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SCIENTIFIC ARTICLE

Anesthesia recovery comparison between remifentanil-propofol and remifentanil-desflurane guided by Bispectral Index® monitoring

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Anesthesia recovery;
Desflurane;
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Balanced anesthesia

Abstract
Background and objectives: There is a strong demand for fast and predictable anesthesia recovery with few side effects. Choice of the hypnotic agent could impact on that. This study investigated the differences between recoveries after remifentanil-propofol and remifentanil-desflurane anesthesias guided by bispectral index (BIS®).
Methods: Forty patients were randomly assigned into 2 groups according to the anesthesia technique applied: remifentanil-propofol (REM-PRO) and remifentanil-desflurane (REM-DES). After the discontinuation of the anesthetics, the times to extubation, to obey commands and to recover the airway protection reflex were recorted. In the post-anesthetic recovery room (PACU) it was recorded the occurrence of nausea and vomiting (PONV), scores of Ramsay sedation scale and of numeric pain scale (NPS), morphine dose and length of stay in the unit.
Results: Data from 38 patients were analyzed: 18 from REM-PRO and 20 from REM-DES group. Anesthesia times were similar (REM-PRO = 193 min, SD 79.9 vs. 175.7 min, SD 87.9 REM-DES; $p = 0.5$). REM-DES had shorter times than REM-PRO group: time to follow command (8.5 min; SD 3.0 vs. 5.6 min; SD 2.5; $p = 0.0$) and extubation time (6.2 min; 3.1–8.5 vs. 9.5 min; 4.9–14.4; $p = 0.0$). Times to recover airway protective reflex were similar: 16 patients from REM-PRO (88.9%) restored the airway protective reflex 2 min after extubation vs. 17 from REM-DES (89.5%); and 2 patients from REM-PRO (11.1%) vs. 2 from REM-DES (10.5%) 6 min after extubation, $p = 1$. Ramsay sedation score, NPS, PONV incidents, morphine dose and PACU stay of length PACU were also similar.

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Conclusion: Remifentanil-desflurane-based anesthesia has a faster extubation time and to follow command than remifentanil-propofol-based anesthesia when both guided by BIS®.

PALAVRAS-CHAVE
Recuperação pós-anestésica;
Desflurano;
Propofol;
Anestesia intravenosa;
Anestesia balanceada

Comparação da recuperação pós-anestésica entre remifentanil-propofol e remifentanil-desflurano guiada pela monitoração do Índice Bispectral®

Resumo
Justificativa e objetivos: Há uma forte demanda por recuperação pós-anestésica *rápida* e previsível com poucos efeitos adversos. A escolha do agente hipnótico pode influenciar isso. Este estudo investigou as diferenças da recuperação no pós-operatório entre as técnicas anestésicas com remifentanil-propofol e com remifentanil-desflurano ambas guiadas pelo índice bispectral (BIS®).
Métodos: Foram randomicamente distribuídos 40 pacientes em dois grupos de acordo com a técnica anestésica aplicada: remifentanil-propofol (REM-PRO) e remifentanil-desflurano (REM-DES). Após a descontinuação dos anestésicos foram registrados os tempos para extubação, obedecer a comandos e recuperar o reflexo de proteção das vias aéreas. Na sala de recuperação pós-anestésica (SRPA) foi registrado a ocorrência de náuseas e vômitos (NVPO), os escores na escala de sedação de Ramsay e na escala numérica de dor (END), a dose de morfina utilizada e o tempo de permanência nesta unidade.
Resultados: Os dados de 38 pacientes foram analisados: 18 do grupo REM-PRO e 20 do grupo REM-DES. Os tempos de anestesia foram semelhantes (REM-PRO = 193 minutos, DP 79,9 vs. 175,7 minutos, DP 87,9 REM-DES; $p = 0,5$). O grupo REM-DES apresentou tempos mais curtos que o grupo REM-PRO: tempo para obedecer a comandos (8,5 minutos; DP 3,0 vs. 5,6 minutos; DP 2,5; $p = 0,0$) e tempo de extubação (6,2 minutos; 3,1-8,5 vs. 9,5 minutos; 4,9-14,4; $p = 0,0$). Os tempos para recuperação do reflexo de proteção das vias aéreas foram semelhantes: 16 pacientes do grupo REM-PRO (88,9%) recuperaram o reflexo de proteção das vias aéreas dois minutos após a extubação vs. 17 do grupo REM-DES (89,5%) e dois pacientes do grupo REM-PRO (11,1%) vs. dois do REM-DES (10,5%) seis minutos após a extubação, $p = 1$. Os escores de Ramsay, NPS, a incidência de NVPO, a dose de morfina e o tempo de permanência na SRPA também foram semelhantes.
Conclusão: A anestesia com remifentanil-desflurano tem um perfil de recuperação da anestesia pós-anestésica mais rápido que o da anestesia com remifentanil-propofol quando ambas guiadas pelo BIS®.

Introduction

The short-acting anesthetics, such as propofol and desflurane, provide safe and effective anesthesia with few side effects and rapid recovery. Desflurane has the lowest blood/gas partition coefficient among volatile anesthetics and enables a greater intraoperative anesthesia control with low inter-individual variability.[1] In turn, total intravenous anesthesia (TIVA) with propofol also provides quick anesthesia emergence and lower incidence of postoperative nausea and vomiting (PONV).[2–4]

The level of anesthesia (whether superficial or deep) influences anesthesia recovery.[1] The bispectral index (BIS®) is an electroencephalogram derived scale firstly developed for monitoring the level of consciousness among patients receiving general anesthesia and sedation.[5] Recently, BIS® monitoring has also proved to be also useful to control anesthesia depth, reduce drug consumption, shorten anesthesia recovery and decrease adverse effects.[5,6]

There is a strong demand for faster anesthesia recovery, as a quicker recovery may be associated with earlier and better care of patent airways, more protection against aspiration, and greater oxygenation.[1] These are essential for ambulatory anesthesia[6,7] and also in other circumstances, such as in elderly, obese and critical patients.[1] From an economic perspective, a quick anesthesia recovery favors fast-tracking, increases case turnover and may improve resource use.[1]

Early anesthesia recovery has been clinically assessed after anesthetic discontinuation by time to follow command; extubation time and protective airway reflex restoration after extubation. Evidences suggest that desflurane offers shorter early anesthesia recovery than propofol-based anesthesia.[7–9] However, most studies had some bias due to an absence of rigid control of anesthesia depth.[3,7,10]

Objectives

The choice of the hypnotic agent could impact on early recovery, not only due to differences in pharmacokinetic profile but also in pharmacodynamics. In the present study we tested the hypothesis that remifental-desflurane balanced anesthesia has a shorter extubation time (primary endpoint) than total intravenous anesthesia with remifentanil-propofol when both guided by BIS®. The secondary endpoints were time to follow command; time to recover the protective airway reflex after extubation; use of vasopressors during the surgery and the patient's vitals at the Post-Anesthesia Care Unit (PACU).

Methods

Trial design

This was a unicenter, non-stratified, double-blind, with 1:1 randomization, clinical prospective trial conducted in a quaternary level hospital in Brazil.

Participants

Eligible participants were all female adults were over 18 years of age, classified by the American Society of Anesthesiologists as physical status I or II, undergoing elective breast surgery with general anesthesia.

Exclusion criteria were history of: chronic use of any psychoactive drug; pregnancy on course or suspicion of; neuromuscular disorders; cerebral vascular disease; dysphagia; dysphonia; gastroesophageal reflux disease; previous larynx and/or upper gastrointestinal tract surgery; allergy to any drug to be used and malignant hyperthermia. Patients who developed hemodynamic instability during surgery, and/or potential need for blood transfusions were excluded from the study. Patients unable to swallow 20 mL of water in an upright position were also excluded.

Study setting

This study was conducted in the *Hospital das Clínicas* of the *Universidade Federal de Minas Gerais*, Brazil, from July until November in 2015. The Fig. 1 shows a flowchart that outlines patient selection, randomization and analyses.

Interventions

Upon enrollment, all subjects were familiarized with the numerical pain scale (NPS), score of ''0'' representing no pain and score of ''10'' the worst pain imaginable, and tested for ability to swallow 20 mL of water (protective airway reflex test). Swallowing was judged successful if

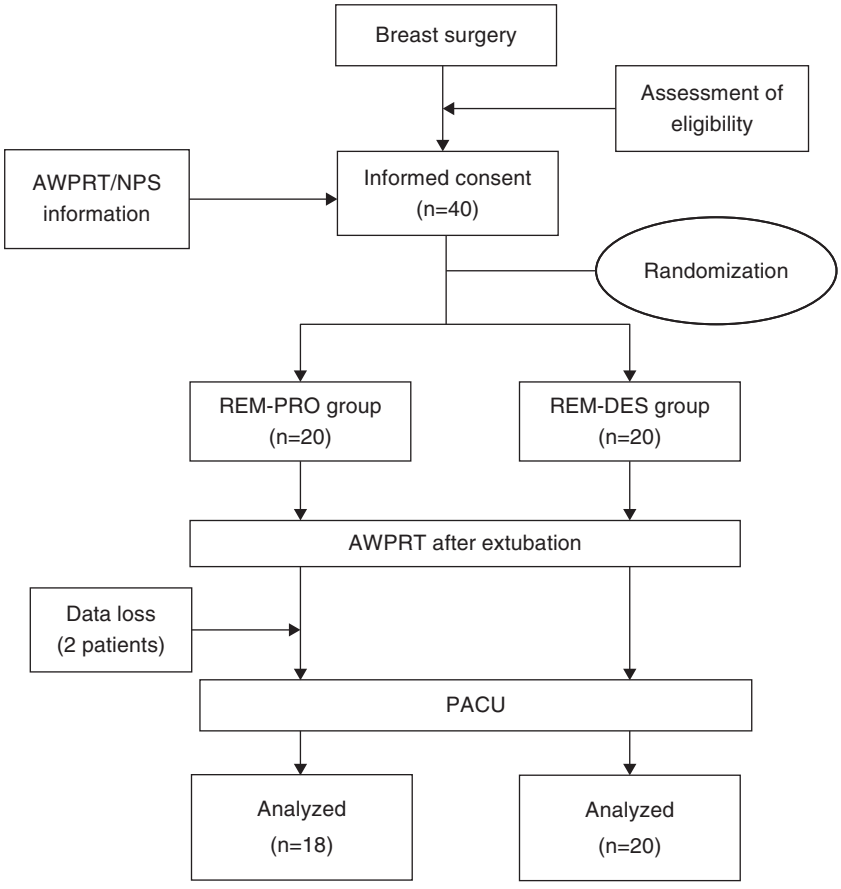

Figure 1 A flowchart that outlines patient selection, randomization and analyses. AWPRT, Airway Protective Reflex Test; NPS, Numerical Pain Scale; PACU, Post-Anesthesia Care Unit.

no coughing or drooling occurred after water passed into patient's mouth and no water remained in her oropharynx upon subsequent visual inspection.[11,12]

In the operating room (OR), patients from both groups were monitored with EKG, pulse oximetry, non-invasive blood pressure (NIBP) and end-tidal measurements (ET) of desflurane, oxygen and carbon dioxide (CO_2). Mechanical ventilation was set to target these parameters: ETCO2 between 30 and 40 mmHg; $FiO_2 = 30\%$, oxygen saturation (SpO_2) $\geq 97\%$. Anesthesia depth was titrated with BIS monitoring (BIS VISTA® Monitoring System, USA) to obtain the values between 40 and 60 intra-operatively. Neuromuscular blockade was guided by train-of-four monitoring (TOF). Infusion workstation was Orchestra® Base Primea with Modules DPS (Fresenius Vial S. A. S., France). The tip of the temperature probe was placed in the patients' nasopharyngeal for temperature monitoring.

General anesthesia was standardized. In both groups, remifentanil was the only opioid used for anesthesia induction and maintenance. Target-controlled infusion (TCI) mode was set and remifentanil administration was based on Minto's pharmacokinetic model.[13] An effect-site target of 5 ng.mL^{-1} was set for induction. Adjustments were made according to established BIS value range. Lidocaine 1.5 mg.kg^{-1}, was given intravenously (I.V.) before propofol administration. Atracurium was the sole neuromuscular blocking agent used. A bolus of 0.5 mg.kg^{-1} I.V. was administered to patients in both groups after unconsciousness, defined by loss of the eyelid reflex. Intubation was made only when train-of-four (TOF) stimulation monitor on the ulnar nerve was zero.

In the REM-PRO group, after remifentanil and lidocaine infusions, propofol plasma-site TCI of 5 μg.ml^{-1} (Marsh's pharmacokinetic model) was set for induction and ajusted according to BIS® values.[14]

In the REM-DES group, after remifentanil and lidocaine infusions, a bolus of propofol 1.5–2.5 mg.kg^{-1} I.V. was administered until loss of consciousness. Anesthesia maintenance was done with desflurane (Desflurane Dräger vaporizer D-Vapor 3000). Adjustments were done according to established BIS® value range.

Hemodynamic instability was defined by systolic blood pressure below 90 mmHg, despite volume loading and intermittent using of vasopressors. Blood transfusion target was set at 8 g.dL^{-1} or whenever the anesthesia provider judged necessary.

The post-operative pain protocol consisted of: dexamethasone 10 mg I.V. (except for diabetics), ketoprofen 100 mg I.V. (except for patients over 60 years of age, or with chronic renal disease or using angiotensin-converting enzyme inhibitors), metamizol (Dipirona®) 2.0 g I.V. and morphine 0.1 mg.kg^{-1} I.V. In addition to dexamethasone, 4.0 mg I.V. were used for PONV prophylaxis.

Before discontinuing anesthetics, TOF should be above 90%. If not, atropine 0.02–0.04 mg.kg^{-1} I.V. and neostigmine 0.04–0.06 mg.kg^{-1} I.V. boluses were administered to achieve it.

Outcomes

The primary endpoint was the extubation time, defined by the discontinuation of anesthetic delivery until the endotracheal tube cuff deflation. When the anesthetics were discontinued, the fresh gas flow was set above patient's respiratory minute volume. Patients were extubated when having respiratory rate greater than 12 breaths per minute; tidal volume above 6 mL.kg^{-1}, $SpO_2 \geq 97\%$ and following a command or heavily coughing during anesthesia emergence.

The secondary endpoints and their definitions were as follows: anesthesia time (time from induction until anesthetics discontinuation) and time to follow command (time from anesthetics discontinuation to follow a standard command). This command consisted of ''*patient's name, squeeze my hand!*'' and was said to each patient by the anesthesia provider every 15 s from anesthetic discontinuation until patient's answer.

The time to recover the protective airway reflex was evaluated by the protective airway test, described earlier, at 2, 6, 14, 22 and 30 min after extubation until the first successful patient's attempt. To perform such test, the patient was positioned at 60° upright position on the surgical bed and asked to swallow 20 mL of water. Protective airway reflex was considered restored if swallowing was adequate (describe above).

At the PACU, patients were monitored with EKG, SpO_2 and NIBP. A blind observer evaluated the patients on admission and every 5 min afterward until being discharged. Measured outcomes also included vital signs; Ramsay scale sedation; NAS and PONV scale (1 = no symptoms; 2 = mild to moderate nausea and/or vomiting, not needing anti-emetics; 3 = severe nausea and/or vomiting, anti-emetics needed; 4 = severe nausea and/or vomiting, not responding to anti-emetics).

Sample size

Sample size was calculated based on the primary outcome of the study (extubation time). According to previous study,[15] a difference of 3.1 min in mean extubation time from propofol and desflurane with a standard deviation (SD) of 3.0 min were considered clinically significant. Sample size calculation revealed that 17 subjects per group were required to achieve a power of 85% with a type one error of 0.05. Because of the potential loss of patients along the study, we included 20 patients on each group.

Randomization

The randomization scheme was developed by a computer program Microsoft Excel® 2013 (Microsoft, Redmond, USA) and covered in sealed envelopes. These envelopes were prepared by an independent anesthesiologist who was not associated with study. Patients were allocated into two groups according to its anesthetic regime: remifentanil-propofol (REM-PRO group) or remifentamil-desflurane anesthesia (REM-DES group).

Blinding

The anesthesia provider was not blinded due to safety reasons. An observer, blinded to the anesthesia assignment, recorded the data.

Table 1 Demographic characteristics of the REM-PRO and REM-DES groups.

	REM-PRO				REM-DES				*p*-value
	n	Mean	Median	%	*n*	Mean	Median	%	
Age (years)	19	56.3 (±15.2)			20	46.7 (±11.1)			0.03[a]
Weight (kg)	19	65.4[b]	62.2 (51–92.5)		20	72.4 (±19.2)	69.5 (43.9–106.5)		0.04
Height (m)	19	1.55 (±0.1)			20	1.6 (±0.08)			0.08
BMI ($kg.m^{-2}$)	19	28.6 (±5.0)			20	29 (±6.1)			0.62
ASA I	4			21.1	8			40	0.15
ASA II	15			78.9	12			60	

Mean (±SD); Median (Minimum–Maximum); BMI, body mass index; ASA, American Society of Anesthesiologists' physical status classification system.
[a] Significant difference.
[b] Non-normal distribution.

Table 2 Anesthesia time, time to follow commands and extubation time in the REM-PRO and REM-DES groups.

	REM-PRO (*n* = 18)	REM-DES (*n* = 20)	*p*-value
Anesthesia time (min)	193.5 (±79.9)	175.7 (±87.9)	0.52
Time to follow command (min)	8.5 (±3.0)	5.6 (±2.5)	0.00[a]
Extubation time (min)	9.5[b] (4.9–14.4)	6.2 (3.1–18.5)	0.00[a]

Mean (±SD); Median (Minimum–Maximum).
[a] Significant difference.
[b] Non-normal distribution.

Statistical methods

Data are presented as means with standard errors (in parentheses) for variable with normal distribution. For variables with non-normal distribution, data are showed with maximum and minimum values. Differences in recovery times between the desflurane and propofol groups were compared using contingency tables with chi-squared analysis or Fisher's exact test. For continuous variables (duration of anesthesia and extubation time), a two-tailed *t*-test was used. Ordinal data and non-Gaussian continuous data were compared between groups using the Mann–Whitney test. All statistics were performed using SPSS Statistics software (IBM, Armonk, USA)

Results

Demographic data are showed in Table 1. Both groups were homogeneous, except from patient mean ages ($p = 0.03$).

Data from one patient from REM-PRO group were lost and excluded from analysis. Another patient from REM-PRO group awoke very agitated, preventing further assessment. Only her demographic data were included in the analysis.

The REM-PRO and REM-DES mean anesthesia times were similar ($p = 0.52$). However, the Pearson correlation analysis (age vs. extubation time and age vs. time to follow command) revealed that age had no influence on the outcomes in either group ($p > 0.05$). There was no difference between the groups regarding the anesthesia times (Table 2), 193.5 min (±79.9) vs. 175.7 min (±87.9) for the REM-PRO and REM-DES respectively. In the REM-PRO group, the mean time to follow command was 8.5 min (±3.0), whereas in the REM-DES, it was 5.6 min (±2.5), *p*-value = 0.003. This represented a difference of 2.9 min (Table 2). In the REM-PRO group, median time to extubation was 9.5 min (4.9–14.4), while in the REM-DES was 6.2 min (3.1–18.5), *p*-value = 0.012 (Table 2).

The airway protection test results were similar between the REM-PRO and REM-DES groups. Among the patients from REM-PRO group, 16 (88.9%) and 2 (11.1%) succeeded in the airway protection test at the 2nd and 6th minute after the extubation respectively. Similarly, in the REM-DES group, 17 (89.5%) and 2 (10.5%) patients succeeded in the airway protection test 2nd and 6th minute after the extubation respectively. One participant from the REM-DES group refused to do the test after the extubation.

There was no difference in the use of vasopressor during surgery between the REM-PRO and REM-DES groups for hypotension treatment. In each group, cardiovascular drugs were used 4 times as a whole, representing 21.1% and 20% respectively ($p = 1$).

On PACU admission and at the following 15 and 30 min, no statistical significant difference was found in any measured outcomes: episodes of hypotension (defined by mean arterial NIBP less than 60 mmHg) and brady/tachycardia (defined by heart rate lower than 60 or higher 100 bpm); use of supplemental oxygen, NPS, Ramsay sedation scale scores, episodes of PONV. Transportation time between extubation and PACU admission; dose of morphine in the PACU; maximum PACU stay times were also not statically different between the groups.

Discussion

This study showed that time to follow command and extubation times were significantly higher in REM-PRO than in

REM-DES group, in other words, 51.7% and 53% longer respectively. Differences in time to follow command (or emergence time) and extubation time among anesthetics are extensively studied,[7,9,16] although the best strategy for short anesthesia emergence and extubation time has not been defined.[7,17]

It is known that the advantages of one anesthetic over another may not necessarily translate into rapid recovery from anesthesia, especially if the patient received other drugs that could tend to equalize differences between these anesthetics.[7,16] Therefore, in this study, no pre-medication was given prior to the surgery and remifentanil was the sole opioid administrated, differing only in hypnotic agents applied. Unlike other studies,[7,9,16,18] the addition of BIS® monitoring helped the anesthetic administration, since the use of somatic and autonomic monitoring to judge the dosage of anesthetic agents can lead to either anesthetic over or under dosage. In a meta-analysis, Liu et al. demonstrated that BIS® monitoring consistently reduced anesthetic use by 19% compared with standard clinical practice for ambulatory anesthesia.[6] In another meta-analysis, Punjasawadwong et al. showed that BIS monitoring reduced anesthetic consumption: a decrease of 1.32 $mg.kg^{-1}.h^{-1}$ and 1.02 MAC equivalents for propofol and desflurane respectively.[5] Thus, in the present study, all patients were subjected to similar anesthesia depth throughout the surgery, and the times to follow command and the extubation times were measured at comparable anesthesia depth. Given that, the quicker recovery in the REM-DES group could only be the result of the differences in propofol's and desflurane's pharmacology.

In a study, BIS® monitoring reduced all components of early post-anesthesia recovery: time to eye opening (1.93 min), time for response to command (2.73 min), time to extubation (2.62 min) and time to orientation (3.06 min).[5] Our findings are also in accordance with the study of Gupta et al.[7] that systematically reviewed post-anesthesia recovery profiles in ambulatory setting with many anesthetics and found that the time to follow command was 1.3 min quicker with desflurane than with propofol-based anesthesia. A meta-analysis conducted by Wachtel et al. reported 23% and 21% reductions in the mean time to follow command and the mean extubation time, respectively, with desflurane.[9] Desflurane has also a more predictable anesthesia emergence, since it reduced the variability in time to extubation and in following command by 26% and 39%, respectively, in comparison with propofol.[9] Interestingly Wu et al.[18] reported that propofol-based TIVA reduced the mean time to extubation by at least 9% in comparison with desflurane. In this study, however, it is important to note that BIS® monitoring was not used, cases were ran by different anesthesiologists, a high gas flow was not set after turning off the desflurane vaporizer and patients received repetitive boluses of neuromuscular blocking agent and fentanyl as necessary throughout the procedures. All of these aspects could delay post-anesthesia early recovery.[7]

Anesthesia recovery has been demonstrated to be dependent on many factors, in particular the anesthesia duration and depth and also on patient's characteristics.[1] Juvin et al. compared desflurane-based with propofol-based anesthesia in morbidly obese patients and showed that desflurane decreased early recovery times by 60% (6.5 min) for time to eye opening; 57% (7.6 min) for time to extubation and 58% (8.6 min) for time to stating name. A meta-analysis conducted by Liu et al.[8] also found that, in obese patients, desflurane-based anesthesia took less time to respond to a command and to open their eyes than with propofol-based anesthesia.

The pharmacoeconomic aspects of using different anesthetics were not addressed in the present study. The cost of the new anesthetics, in particular desflurane, is a great concern. However, although the direct drug consumption is the easiest way of assessing the costs, anesthesia-related expenses are much broader. Not only drugs should be taken into consideration, but also personnel, equipment used for drug infusion and anesthesia monitoring, surgical aspects, anesthesia recovery and discharge times.[1] In fact, anesthetics constitute less than 4% of the total anesthetic costs for short case procedure,[19] whereas organizational and operational issues, especially personal costs, have a far greater impact on overall spending and may account for two-thirds of total anesthetic expense.[20] Additionally, the use of desflurane has been shown to decrease direct costs in comparison with TIVA, especially when considering wastage.[1,4] Furthermore, reducing fresh gas flow has a profound effect on inhaled anesthetic consumption.[1]

According to Dexter et al.,[21] extubation time influences operation room (OR) workflow: longer extubation times increase the odds of at least one person being idle in the OR (waiting for tracheal extubation), thereby slowing workflow. Reduction in extubation time may decrease the labor costs of the OR use time.[22] This may be the case in procedures with long extubation time, when the extubation time is the bottleneck to the patient leaving the OR, or when the OR is overutilized or booked for more than 8 h and the staffing can be reduced to 8 h.[22] Still, the greatest reduction in direct cost will apply to hospitals at which all ORs are consistently overutilized. In any situation, each minute decreases from OR time reduces from 1.1 to 1.2 min in overall regularly scheduled labor costs.[22] Consequently, a small reduction in OR time by reducing the extubation time, as reported in this study, would reasonably be considered as a saving, since our usual OR workday is longer than 8 h. Additionally, a faster and more predictable post-anesthesia recoveries may lead to intangible benefits, for instance: fewer unhappy surgeons complaining to hospital administrators.[22] Interestingly, when surgeons score anesthesiologists' attributes on a scale from 0, ''no importance'', to 4, ''a factor that would make me switch groups/hospital'', their average score is 3.9 when inquired for ''patient quick to awaken''.[23]

There was no difference in the use of cardiovascular drugs in either group. This shows that hemodynamic stability was satisfactorily provided by the similar anesthetic level of each of the maintenance regimes as also reported by Camci et al.[24]

Mckay et al.[11,12] demonstrated that desflurane allows an earlier return of protective airway reflexes than sevoflurane. Consequently, our hypothesis was that a shorter emergence and extubation times with desflurane anesthesia, in comparison with propofol, would also translate into a faster recovery of the protective airway reflexes. However, when it tested in this study, the results were similar in both groups. In studies performed by Mckay et al.,[11,12] midazolam was given as a pre-medication, fentanyl was administered as

needed throughout the procedures and no BIS® monitoring was applied to both studies. In contrast, in the present study, no pre-medication was given, a short-lived opioid (remifentanil) was administered and BIS® monitoring was used in all patients. One could speculate that these factors might have diminished the differences on protective airway reflexes between the groups evaluated.

At the PACU, the intermediated post-anesthesia recovery profile were akin in both groups. Vital signs were stable in accordance with a study conducted by Loop and Priebe.[4] Still, level of sedation was satisfactory in both groups, as showed by the predominance of the Ramsay score of 2 on admission, after 15 and 30 min. Because of the rapid offset of action of remifentanil, immediate postoperative pain was a great concern. Pain scores were similar in both groups in agreement with other studies.[25,26] However, although our pain control protocol praised multimodal pain management, the high pain scores (NPS > 5) observed in both groups throughout the PACU stay indicates poor pain control. Diabetic, elderly patients, angiotensin receptor blockers and angiotensin-converting enzyme inhibitor takers, which represented a significant fraction of our patients (28.9%), did not receive either ketoprofen or dexametasone or both, a fact that may explain the high pain scores noted reported. Another concern regards desflurane and its higher incidence of PONV in comparison with propofol.[27] Despite that, the incidences were equal in both groups in the present study. The use of BIS® monitoring also explains this finding as meta-analysis demonstrated that it reduces the risk of PONV, probably due to the reduction in anesthetic use.[5,6]

The major limitation of this study was the lack of data regarding remifentanil, desflurane and propofol administered doses to each patient. Additionally, end-tidal desflurane, propofol plasma-site and remifentanil effect-site concentrations were not recorded at the end of surgery and at extubation. These possible confounding factors were indirectly controlled by keeping BIS® value within appropriate range during surgeries for all patients. However, that does not compromise the findings, since patients were extubated after fulling objective and clinical criteria (respiratory rate greater than 12 breaths per minute; tidal volume $\geq 6\,mL.kg^{-1}$, $SaO_2 \geq 97\%$, prompt response to a standard command; or heavy coughing during anesthesia emergence). In respect to the significant differences in patient mean ages between the groups, the Pearson correlation analysis (age vs. time to follow command and age vs. extubation time) revealed that age had no influence on time to follow command and extubation time in either groups ($p > 0.05$). Still, although inhalation induction would be the best study design for patients receiving desflurane in this study, propofol was the only hypnotic agent used for induction in both groups. Desflurane's great pungency increases airway reactivity and also stimulates the sympathetic system, which make its induction impractical.[1]

Conclusion

Remifentanil-desflurane-based anesthesia has a faster time to follow command and extubation time than remifentanil-propofol-based anesthesia when both guided by BIS® with similar indeterminate recovery at PACU.

Registration

This study was approved by the Ethics Committee of the Federal University of Minas Gerais (CAAE – 31820014.8.0000.5149). Patients were recruited for enrollment preoperatively on the day of the surgery and gave written informed consent before enrollment (Fig. 1). The study was registered at ClinicalTrials.gov (NCT02631525).

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Conflicts of interest

The authors declare no conflicts of interest.

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