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Comparison of the effects of dexmedetomidine and remifentanil on perioperative hemodynamics and recovery profile of patients undergoing laryngeal microsurgery

A prospective randomized double-blinded study

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Abstract

Background: Laryngeal microsurgery (LMS) causes hemodynamic instability and postoperative agitation, cough, pain, nausea, and vomiting. Moreover, because of a short operation time, it is associated with challenging anesthetic management. The aim of this study was to compare the usefulness of continuous administration of dexmedetomidine and remifentanil in inducing general anesthesia in patients undergoing LMS.

Methods: This is a prospective randomized control design. Continuous intravenous infusion of dexmedetomidine (group D) or remifentanil (group R) was administered from 10 minutes before the induction of anesthesia to the end of surgery. In both groups, 1.5 mg/kg propofol and 0.5 mg/kg rocuronium were administered for the induction of anesthesia, and desflurane were titrated during the measurement of the bispectral index. We recorded hemodynamic data, recovery time, grade of cough, pain score, and analgesic requirements during the perioperative period.

Results: 61 patients were finally analyzed (30 for group D, 31 for group R). The incidence of moderate to severe postoperative sore throat was higher in group R than in group D (42% vs 10%, $P = .008$), and the quantity of rescue fentanyl used in post-anesthesia care unit was significantly higher in group R than in group D (23.2 ± 24.7 mg vs 3.3 ± 8.6 mg; $P < .001$); however, the time required for eye opening was significantly longer in group D than in group R (599.4 ± 177.9 seconds vs 493.5 ± 103.6 seconds; $P = .006$). The proportion of patients with no cough or single cough during extubation was comparable between the 2 groups (group D vs group R: 73% vs 70%) as was the incidence of hemodynamic instability.

Conclusion: Although there was a transient delay in emergence time, dexmedetomidine reduced postoperative opioid use and the incidence of sore throat. Dexmedetomidine may be used as an alternative agent to opioids in patients undergoing LMS.

Abbreviations: ASA = American Society of Anesthesiologists, BIS = bispectral index, HR = heart rate, LMS = laryngeal microsurgery, MAC = minimal alveolar concentration, MAP = mean arterial blood pressure, PACU = post-anesthesia care unit, VNRS = verbal numeric rating scale.

Keywords: dexmedetomidine, larngeal microsurgery, remifentanil

1. Introduction

Since Pollard described the concepts of anesthetic considerations in laryngeal microsurgery (LMS),[1] many anesthetists have been interested in perioperative management associated with this surgery. Within the short operative period of LMS, sufficient induction of anesthesia is required during airway manipulation.[2,3] However, excessive use of anesthetics causes hemodynamic instability and delayed recovery, which is a challenge for

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YSK and HWC contributed equally to this work.

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The datasets generated during and/or analyzed during the current study are publicly available.

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anesthetists.[4] Usefulness of short-acting opioids, such as remifentanil, in intraoperative hemodynamic stabilization and fast recovery of patients undergoing LMS has been reported,[3,5] but the use of these drugs is associated with several postoperative complications, including postoperative pain[6] and acute opioid tolerance.[7]

Dexmedetomidine may yield arousable sedation as well as analgesia without causing respiratory depression.[8] Currently, it is widely used as a sedative in the surgery or intensive care unit. Dexmedetomidine has been reported to show more favorable results than other sedatives, including midazolam, in terms of analgesia[9,10] and patient and clinician satisfaction,[11,12] without causing additional cardio-respiratory complications.

To achieve both fast recovery and reduced side effects, we focused on the characteristics of dexmedetomidine.[13] We assigned the incidence of sore throat as a primary outcome. We hypothesized that the intraoperative use of dexmedetomidine would reduce postoperative pain, opioid consumption and other complications. The aim of this study was to compare the usefulness of continuous administration of dexmedetomidine and remifentanil while inducing desflurane anesthesia in patients undergoing LMS.

2. Methods

2.1. Study population

This single-center prospective, randomized controlled trial was conducted from 2017 to 2019 at the Korea University Guro Hospital. After obtaining approval from the Korea University Guro Hospital Institutional Review Board (IRB number: 2017GR0160), the trial was registered in the UMIN clinical trial registry (trial identifier: UMIN000030217) prior to patient enrollment. The current study was presented in accordance with the guidelines of the Consolidated Standards of Reporting Trials. After providing an explanation of the trial, written informed consent was obtained from all participants.

Patients aged 20 to 70 years diagnosed with Reinke's edema, laryngeal papilloma, vocal cord polyp, sulcus vocalis, or vocal cord cyst by otolaryngologist with American Society of Anesthesiologists (ASA) physical status I to II who were scheduled to undergo LMS under general anesthesia were included in the study. Exclusion criteria were patient refusal, patient with hemodynamic instability, BMI over 30 kg/m^2, cardiovascular disease except hypertension, difficult airway expected (more than a quarter of the vocal cord covered or hard to assess airway using rigid laryngoscope during preoperative evaluation), chronic cough, asthma, recent respiratory or upper airway disease within 2 weeks, chronic kidney disease stage 4 to 5 or declined liver function classified as Child-pugh class C, history of drug allergies. Patients taking ACE inhibitors, pregnant or lactating patients, and patients unable to communicate were also excluded.

Demographic data including age, weight, height, and ASA class were collected from all patients. The patients were randomly assigned to the dexmedetomidine (group D) or remifentanil (group R) group, and they were unaware of the group assignment before the surgery. A single investigator was responsible for the group assignment of patients. Randomization was achieved using a web-based computer-generated list (www.randomization.com). The subject numbers were placed in opaque, sealed envelopes that were opened in the operating room by an independent anesthesiologist who was not involved in the study.

2.2. Anesthetic protocol

We monitored to the all patient with non-invasive blood pressure measurement, electrocardiography, pulse oximetry, temperature and bispectral index (BIS) during the perioperative period. The baseline values of each parameter were recorded before the induction of anesthesia.

Preoxygenation was performed to all the patients with oxygen mask, which supplies 5 L/min of oxygen before induction. For group D, 1.0 mcg/kg of dexmedetomidine diluted with saline was infused for 10 minutes as a loading dose. Thereafter, saline 5 cc bolus was administered 1 minute before induction. Induction of anesthesia was achieved using propofol 1.5 mg/kg, rocuronium 0.5 mg/kg, and mask ventilation with desflurane (1 MAC, age compensated), and oxygen was supplied at a rate of 8 L/min for 2 minutes 30 seconds, which was followed by endotracheal intubation using a videolaryngoscope. We used reinforced 6.5 mm I.D. (inner diameter) tube for male and 6.0 mm I.D. for female, and all breathing circuit were used 150 cm heated and humidified circuit (Mega Acer kit, acemedical, Goyang, Korea). 0.005 to 0.01 mcg/kg/min of dexmedetomidine was continuously infused as the maintenance dose during the surgery. For group R, we infused saline instead of dexmedetomidine for 10 minutes as a placebo loading dose with a same flow rate to the group D calculated by infusion pump. Thereafter, 1.0 mcg/kg of remifentanil diluted with 5cc saline was administered 1 minutes before induction. There were same protocols to the group D for induction doses of propofol, rocuronium and desflurane and endotracheal tube type and size. 0.05 to 0.1 mcg/kg/min of remifentanil (flow rate comparable to 0.005–0.01 mcg/kg/min of dexmedetomidine) was infused as the maintenance dose.

To explain in detail the drug preparation, a single investigator who was responsible for the group assignments prepared the bolus and infused solution of the study drug. For preparation of the loading dose of the study drug, either 0.9% isotonic saline (group R) or dexmedetomidine (0.1 mg; group D) was diluted in 0.9% isotonic saline to a final volume of 50 mL (final concentrations: dexmedetomidine 2 mcg/mL) in a 50 mL polyethylene syringe (KOVAX-SYRINGE; Korean Vaccine, Seoul, Korea), which was labelled as "Loading X". For preparation of the bolus of the study drug, either 0.9% isotonic saline (group D) or remifentanil (1mcg/kg; group R) was diluted in 0.9% isotonic saline to a final volume of 5 mL in a 5-mL polyethylene syringe (KOVAX-SYRINGE; Korean Vaccine, Seoul, Korea), which was labelled as "Bolus X". For preparation of the infused solution of the study drug, either dexmedetomidine (0.1 mg) or remifentanil (1 mg) was diluted in 0.9% isotonic saline to a final volume of 50 mL (final concentrations: dexmedetomidine 0.2 mcg/mL and remifentanil 2 mcg/mL). The solution was then drawn into a 50-mL polyethylene syringe (KOVAX-SYRINGE; Korean Vaccine, Seoul, Korea) and placed on an infusion pump (INJECTOMAT MC AGILIA; Fresenius Kabi, Bad Homburg, Germany). The infusion pump was labelled as "Infusion X".

Mechanical ventilation was maintained at a tidal volume of 8 mL/kg and an inspiration-to-expiration ratio (I:E ratio) of 1:2, and ventilation frequency (10–14/min of respiratory rate) was adjusted to maintain end-tidal carbon dioxide ($P_{et}CO_2$) at 30 to 35 mm Hg (Primus, Dräger, Lübck, Germany). The limit of the peak inspiratory pressure was 40 mm Hg. When auto-PEEP or other problems of ventilation were suspected, we carefully inspected the overall situation to detect errors in aspects related to the endotracheal tube (size, depth, and kinking), ventilation

Table 1

Tools for assessing intra-operative quality between the 2 groups.

Grade of intubating condition, grade of intraoperative laryngoscopy			
Assessed variables	**Excellent**	**Good**	**Poor**
Laryngoscopy	Easy	Fair	Poor
Jaw relaxation	Relaxed	Not fully relaxed	Poorly relaxed
Resistance to blade	No resistance	Slight resistance	Active resistance
Position of vocal cord	Abducted	Intermediate/moving	Closed
Diaphragmatic movements or cough	None	<2 weak movements for <5 s	>2 movements for <5 s
Excellent: all factors are excellent, Good: all factors are either excellent or good, Poor: a single factor is evaluated as poor			

Grade of cough during emergence	
0	No cough
1	Single cough
2	Persistent cough lasting within 5 s
3	Persistent cough lasting ≥5 s or bucking

Emergence agitation scale (Ricker sedation-agitation scale)	
1	Minimal or no response to noxious stimuli
2	Arousal with physical stimuli but non-communicative
3	Difficult to arouse but awakens to verbal stimuli or gentle shaking
4	Calm and follows commends
5	Anxious or physically agitated and calm with verbal instructions
6	Requires restrains and frequent verbal reminders of limits
7	Pulling at tracheal tube, trying to remove catheters or striking at staff.

Postoperative sore throat	
0	No
1	Mild
2	Moderate
3	Severe

(adequate/inadequate), patient's position, and anesthetic circuit as well as to detect the presence of water accumulation in the ventilator tube, long inspiratory time, and bronchospasm. Anesthesia was maintained with desflurane inhalation in 50% air-oxygen mixture at the rate of 3.0 L/min to achieve a BIS of 40 to 60 and also with continuously adjusted intravenous infusions of dexmedetomidine (0–1 mcg/kg/h) for group D, or remifentanil (0–0.15 mcg/kg/h) for group R to achieve a mean blood pressure of 65 to 95 mm Hg and a heart rate (HR) of 80 to 100 beats/min.

Hemodynamic instability events were defined identically for both groups. Tachycardia was defined as an HR of >90 beats/min. Hypertension was defined as a mean arterial blood pressure (MAP) of >100 mm Hg if its baseline value was <83 mm Hg, or it was also defined as a 20% increase from the baseline MAP if the baseline value was >83 mm Hg. Bradycardia was defined as an HR of <45 beats/min. Hypotension was defined as an MAP of <60 mm Hg. When hypotension or hypertension occurred during the perioperative period, ephedrine 4 mg or nicardipine 300 mcg was administered intravenously, and checked the number of medication. We also counted the number of times the HR or blood pressure increased or decreased.

The hemodynamics and BIS were recorded at baseline, at the time of intubation, 1 minutes after intubation, 5 minutes after intubation, at the time of rigid scope insertion, 3 minutes after rigid scope insertion, and the end of surgery and analyzed.

At the end of surgery, the administration of desflurane + dexmedetomidine (group D) or desflurane + remifentanil (group R) was stopped, fresh gas flow was increased to 8 L/min of oxygen, and sugammadex 2 mg/kg was administered to reverse the neuromuscular blockade. After each patient showed recovery, spontaneous breathing, and consciousness, extubation was performed, and the patient was transferred to the post-anesthesia care unit (PACU).

In operation room, the grade of intubation condition, intraoperative rigid laryngoscopy, and cough during emergence were evaluated by 2 anesthesiologists simultaneously (Table 1). The quality of tracheal intubation conditions and grade of intraoperative laryngoscopy were evaluated according to the previously described scoring system proposed by Viby-Mogensen et al[14] (Table 1). Five factors were considered for assessment (jaw relaxation, ease of laryngoscopy, vocal cord position, presence of cough, and patient movement) as excellent (1), good (2), or poor (3). By using the above criteria, the overall intubating conditions were judged as follows: "excellent," if scores of all conditions were 1; "good," if the score of any of the conditions was 2; and "poor," if the score of any of the conditions was 3. Laryngoscopies (both during intubating and laryngeal surgery) were considered as easy (jaw relaxed, no resistance to laryngoscope blade), fair (jaw not fully relaxed, slight resistance to blade), or difficult (poor jaw relaxation, active resistance of the patient to laryngoscopy). They were considered excellent (all variables were excellent), good (all variables were either excellent or good), or poor (the presence of a single variable listed under poor).

In the PACU, an independent anesthesiologist who was blinded to information of patient group, assessed the recovery time (time required for eye opening), sedation scale (the Richmond Agitation and Sedation Scale) score, verbal numeric rating scale (VNRS; 1–10) score for pain every 10 minutes for 60 minutes, cumulative quantity of fentanyl use, and occurrence of adverse

events. Thirty minutes after the entry of each patient to the PACU, the grade of sore throat and emergence agitation were evaluated (Table 1). Sore throat with VNRS 2 to 3 was judged as mild, while 4 to 6 as moderate, and 7 to 10 as severe. When the patient complained of nausea or vomiting, 10 mg of metoclopramide was administered intravenously, if not contraindicated.

2.3. Statistical analysis

A power analysis based on a previous study[15] which suggested that a minimum sample size of 28 patients would be required for each group to achieve a significance level of 5% and power of 95%. To allow for an exclusion rate, the study population was prospectively set at 64 patients for randomization.

The analyzed data were tested for normality using the Kolmogorov–Smirnov test. Either a parametric or non-parametric analysis was performed depending on the results of the Kolmogorov–Smirnov analysis. Data are expressed as the mean ± SD and compared using independent *t* test or Mann–Whitney *U* test for intergroup analysis. For repeated measurements including BIS, sedation, VNRS, and hemodynamic parameters, repeated measures analysis of variance was used to analyze group effects. When the sphericity condition of the data was not satisfied, the results from multivariate analyses were adopted. On the contrary, when the sphericity condition of data was satisfied, we adopted the results of tests showing within-subjects effects. Categorical variables were compared using chi-squared test or Fisher's exact test, as appropriate.

Statistical analyses were performed using SPSS 22 (IBM, Armonk, NY, Statistical Package for the Social Sciences 22). A *P* value of $<.05$ was considered significant.

3. Results

The CONSORT flow diagram is presented in Figure 1. Finally, a total of 61 patients were enrolled in this study (30 and 31 patients

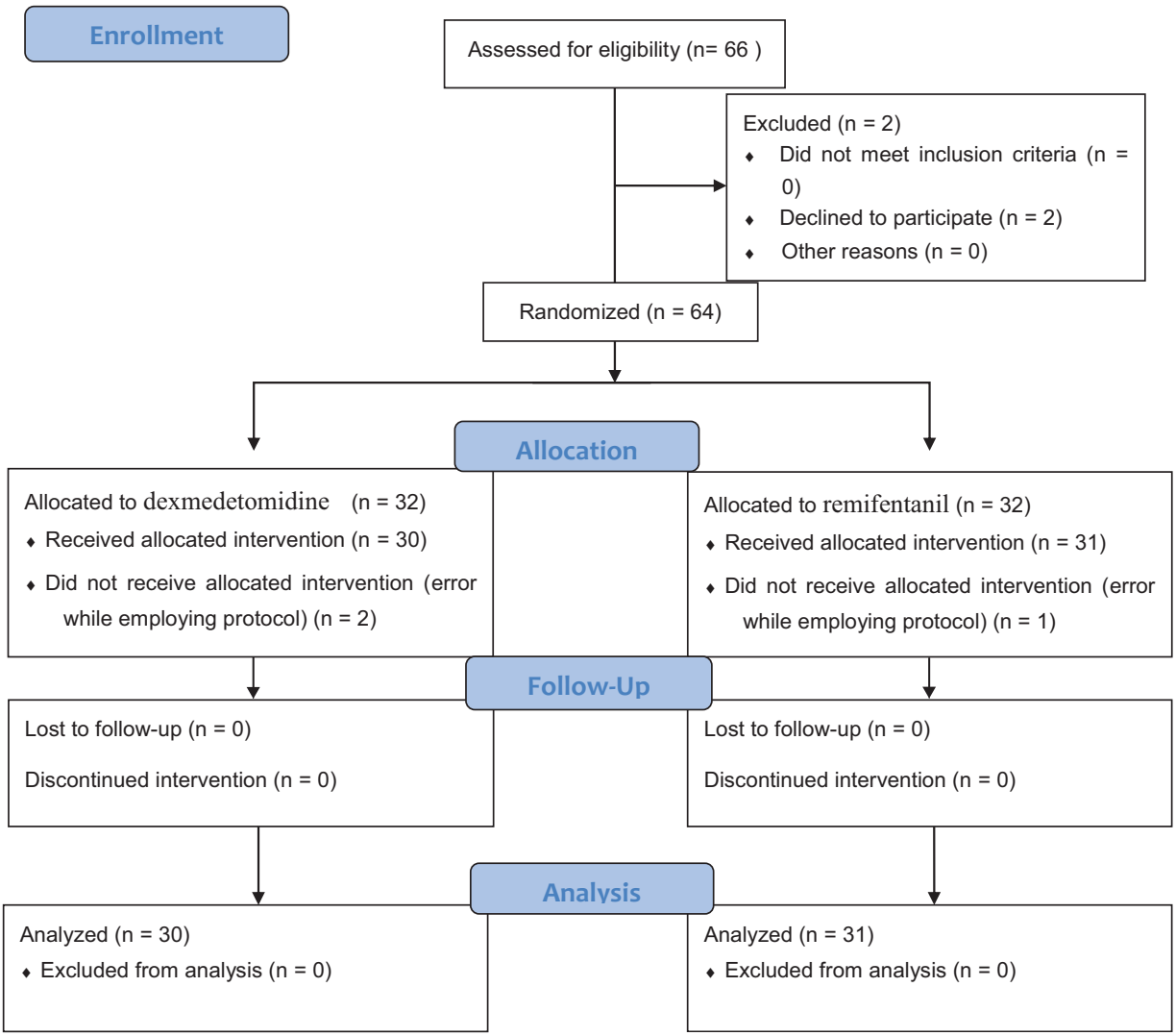

Figure 1. Consort diagram. Initially, 64 patients were randomly assigned to 1 of 2 groups as follows: the dexmedetomidine infusion group (group D) or the remifentanil infusion group (group R). 61 patients (30 in group D and 31 in group R) completed this study.

Table 2

Demographic data.

	Group D ($n=30$)	Group R ($n=31$)	*P* value
Age (yr)	50.9 (11.8)	52.1 (11.7)	.69
Sex (M/F)	18/12	19/12	.92
Height (cm)	161.2 (9.0)	163.6 (8.2)	.66
Weight (kg)	65.5 (9.3)	64.3 (11.5)	.28
Body mass index (kg m^{-2})	23.7 (2.4)	23.9 (2.8)	.77
ASA-PS (1/2)	12/18	11/20	.72
HTN (no/yes)	22/8	25/6	.50
Preoperative hemoglobin level	14.4 (1.3)	14.1 (1.5)	.41

Values are represented as mean (SD) and number of patients. M: male, F: female, Group D: dexmedetomidine infusion group, Group R: remifentanil infusion group, ASA-PS: American Society of Anesthesiologists physical status, HTN: hypertension.

in groups D and R), excluding 3 patients who dropped out during the trial.

Demographic data including sex, age, weight, height, body mass index, preoperative hemoglobin level, presence of hypertension, and ASA class showed no significant differences between the 2 groups (Table 2).

3.1. Perioperative findings in the operation room

The grade of intubation condition, intraoperative rigid laryngoscopy were comparable in the both groups (Table 3).

The incidence of an abrupt increase in HR was significantly low in group D (Table 3). HR, mean blood pressure, and BIS values were comparable between the 2 groups at each specific point during surgery, but multivariate analyses revealed that the variations in HR, blood pressure, and BIS were significantly different (less tachycardia, hypotension and lower BIS in group D compared to those in group R, $P=.004$, $<.001$, 0.007, respectively) (Fig. 2). The number of use of cardiovascular medications including nicardipine and ephedrine was significantly higher in group R (0.55 ± 1.15) than in group D (0.10 ± 0.31; $P=.044$).

Quantities of intraoperative dexmedetomidine (group D) and remifentanil (group R) used by patients were 193.45 ± 142.65 and 147.85 ± 111.30 mcg, respectively (Table 3). The duration of anesthesia or surgery and end-tidal desflurane concentrations were comparable between the 2 groups, but the time required for eye opening after surgery was significantly shorter in group R (493.5 ± 103.6 seconds) than in group D (599.4 ± 177.9 seconds; $P=.006$) (Table 3). The severity of cough during extubation in group D were not inferior to those in group R (Table 3).

Table 3

Perioperative outcomes.

	Group D ($n=30$)	Group R ($n=31$)	*P* value
Dexmedetomidine (mcg)	193.5 (142.7)		N/A
Remifentanil (mcg)		147.9 (111.3)	N/A
Anesthesia time (min)	35.3 (11.9)	34.6 (11.0)	.81
Surgical time (min)	9.7 (8.4)	12.0 (11.0)	.36
Time to eye opening (s)	599.4 (177.9)	493.6 (103.6)*	<.01
Intraoperative events			
Tachycardia	1.9 (2.9)	3.8 (3.1)*	.02
Bradycardia	0.5 (1.5)	0.0 (0.0)	.07
Hypertension events	2.3 (1.9)	1.6 (1.6)	.12
Hypotension events	0.2 (0.8)	0.4 (0.8)	.33
Use of nicardipine	0.1 (0.3)	0.4 (1.0)	.12
Use of ephedrine	0.0 (0.0)	0.1 (0.4)	.18
Use of nicardipine or ephedrine	0.1 (0.3)	0.5 (1.2)*	.03
Grade of intubation condition (1/2/3)	23/6/1	26/3/2	.53
Grade of rigid scope insertion (1/2/3)	29/1/0	27/2/2	.51
Grade of cough during extubation (0/1/2/3)	10/13/3/4	14/8/3/6	.54

Values are represented as mean (SD) and number of patients. Group D: dexmedetomidine infusion group. Group R: remifentanil infusion group. *$P < .05$ compared to group D. Intraoperative events were demonstrated by mean ± standard deviation of events number per patient, and use of nicardipine and ephedrine were also demonstrated by mean ± standard deviation of administration number per patient (nicardipine was administrated by 500 μg, ephedrine was administrated by 4 mg).

3.2. Postoperative findings in the PACU

Postoperative pain scores in the PACU were consistently higher in group R ($P=.032$ for multivariate analysis) (Fig. 3A).

Sedation scores were significantly different at 10, 20, 30, and 40 minutes but not at 50, 60 minutes after the patients were transferred to PACU ($P<.001$, .001, .009, .045, .542, and 1.000, respectively) (Fig. 3B). The incidence of sore throat, and fentanyl consumption were significantly higher in group R than in group D ($P<.01$, and $<.001$, respectively) (Table 4). The incidences of emergence agitation and postoperative nausea and vomiting were comparable between the 2 groups (Table 4). Other adverse events including desaturation were not reported in the both groups.

4. Discussion

In this study, we showed the usefulness of dexmedetomidine compared to that of remifentanil. As we expected, dexmedetomidine showed better postoperative analgesic effects with reducing sore throat which was our primary endpoint, and provided greater perioperative hemodynamic stability than remifentanil when used as a complementary agent to desflurane anesthesia.

In clinical situations, dexmedetomidine has been applied in various ways. We focused on the use of dexmedetomidine as a part of balanced anesthesia, especially as a substitute of opioids.

There is no disagreement that many clinicians use opioids as primary agents for blunting sympathetically mediated hemodynamic changes in response to stressful stimuli.[2] Most opioids act as G-protein coupled mu-receptor agonists[16] and show a dose-dependent decrease in HR, blood pressure, respiratory rate, and tidal volume.[17] Among them, remifentanil has the shortest half-life, which is associated with the fastest recovery, regardless of the infusion period.[18] However, previous studies suggested that it is associated with postoperative pain, acute opioid tolerance, and opioid-induced hyperalgesia.[5,7] From the perspective of early recovery after surgery, remifentanil has a critical disadvantage.

Dexmedetomidine is a highly selective short-acting alpha-2 agonist.[18] As the sedative effect of alpha-2 receptor activation is counteracted by the central alpha-1 receptor, dexmedetomidine is a more potent sedative than other alpha-2 agonists, such as clonidine.[19] Unlike that induced by other gamma-aminobutyric acid-related anesthetics, dexmedetomidine-induced sedation resembles a natural sleep pattern.[20] In addition, by binding to the central and spinal cord alpha-2 receptor, dexmedetomidine provides an analgesic effect.[18] Guo et al[21] showed that dexmedetomidine is directly injected into the locus coeruleus, which leads to the development of antinociception in a rat model and activation of alpha-2 receptor in the spinal cord, suggesting a supraspinal pathway.

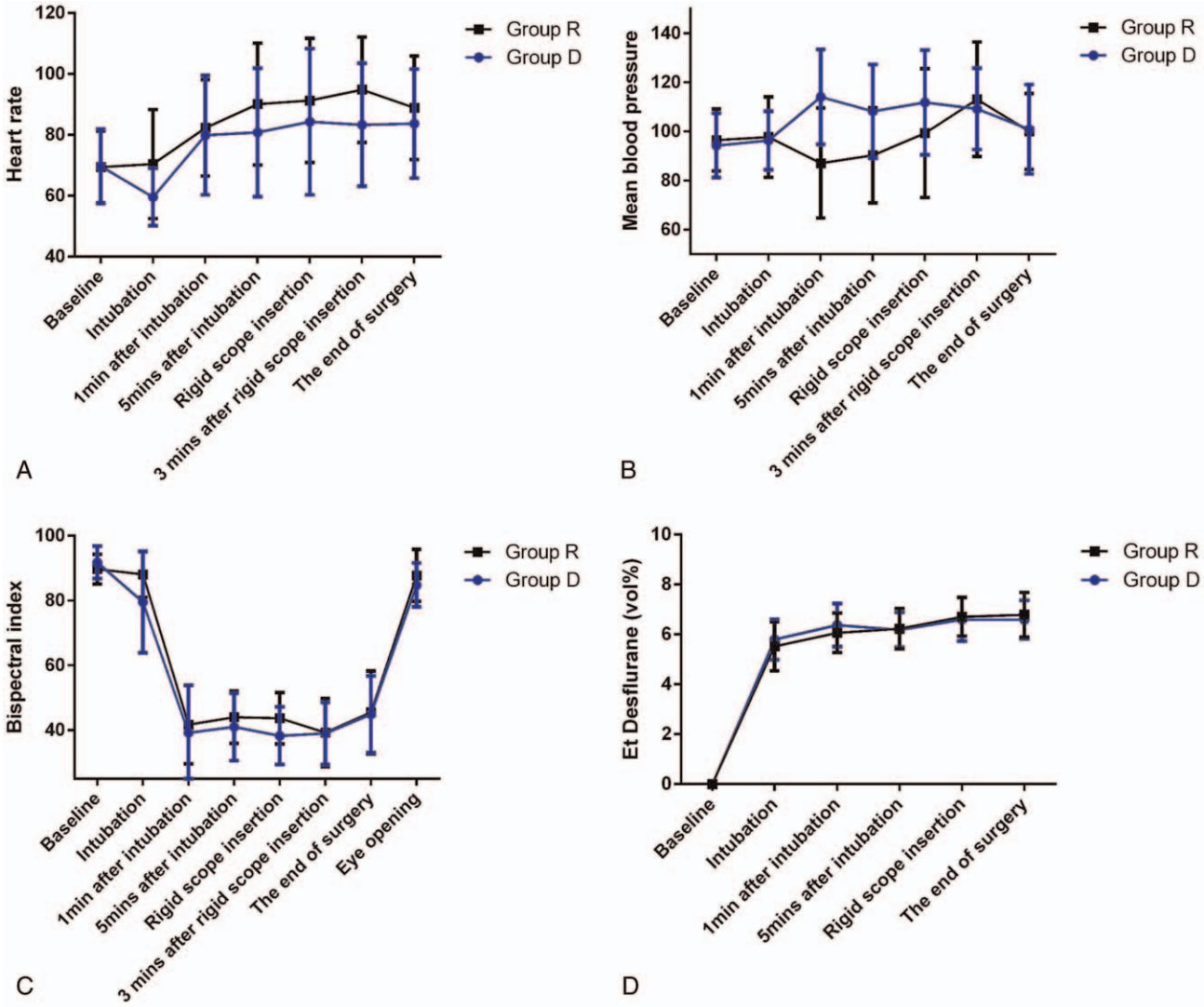

Figure 2. Changes in the heart rate (A), mean blood pressure (B), BIS (C), and end-tidal desflurane concentration (D); The graphs show the mean value and standard deviation of each variable for each time point during general anaesthesia. All data were collected at baseline, 1, 5 min after intubation, at the time of rigid scope insertion for LMS surgery, 3 min after rigid scope insertion, and at the end of the surgery. Group D: dexmedetomidine infusion group. Group R: remifentanil infusion group. All data are comparable between the 2 groups.

Recently, Kaye et al[13] suggested a role of dexmedetomidine in enhanced recovery after surgery. They considered the use of dexmedetomidine as part of a multimodal opioid-sparing approach for the management of postoperative pain. In medical practice, many patients undergoing surgery have been exposed to opioids for the first time. There is much evidence that repeated use of mu-receptor agonists causes tolerance, opioid-induced hyperalgesia, and dependency.[22,23] Synaptic plasticity in opioid-sensitive nerve networks is thought to play an important role in opioid tolerance and adaptation in addition to the mu-receptor itself and cellular and systemic pathways.[22] Although these adaptations often occur during chronic exposure, only a single episode of opioid intoxication may also cause acute tolerance in seconds to minutes in animal or cell studies.[23] Considering these problems, multimodal analgesia, which plays a key role in enhanced recovery after surgery while reducing opioid-related side effects, is important.[4] Meanwhile, dexmedetomidine is known to be less dependent than opioids. A few cases of dexmedetomidine withdrawal syndrome have been reported in limited circumstances.[24] Instead, dexmedetomidine was applied in other drug abuse treatments.[25,26] Under opioid-induced hyperadrenergic state, the use of alpha-2 agonists may decrease sympathetic outflow and counteract the physiological effects.[13]

In our study, there were several indicators for pain assessment. Intraoperative use of dexmedetomidine was more effective in inducing postoperative pain control than was remifentanil. As we expected, incidence of sore throat, which was our primary endpoint, pain score and fentanyl consumption were significantly higher in group R (remifentanil) than in group D (dexmedetomidine). The results were consistent with previous studies.[9,10] It seemed clear that dexmedetomidine helped manage postoperative pain.

In addition, there were several other areas where dexmedetomidine was effective in the perioperative period. Hemodynamic stability was one of the secondary endpoints. Previous studies have suggested the beneficial effect of dexmedetomidine on

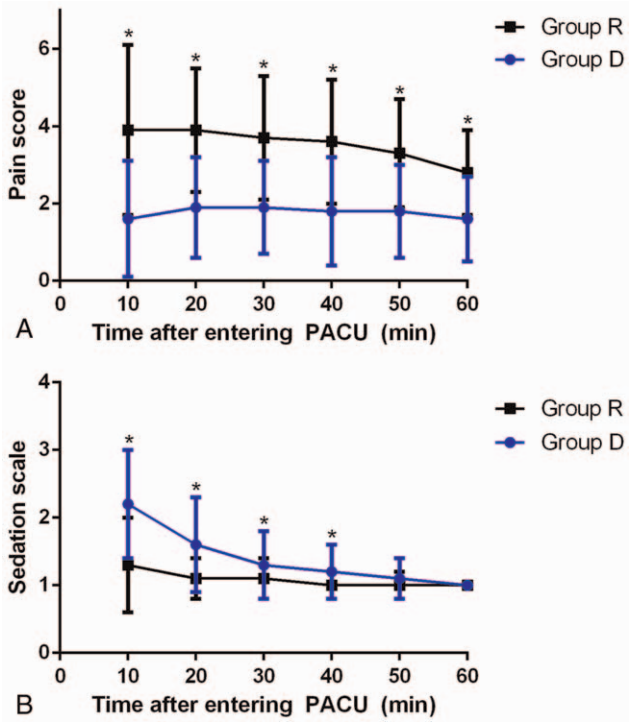

Figure 3. Changes in the outcomes of the 2 groups at the PACU. The graphs show the mean value and standard deviation of pain score (A) and sedation scale (B) for each time point. "*" means the statistically significantly data compared to group D ($P < .05$).

hemodynamic stability.[27,28] Dexmedetomidine may induce biphasic hemodynamic alterations. Alpha-2 mediated vasoconstriction may result in transient tachycardia and elevated blood pressure. However, once the baroreceptor is upregulated and vagal tone is activated, dexmedetomidine may induce hypotension with sympatholytic effects.[18] In our study, our dexmedetomidine regimen represented lesser hypotension during the early phase of surgery than our remifentanil regimen. Abrupt increases in HR and tachycardia were also reported less frequently throughout surgery in the dexmedetomidine group. These findings suggest that although both agents did not result in dramatic changes in hemodynamics, to avoid hypotension in the induction period, our dexmedetomidine regimen would be an appropriate option.

Emergence agitation was also one of the secondary endpoints. Emergence agitation often occurs in the PACU. Dexmedetomidine is known to decrease the occurrence and severity of emergence agitation in pediatric patients.[13] Other sedatives that act on gamma-aminobutyric acid can potentially alter the levels of deliriogenic neurotransmitters, resulting in negative consequences.[29] In our study, the incidence and severity of emergence agitation seemed lower in group D than in group R, but the difference were not significant. One of the reasons why emergence agitation did not differ significantly in the results of this experiment was that the experimental design was not suitable for evaluating emergence agitation. (The relatively low incidence of emergence agitation in adults was another reason.) Based on our result of emergence agitation severity, 0.444 of effect size was calculated, which means 81 patients in each group (without consideration of the drop-out rate) are required to evaluate emergence agitation with a significance level of 5% and a power of 80%.

Sharma and Mehta[30] reported that dexmedetomidine provided better intubating conditions, including mask ventilation, jaw relaxation, and vocal cord position, than the placebo. However, they did not explain the mechanism of these phenomena. Although the evidence is poor, it seems that the actions of alpha-2 receptors, including constriction of vascular smooth muscle,[31] decrease in the motility of smooth muscle[32] and decrease in secretion from the salivary gland[33] may have influenced this phenomenon. Meanwhile, remifentanil also has a beneficial effect during intubation. Puchner et al[34] showed that the use of remifentanil was associated with a lower grimace, cough, and movement during awake intubation that was the combination of midazolam and fentanyl. To the best of our knowledge, no well-designed study has compared dexmedetomidine and remifentanil under intubation conditions. In our experimental results, remifentanil appeared to be slightly better than dexmedetomidine, but this difference was not significant.

Previous studies have reported that dexmedetomidine may decrease postoperative nausea and vomiting compare to remifentanil[35] or placebo.[36] We also investigated the effects of these drugs on nausea and vomiting. There were only 7 cases of mild nausea (3 in dexmedetomidine and 4 in remifentanil) in our study, so we could not confirm which of these drugs was better. It is known that nausea is one of the side effects of dexmedetomidine,[13] but its extent seemed to be smaller than that associated with opioids. In this study, because the operation time was short and the amounts of study drug used were relatively small, the effect on nausea seemed insignificant.

Although we investigated many advantages of dexmedetomidine, there was a significant shortcoming. In our study, patients in group D showed awakened with a delay of about 100 seconds and remained sedated for 40 minutes in the PACU; however, there was no respiratory depression or other severe complications. Delayed recovery may lead to additional expenditures on medical expenses and adversely affect surgical management. In our center, this cost has been calculated to be reasonable, but it may differ in other provinces or countries. Therefore, risk and benefit should be thoroughly considered while applying dexmedetomidine or remifentanil.

We observed a statistically significant difference in the pattern of BIS change. Dexmedetomidine showed slightly lower BIS during surgery. Dexmedetomidine may further reduce intraoperative recall, but this interpretation was limited by a lack of evidence of the mechanism. In addition, because the 2 agents showed their own strengths and weaknesses in this study, we cannot determine which one is better. Therefore, rather than

Table 4

Outcomes in post-anesthetic care unit (PACU).

	Group D ($n=30$)	Group R ($n=31$)	*P* value
Fentanyl consumption per patient (mcg)	3.3 (8.6)	23.2 (24.7)*	<.001
Postoperative sore throat (0/1/2/3)	19/8/3/0	6/12/11/2*	< 0.01
Emergence agitation (1/2/3/4/5/6/7)	4/7/5/8/6/0/0	3/3/2/12/9/2/2	.30
Nausea and vomiting (Y/N)	3/27	4/27	1.00
SpO_2 < 95% (Y/N)	0/30	0/31	1.00

Values are represented as mean (SD) and number of patients. Group D: dexmedetomidine infusion group. Group R: remifentanil infusion group. PACU: post-anesthetic care unit. *$P < .05$ compared to group D. Postoperative sore throat 0; none, 1; mild, 2; moderate, 3; severe.

seeking a simple answer, we have to think about each situation. Our data may provide useful information to understand the clinical characteristics of the 2 agents. In some cases, it may be helpful to obtain a proper answer for a balanced combination of dexmedetomidine and remifentanil while considering various factors. We also expected that both dexmedetomidine and remifentanil may have beneficial effects by reducing desflurane requirements, because adjuvant anesthetics may reduce complications by sparing the total dosage of the main anesthetics. In our study, the desflurane-sparing effects of the 2 drugs at the experimental dose were comparable considering that the level of desflurane during operation were not different.

There were some limitations. Because this study was conducted in healthy people, delirium or other complications were not sufficiently observed.[37] The effects of dexmedetomidine and remifentanil may be amplified in patients with cardiovascular disorders. In addition, the possibility of drug-interaction with desflurane cannot be excluded. Especially, desflurane may induce increased HR and airway irritation[38] which may result in significant effects in our study. There was also another limitation in the research design. In the first place, the primary outcome was sore throat, which was a very natural result, not hemodynamic instability or other indicators. Therefore, evidences are still weak for minor outcomes. Further studies are required in patients with specific conditions under various research hypothesis.

5. Conclusions

Dexmedetomidine showed reduced sore throat incidence, pain intensity and opioid sparing effects as well as hemodynamic stability. Although there was a transient delay in emergence time, dexmedetomidine can be properly applied as an alternative agent to enhance recovery after LMS.

Author contributions

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