded.

Statistical Analysis

The data obtained from our study were loaded on the SPSS (ver: 22.0) program, the significance test of the difference between the two means, variance analysis in repeated measures, Bonferroni test were used when the parametric test assumptions were fulfilled; and Man Whitney U test, Friedman test, Wilcoxon test and Chi-square test were used when they were not, and the error level was taken as 0.05.

Results

26 (65%) of the patients were female and 14 (35%) were male. 12 (60%) of the patients in the study who were in the low flow group were female while 8 (40%) were male. Of the patients in the high flow group, 14 (70%) were female while 6 (30%) were male. There were no significant differences between the groups in terms of gender ($X^2 = 0.44$: $p = 0.507$: $p > 0.05$). The mean age of the patients in the low flow group was 46.25

(± 13.09), and in the high flow group, the mean age was 47.95 (± 14.82). There was no significant difference between the groups in terms of age ($p > 0.05$). Patients in the low flow group had a weight of 76.10 (± 8.80) and those in the high flow group had a weight of 74.0 (± 9.95). The difference between the two groups in terms of weight was not significant ($p > 0.05$) (Table 1).

Table 1: The demographic data of individuals in the study.

Groups	Gender/Sex		Age (year)			Kilogram (kg)		
	Female	Male	Mean	S.D.	Result	Mean	S.D.	Result
Low Flow Group (N = 20)	12(%60)	8(%40)	46.25	13.00	t = 0.39	76.10	8.80	t = 0.70
High Flow Group (N = 20)	14(%70)	6(%30)	47.95	14.48	p = 0.698	74.00	9.95	p = 0.484

*$p < 0.05$ significant
S.D: Standard Deviation

15 (37.5%) of the patients were ASA I physical status and 25 (62.5%) were ASA II physical status. 6 (30%) of the patients in the study who were in the low flow group were ASA I while 14 (70%) were ASA II. Of the patients in the high flow group, 9 (45%) were ASA I while 11 (55%) were ASA II. The annex disease of the patients in the low flow group were 8 (42.10%) DM, 7 (36.84%) HT, 3 (15.78%) asthma and 1 (5.26%) thyroid disease. The annex disease of the patients in the high flow group were 5 (29.41%) DM, 8 (47.05%) HT, 4 (23.52%) asthma. The indications of surgery of the patients in the low flow group were 9 (45%) cholecystectomy, 5 (25%) intestinal (Mass-bx), 6 (30%) herniation (inguinal-umblical). The indications of surgery of the patients in the high flow group were 7 (35%) cholecystectomy, 8 (40%) intestinal (Mass-bx), 5 (25%) herniation (inguinal-umblical). There were no significant differences between the groups in terms of ASA, annex disease and indications of surgery (Table 2).

Table 2: Thecomparison of thevalues of theASA,annexdisease, indications of surgery.

Gruplar	ASA		Annex Disease			Indications of Surgery			
	ASA I	ASA II	DM	HT	Asthma	Thyroid Disease	Cholecystectomy	Intestinal (Mass-bx)	Herniation (In-guinal - umblical)
Low Flow Group (N = 20)	6(%30)	14 (%70)	8	7	3	1	9	5	6
High Flow Group (N = 20)	9(%45)	11(%55)	5	8	4	-	7	8	5

When the SpO_2 values of the patients in both groups measured in different time periods were compared, it was found that there was a significant difference between 30th, 45th, 60th, 90th and 120th minutes ($p < 0.05$). SpO_2 values measured at other times were not significantly different ($p > 0.05$) (Table 3).

Table 3: Comparison of SPO_2 values of individuals in both groups.

Measurement Times	Low Flow Group		High Flow Group		Result
	Mean	Standard Deviation	Mean	Standard Deviation	
Preoperatively	97.15	1.53	96.85	1.56	t = 0.61 p = 0.544
After intubation	99.35	0.48	99.45	0.75	t = 0.49 p = 0.623
15 minutes	99.35	0.87	99.70	0.57	t = 1.43 p = 0.142
30 minutes	99.05	0.68	99.60	0.59	t = 2.70 p = 0.010[a]
45 minutes	98.85	0.93	99.40	0.75	t = 2.05 p = 0.047[b]
60 minutes	98.60	0.82	99.70	0.57	t = 4.91 p = 0.001[c]
90 minutes	98.30	0.92	99.50	0.75	t = 4.67 p = 0.001[d]
120 minutes	98.25	0.85	99.30	0.57	t = 4.58 p = 0.001[e]

[a]$p < 0,05$; SPO_2 in both groups compared to 30 minutes
[b]$p < 0,05$; SPO_2 in both groups compared to 45 minutes
[c]$p < 0,05$; SPO_2 in both groups compared to 60 minutes
[d]$p < 0,05$; SPO_2 in both groups compared to 90 minutes
[e]$p < 0,05$; SPO_2 in both groups compared to 120 minutes

When the FiO_2 values of the patients in both groups measured in different time periods were compared, it was found that there was a significant difference between 30th, 45th, 60th, 90th and 120th minutes ($p < 0.05$). FiO_2 values measured at other times were not significantly different ($p > 0.05$) (Table 4).

Table 4: Comparison of FiO_2 values of individuals in both groups.

Measurement Times	Low Flow Group		High Flow Group		Result
	Mean	Standard Deviation	Mean	Standard Deviation	
After intubation	95.15	2.88	95.35	2.85	t = 0.22 p = 0.827
15 minutes	92.95	1.73	95.45	1.98	t = 0.84 p = 0.401
30 minutes	89.50	2.87	95.25	1.86	t = 3.59 p = 0.001[a]
45 minutes	87.60	2.11	95.70	1.68	t = 10.08 p = 0.001[b]
60 minutes	86.75	1.86	95.60	1.53	t = 16.22 p = 0.001[c]
90 minutes	86.05	1.84	96.15	2.05	t = 20.22 p = 0.001[d]
120 minutes	85.95	1.46	95.65	1.89	t = 29.24 p = 0.001[e]

[a]p < 0,05; FiO_2 in both groups compared to 30 minutes
[b]p < 0,05; FiO_2 in both groups compared to 45 minutes
[c]p < 0,05; FiO_2 in both groups compared to 60 minutes
[d]p < 0,05; FiO_2 in both groups compared to 90 minutes
[e]p < 0,05; FiO_2 in both groups compared to 120 minutes

When the lactate and COHb values measured at different times of the individuals in both groups were compared, the difference was not significant ($p > 0.05$) (Table 5).

Table 5: Comparison of lactate and COHb values of individuals in both groups.

Measure-ment Times	Low Flow Group (Lactate)		High Flow Group (Lactate)		Result (Lactate)	Low Flow Group (COHb)		High Flow Group (COHb)		Result (COHb)
	Mean	S.D.	Mean	S.D.		Mean	S.D.	Mean	S.D.	
30 minutes	0.99	0.27	0.98	0.17	t = 0.13 p = 0.892	1.09	0.41	1.05	0.33	t = 0.33 p = 0.739
90 minutes	1.20	0.38	1.03	0.28	t = 1.60 p = 0.118	1.18	0.51	1.11	0.23	t = 0.50 p = 0.614

*p < 0.05 significant
S.D: Standard Deviation

When the MBP, HR, BIS, tympanic temperature, $EtCO_2$, extubation time, tongue removal time and Aldrete recovery score values also measured at different times of the individuals in both groups were compared, the difference was not significant.

Discussion and Conclusion

Low-flow anesthesia has risks such as hypoxia, low or high dose use of volatile anesthetics, hypercapnia and accumulation of potentially toxic trace gases. Therefore, it is suggested that low-flow anesthesia techniques should be preferred at the beginning with no serious disease, minor and moderate operations[5,6]. For this reason, patients in the ASA I-II risk group were included in our study. The distribution of our cases according to operations is also similar.

During the application of low flow methods, devices must be used that have appropriate continuous monitoring of airway pressure, expired gas volume, FiO_2, volatile anesthetic agent concentration and CO_2 concentration can be monitored continuously, and alarm limits should be carefully adjusted[6]. We used a (Dräger-Primus) anesthesia machine in our study, which allows these observations and electronically monitoring of fresh gas flow.

The desflurane concentration of the gases inhaled can be changed in a short time while the fresh gas flow is low, since desflurane allows rapid induction and recovery and the vaporizer can be set at a wide dose range. This prevents the inadequate depth of anesthesia due to the inadequacy of low-flow anesthesia, or vice versa, allowing rapid intervention in cases of deep anesthesia[7,8]. For this reason, we used desflurane in low-flow anesthesia for our study.

Baum et al. reported in their study comparing low and minimal flow desflurane anesthesia; that in minimal flow desflurane anesthesia, desflurane concentration should be increased by 1 - 2%, while at low flow rate sufficient concentration is achieved without changing the vaporizer setting[8]. Hargasser et al. reported that the flow was sufficient to maintain desflurane density ratios in the case of a low flow of 1 lt min^{-1} without altering the vaporizer setting at the 30th minute of high flow[9]. In our study, we observed that sufficient concentration could be achieved with 6% desflurane in all cases of both the high flow group and the low flow group.

It has been reported that the risk of hypoxic gas mixture is reduced in nitrous oxide-free low-flow anesthesia applications and that patient safety is increased against the possibility of hypoxemia[8]. The duration of the initial phase with nitrous oxide-free low-flow anesthesia is only controlled by the time required to ensure the agent concentration to ensure adequate anesthesia depth, which is determined by the pharmacokinetic properties of the agent used and the technical characteristics of the agent's vaporizer[10]. In our study, to ensure standardization in both groups, anesthesia maintenance was achieved without using a mixture of nitrous oxide in both the high flow and low flow groups by keeping the high flow durations applied at the beginning equal.

Different approaches are used to evaluate hemodynamic parameters in the maintenance of anesthesia. Dupont et al. maintained the mean arterial pressure and heart rate at approximately ± 20 units based on baseline values and, in the case of exceeding the stated values, added additional opioid doses and increased inhalation agent concentration if there was not enough effect[11]. In our study, hemodynamic data obtained with dose titration of remifentanil infusion were kept at 6% desflurane concentration in both groups; The MBP values were similar in both groups, and the differences were not significant.

In some studies, increase in heart rate and left ventricular end-diastolic pressure; and the decrease in mean arterial pressure, left ventricular systolic pressure, and stroke volume was observed during desflurane administration at 1 - 1,5 MAC[12]. Gormley et al. reported that the use of desflurane in vaporizer settings above 6% caused an increase in heart rate and blood pressure by increasing transient sympathetic activity[13]. Elmacıoğlu et al. examined the effects of desflurane in low flow anesthesia and reported that hemodynamic stability was maintained in the perioperative period when desflurane anesthesia was administered with fresh flow rates of 0.5 - 1 - 2 lt min^{-1}[14]. It has been shown that remifentanil, one of the new opioids, successfully inhibits blood pressure and heart rate increase caused by volatile anesthetics and surgical stimulation[14,15]. We kept the vaporizer setting at 6% constant in our study. In our study, HR values were similar in both groups, meaning no significant changes were found. Desflurane was found to be sufficient at 6% concentration in both groups, suggesting that the vaporizer settings did not need to be changed. In both groups, we think that using remifentanil at 1 μg kg^{-1} in the induction and 0,5 - 20 μg kg^{-1} per min in succession, prevents the increase in sympathetic activity that may be caused by desflurane.

Çukdar et al. reported that in their study comparing low- and high-flow desflurane anesthesia, the SpO_2 level, in any case, did not fall below 97%[6]. Despite SpO_2 values being normal in our study; although clinically meaningless, the value of SpO_2 was statistically significantly lower when measured at 30th, 45th, 60th, 90th and 120th minutes. We did not encounter hypoxia which may be due to desflurane during our application. As a result, we observed that low fresh gas flow and desflurane-remifentanil combinations could be used safely without any risks of hypoxia.

Kızıltepe et al.monitored the FiO_2 concentration using a 50% O_2, 50% air mixture in the study and reported that there were insignificant reductions in inspired and expired O_2 concentration during the operation, but this reduction did not fall below 30% and they found no evidence of hypoxia in arterial blood gas analysis[16]. Payas et al. noted in studies where the low fresh gas flow is used, that the difference between given oxygen and FiO_2 gets bigger over time and that the FiO_2 value decreases significantly with time but FiO_2 does not go below 30% in any of the groups[17]. In our study with the low fresh gas flow, the SpO_2 value did not drop below 97% and the FiO_2 value did not go below 30% in any of the cases. In our study, although the FiO_2 percentages were within the normal limits, the FiO_2 percentages in the low flow group did not fall below the 30% critical lower limit, but measurements at the 30th minute, 45th minute, 60th minute, 90th minute and 120th minute were found to be statistically significantly lower. This result was assessed in accordance with the time course of inspired O_2 and the known effects of low flow anesthesia applications on inspiratory gas concentrations. Tokgöz et al. reported that lactate, one of the markers of anaerobic respiration, was found to be higher in the low-flow group than in the high-flow group in the blood gas studies when they compared low and high flow desflurane anesthesia methods[18]. In our study, lactate values were not found in the risky range in the blood gas analyzes of the patients in both groups, and the difference between the groups was not significant. This result suggests that low-flow anesthesia allows adequate oxygenation at the cellular level.

Bispectral index analysis method is accepted as one of the objective indicators of the depth of anesthesia[19]. It has been reported that BIS values during general anesthesia should be kept in the range of 40 - 60 to avoid awareness and recollection[20]. The effects of different opioids used in the studies on BSI also vary. For example; remifentanil was found to have a dose-dependent decreasing effect on the BIS index[21]. One study reported that bolus dose administered remifentanil lowered the BIS value independently of intubation and surgical stimulation[22]. In our study, it was observed that the BIS values were similar in both groups in a mean range of 40 - 60 and none of the patients had superficial anesthesia or deep anesthesia. The use of BIS in general anesthesia in our study showed significant benefits such as preventing excessive or unnecessary drug administration to the patient, providing adequate depth of anesthesia and contributing to the follow-up period.

Recovery in inhalation anesthetics depends on the oil solubility of the agent, concentration, duration of use, and the patient's alveolar ventilation level. After about 2 hours of anesthesia using inhalation agents, the early recovery period takes place in about 15 minutes. Because the drugs of inhalation constitute only a fraction of the balanced anesthesia, the process of waking up and recovery depends on non-inhalation factors, too. In this case, the actual effects of the inhalation anesthetics will be suppressed and the results will change[23-25]. Other agents (induction, curative, muscle relaxants etc.) we used to minimize these effects were kept as standard. In their study on recovery times, Nathanson et al. observed that the extubation time was 8.2 ± 3.2 min, the eye opening time was 7.8 ± 3.8 min and the orientation time was 11.2 ± 5.1 min[26]. Philip et al. found that the extubation time was 6.0 ± 0.2 min, the eye opening time was 7.0 ± 0.3 min and the orientation time was 9.0 ± 0.4 min[27]. In our study, extubation time was 11.2 ± 2.1 min, tongue removal time was 13.4 ± 1.7 min, Aldrete recovery score was 16.3 ± 1.7 min in the low flow group; and in the high flow group, extubation time was 10.8 ± 2.3 min, tongue removal time was 13.1 ± 1.9 min, Aldrete recovery score was 16.1 ± 1.4 min. As a result of our study, it was seen that the recovery times in both groups were similar to each other. In terms of these recovery characteristics, the differences between the two groups were not found to be significant. We observed that both applications can safely be used with their rapid and full recovery features.

As a result of interaction with soda lime, it is known that carbon monoxide (CO) is formed in the use of desflurane[28-30]. In low-flow anesthesia applications, humidity is better preserved during re-ventilation compared to other techniques[31]. Preservation of the absorbent humidity is a unique feature of low flow anesthesia administration methods and it is stated that the amount of carbon monoxide (CO) produced is clinically insignificant[32]. However, to avoid possible interference of soda lime and desflurane and prevent possible CO accumulation and increase in COHb, the CO_2 absorbent was changed at the end of each day. Because of the possible risk of COHb increase in our study, blood gas analyzes of patients did not show carboxyhemoglobin levels in the risky range, and the difference between the groups was not significant.

There are still many studies on the low flow anesthesia but we think that it is not reach the required place. Although low flow anesthesia is a commonly used method in routine practice, we still observe conservative approaches to high flow anesthesia. In our study; low flow anesthesia applications, because of the difficulty of following anesthesia depth we also used BIS monitorization in our study to determine the standardization in both the low flow group and the high flow group. We had to keep laparoscopic cases out of study because of the posibility of the some parameters could be affect. In addition, the short study time of the study caused the sample size to be limited.Although there are factors that restrict our study, we have observed that we can safely use low flow anesthesia in especially ASA 1 - 2 cases. We believe that it will become the standard practice in general anesthesia because of the reduction of unnecessary high oxygen flow, more comfortable and more physiological for the patient.

As a result; low flow anesthesia method, which features many advantages, can be safely used just as high flow anesthesia when it is applied in conjunction with sufficient knowledge, suitable anesthesia devices and necessary monitors. We believe that low-flow anesthesia can be used extensively in routine practice with a broader range of different clinical trials that are evaluated ecologically, economically, and academically.

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