Effect of Dexmedetomidine on Preventing Agitation and Delirium After Microvascular Free Flap Surgery: A Randomized, Double-Blind, Control Study

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Purpose: To determine whether dexmedetomidine sedation in the postanesthesia care unit (PACU) could decrease agitation and delirium after free flap surgery.

Materials and Methods: Eighty patients were randomly divided into 2 groups. In the experimental group, dexmedetomidine was given at an hourly infusion rate of 0.5 μg/kg for 1 hour before the operation was completed and continued in the PACU at 0.2 to 0.7 μg/kg continuously until the next morning. In the control group, normal saline was given during the same periods. Patients in the 2 groups received sufentanil and midazolam for sedation and pain relief when necessary. Agitation was monitored with the Riker Sedation-Agitation Scale in the PACU and delirium was monitored with the Confusion Assessment Method for the Intensive Care Unit for 5 days postoperatively.

Results: The overall incidence of agitation was similar between the 2 groups. However, when the influence of patient shifting was excluded, the incidence of agitation in the dexmedetomidine group was apparently lower than that in the control group (10.3 vs 30%; $P = .029$). No difference was found in the occurrence of delirium between the experimental and control groups (5.1 vs 12.5%; $P = .432$).

Conclusion: Dexmedetomidine does not change the overall incidence of agitation after free flap surgery; however, it does decrease agitation after PACU admission. It does not prevent delirium within 5 days postoperatively.

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Tumor resection with microvascular free flap reconstruction of defects is a major procedure in maxillofacial surgery. It is characterized by a long operation time, multiple surgical sites, and considerable blood loss. Patients are usually kept intubated or receive preventive tracheotomy after the operation,[1,2] and restricted movement of their heads is often required for 3 to 5 days to avoid severe traction on anastomosed blood vessels.[1,2] Postoperatively, factors such as pain, airway stimulation, and immobilization and the residual effect of anesthetics make these patients easily agitated during recovery from anesthesia.[3] Some patients even develop delirium within several days after surgery. It has been reported that agitation occurs in nearly 65% of patients after flap reconstruction[3] and that the incidence of postoperative delirium ranges from 2[4] to 70%[5] after free flap surgery. In the authors' hospital, agitation is common after free flap surgery, and patients are usually sedated with sufentanil and midazolam when necessary. Severe agitation and delirium can increase

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the difficulty of nursing, resulting in patient self-injury or even failure of the transferred flap. Thus, it is important to keep patients well sedated.

Dexmedetomidine is a highly specific α_2-adrenoreceptor agonist. It has sedative and analgesic effects, does not inhibit patients' spontaneous respiration, and is used mostly in the intensive care unit (ICU).[6] Early studies have shown that dexmedetomidine decreases agitation in pediatric patients during recovery from general anesthesia,[7-9] decreases delirium in mechanically ventilated adult patients in the ICU,[10] and shortens the course of patient delirium after cardiac surgery.[11] Thus, the authors hypothesized that it could decrease agitation or even delirium in patients after free flap surgery. In adult patients, reports of using dexmedetomidine to prevent emergence agitation are limited, and there have been only a few studies in oral and maxillofacial surgery.[12] Although beneficial for sedation and without a deleterious influence on the transferred flap,[13] dexmedetomidine use has not been reported after free flap surgery. Clinically, patients appear calmer when administered dexmedetomidine for sedation during the recovery period, but there is a lack of proof from a randomized controlled study. Furthermore, the influence of dexmedetomidine on postoperative delirium after discontinuation is unclear.

The aim of this study was to investigate whether continuous dexmedetomidine sedation in the postanesthesia care unit (PACU) decreases agitation and makes patients more comfortable after free flap surgery, and whether the use of dexmedetomidine in the PACU can prevent patient delirium within several days after free flap surgery.

Materials and Methods

STUDY DESIGN AND ENROLLMENT CRITERIA

This was a prospective, randomized, double-blinded, placebo-controlled study. The study was approved by the ethics committee of Peking University School and Hospital of Stomatology (Beijing, China; number PKUSSIRB-2012006) and registered at https://clinicaltrials.gov (identifier, NCT01904760). It was conducted in the Department of Oral and Maxillofacial Surgery at Peking University School and Hospital of Stomatology from June 2013 to October 2013. Written informed consent was obtained from all patients before surgery. Patients were enrolled if they were 18 to 80 years old, classified as having American Society of Anesthesiologists physical status I or II, and scheduled for selected maxillofacial surgery with microvascular free flap reconstruction. Exclusion criteria included bradycardia (preoperative heart rate <50 beats/minute), second- or third-degree atrioventricular block, systolic blood pressure (SBP) lower than 80 mmHg, known allergy to α_2 agonists, psychiatric illness, severe dementia, pregnancy, and absence of written informed consent.

RANDOMIZATION

Patients were randomized by a computer-generated random-number sequence. The random number was disclosed only when the flap reconstruction procedure was started, and the study drug was prepared by a nurse anesthetist. The study drug (dexmedetomidine; Hengrui Medical Company, Jiangsu, China) was prepared at a concentration of 4 μg/mL and 0.9% saline was used for patients assigned to the control group. Patients and all caregivers, including anesthetists, PACU medical staffs, and postoperative investigators, were blinded to the treatment given.

STUDY PROTOCOL

Perioperative Management

All patients received the same anesthetic protocol and perioperative management. Patients were routinely monitored with electrocardiography, pulse oximetry (oxygen saturation), capnography, and invasive BP. Anesthesia was induced with midazolam, sufentanil, propofol, and rocuronium. After nasotracheal intubation was established, mechanical ventilation was initiated with a tidal volume of 8 mL/kg and a respiratory rate of 12 breaths/minute. General anesthesia was maintained with inhalational sevoflurane, nitrous oxide, and oxygen. Oxygen saturation was kept above 97% and end-tidal carbon dioxide was kept at 35 to 45 mmHg. Additional doses of sufentanil and a target-controlled infusion of remifentanil were used according to surgical stimuli. Patients' SBP was maintained above 90 mmHg and heart rate (HR) was maintained above 50 beats/min. A 5-μg dose of sufentanil was administered 30 minutes before the end of the operation to decrease postoperative pain. A minimum of 2% sevoflurane inhalation was maintained until leaving the operating room. All patients were given continuous postoperative analgesia for 2 days by a pump device that administered sufentanil 1 μg/kg and granisetron 3 mg in saline 100 mL at a rate of 2 mL/hour. Depending on the extent of resection, patients' endotracheal tubes were maintained overnight or a preventive tracheotomy was performed at the end of the operation. After the operation, patients were transferred to the PACU, which has 8 beds and is the ICU of the authors' hospital. All patients breathed spontaneously after the operation and were monitored continuously in the PACU. The next morning, maintained endotracheal tubes were removed at approximately 7:00 AM, and patients were transferred back to the wards for further monitoring at 8:00 AM. Patients were followed for 5 days postoperatively; sedatives and analgesics were given whenever needed.

Study Drug Administration

Infusion of the blinded study drug was started approximately 60 minutes before the end of surgery. Patients received dexmedetomidine or 0.9% saline (equivalent to dexmedetomidine at approximately 4 μg/mL) at an hourly rate of 0.5 μg/kg until the operation was completed; infusions were continued in the PACU at hourly rates of 0.2 to 0.7 μg/kg until 6:00 AM the next morning. The rate of study drug infusion was adjusted by physicians in the PACU to keep the patients sedated. The optimal goal was to keep patients calm and cooperative, with their heads in the required position. If agitation was confirmed, low doses of sufentanil (0.05 to 0.1 μg/kg) were given and followed with midazolam 0.01 to 0.05 μg/kg when necessary. This was repeated every 10 to 20 minutes until patients were fully sedated. Low doses of sufentanil or midazolam also were given when the patients complained of pain or difficulty sleeping. The study drug was paused if SBP decreased below 90 mmHg or HR decreased below 50 beats/min and then followed by a low dose of ephedrine or atropine when necessary.

VARIABLES

The primary predictor variable was the 2 study groups (dexmedetomidine vs control). Other variables, such as age, gender, type of flap surgery, intraoperative fluid and sufentanil consumption, blood loss, tracheotomy after the operation, and length of PACU stay, were collected during the study.

The primary outcome variable was the incidence of agitation during patients' stay in the PACU. Agitation was assessed with the Riker Sedation-Agitation Scale (SAS) and defined as a score of at least 5 (1, unable to rouse; 2, very sedated; 3, sedated; 4, calm and cooperative; 5, agitated; 6, very agitated; 7, dangerous agitation).[14]

A secondary outcome variable was the incidence of postoperative delirium within 5 days after the operation. Delirium was determined by the Confusion Assessment Method for the ICU (CAM-ICU).[15] Other secondary outcome variables included patients' pain, sleep, and comfort scores in the PACU, hemodynamic data in the PACU, use of sufentanil and midazolam in the PACU, and adverse postoperative events.

DATA COLLECTION METHODS

Patients' vital signs and sedation levels were monitored continuously in the PACU. Hemodynamic data, including HR and BP, were recorded when entering the PACU; at 1, 2, 4, 6, and 12 hours after admission; and when leaving the PACU. Agitation was recorded by the nurses in charge and was confirmed by the investigator in the PACU according to the SAS (SAS score, ≥5). Before leaving the PACU, patients were asked to rate their overall sleep quality, pain, and comfort level using a numerical scale of 1 to 10 (0 = worst and 10 = best for sleep and comfort assessments; 0 = no pain and 10 = most pain for pain assessment). Sufentanil and midazolam use in the PACU also was recorded.

Patients were followed for 5 days postoperatively. Postoperative delirium was evaluated by the investigator using the CAM-ICU[15] at approximately 5:00 PM on each of the 5 days. Patients' level of consciousness (evaluated with the Richmond Agitation-Sedation Scale [RASS]), sleep quality during the previous night (rated as worst, poor, normal, better, or best), pain score (0 to 10; 0 = no pain, 10 = most pain), and the presence of other symptoms (eg, nausea and vomiting, low back pain, or headache) were recorded. Surgical complications, such as vascular crisis and flap surgery failure, also were monitored.

STATISTICAL ANALYSIS

Sample Size Estimation

The sample size was determined by power analysis. According to the published literature,[3] the incidence of agitation after free flap surgery is approximately 65%; thus, a sample of 36 patients per group, with an α value equal to 0.05, allowed a power of 80% to detect a 50% difference between groups. The sample was increased to 80 patients (40 patients per group) to avoid protocol violation because of dropouts.

Data Analysis

Continuous data and ranked data are presented as mean ± standard deviation or median (interquartile range) as appropriate. The Kolmogorov-Smirnov test was used to test for normality. Differences between the 2 groups were assessed with the independent *t* test or the Mann-Whitney *U* test for unpaired data (eg, pain, sleep, and comfort scores in the PACU and sufentanil and midazolam use in the PACU). Analysis of variance for repeated measurement data was used to analyze hemodynamic data. Categorical data were presented as number (percentage) and were analyzed with the χ^2 and Fisher exact tests (eg, agitation in the PACU, postoperative delirium, subgroup analysis, and postoperative complications). Statistical analysis was performed with SPSS 17.0 for Windows (SPSS, Inc, Chicago, IL). A *P* value less than .05 was accepted as statistically significant.

Results

From June 2013 to October 2013, written informed consent was obtained from 90 patients before surgery. Seven patients were excluded from the study because of intraoperative cancellation of

free flap reconstruction. One patient was excluded because of severe bradycardia (HR <50 beats/minute) before anesthetic induction. Two patients were excluded because of surgical cancellation owing to medical problems. Therefore, 80 patients were randomized and given the study drug or saline. Of these, 1 patient was excluded from the statistical analysis because of protocol violation (the study drug was not given in the PACU because the patient stayed there for <2 hours). The remaining 79 patients were included in final statistical analysis. There were 39 patients in the experimental group and 40 patients in the control group.

The patient characteristics and surgical data are listed in Table 1. There were no differences between groups in demographics, medical history, type of flap surgery, operation length, total intraoperative fluid and sufentanil consumption, blood loss, postoperative tracheotomy, and length of PACU stay ($P > .05$; Table 1).

The HR in the experimental group was significantly lower than that in the control group at all time points ($P < .05$). The SBP in the experimental group was lower than that in the control group at all time points; the difference was statistically significant at 6 and 12 hours after PACU admission ($P < .05$). Diastolic BP in the experimental group was lower than that in the control group at 12 hours after PACU admission ($P < .05$; Table 2).

The overall incidence of agitation in the PACU was similar between the 2 groups (38.5% [15 of 39] for experimental group vs 45% [18 of 40] for control group; $P = .556$). Because patients tended to be more irritated when they were shifted from flatbed carts to the PACU beds and checked by the nursing staff, the incidence of agitation was subdivided into agitation after PACU admission. The 11 patients in the experimental group and 6 patients in the control group who were agitated only during admission were excluded, showing that the incidence of agitation after admission was lower in the experimental group than in the control group (10.3% [4 of 39] vs 30% [12 of 40], respectively; $P = .029$; Table 3).

No differences were found between the 2 groups for the use and dosage of sufentanil and midazolam in the PACU ($P > .05$; Table 3). Although patients in the experimental group subjectively seemed to be calmer in the PACU, no differences were found between the experimental and control groups with regard to their scores for sleep (5.0 [3.0 to 7.0] vs 5.0 [3.0 to 7.5], respectively; $P = .507$), pain (4.0 [2.0 to 5.0] vs 4.0 [0.3 to 5.0], respectively; $P = .534$), and comfort (5.0 [4.0 to 8.0] vs 5.0 [3.0 to 7.0], respectively; $P = .484$; Table 3).

The incidence of delirium within 5 days postoperatively was similar between the 2 groups (experimental group, 5.1% [2 of 39] vs control group, 12.5% [5 of 40]; $P = .432$). Patients' primary complaints, such as sleep

Table 1. PATIENT CHARACTERISTICS AND SURGICAL DATA

Variable	Experimental Group	Control Group	*P* Value
Sample size	39	40	NA
Age (yr)	50.3 ± 15.0	50.6 ± 12.3	.938
Men/women	21/18	21/19	.905
Height (cm)	166.7 ± 6.9	167.4 ± 7.9	.696
Weight (kg)	59.2 ± 11.9	62.9 ± 13.4	.198
Medical history			
Hypertension	5 (12.8)	8 (20)	.390
Coronary artery disease	1 (2.6)	2 (5)	.571
Diabetes	2 (5.1)	1 (2.5)	.541
Cerebral infarction	2 (5.1)	0 (0)	.241
Type of flap surgery			
Fibula/forearm/thigh	23/13/3	26/9/5	.497
Length of operation (minutes)	399.1 ± 94.6	402.7 ± 92.6	.865
Total intraoperative fluids (mL)	2,815.4 ± 557.5	2,855.0 ± 444.9	.728
Intraoperative sufentanil consumption (μg)	25.6 ± 8.2	25.9 ± 9.9	.848
Estimated blood loss (mL)	432.0 ± 132.6	403.7 ± 125.3	.055
Tracheotomy after operation	24 (61.5)	20 (50)	.302
Length of PACU stay (hours)	14.5 ± 2.3	13.7 ± 2.8	.156

Note: Continuous variables are presented as mean ± standard deviation. Descriptive variables are presented as number (percentage).

Abbreviations: NA, not applicable; PACU, postanesthesia care unit.

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Table 2. HEART RATE AND BLOOD PRESSURE DURING PATIENTS' STAY IN THE POSTANESTHESIA CARE UNIT

Variable	Group	T_{in}	T_1	T_2	T_4	T_6	T_{12}	T_{out}
HR (beats/min)	Experimental	78.8 ± 11.9*	72.5 ± 12.4*	70.6 ± 12.8*	72.8 ± 12.7*	74.9 ± 12.2*	75.6 ± 12.8*	78.7 ± 10.6*
	Control	95.9 ± 12.2	88.7 ± 11.9	94.5 ± 10.2	90.2 ± 12.2	86.5 ± 17.4	80.2 ± 10.4	85.3 ± 12.2
SBP (mmHg)	Experimental	122.3 ± 16.0	127.9 ± 15.6	122.1 ± 19.8	122.4 ± 14.4	113.8 ± 12.2*	107.3 ± 13.7*	110.0 ± 14.8
	Control	132.8 ± 18.8	129.8 ± 16.7	127.9 ± 15.9	124.0 ± 14.7	120.5 ± 15.3	114.8 ± 14.2	114.6 ± 16.1
DBP (mmHg)	Experimental	72.4 ± 14.9	74.2 ± 11.2	72.4 ± 10.5	69.9 ± 10.0	65.0 ± 9.7	60.4 ± 11.2*	63.5 ± 10.9
	Control	75.7 ± 14.4	73.6 ± 10.1	72.3 ± 11.4	70.2 ± 10.3	65.2 ± 9.9	65.2 ± 8.1	67.4 ± 14.2

Note: Data are presented as mean ± standard deviation.

Abbreviations: DBP, diastolic blood pressure; HR, heart rate; SBP, systolic blood pressure; T_1, 1 hour after admission to the postanesthesia care unit; T_2, 2 hours after admission to the postanesthesia care unit; T_4, 4 hours after admission to the postanesthesia care unit; T_6, 6 hours after admission to the postanesthesia care unit; T_{12}, 12 hours after admission to the postanesthesia care unit; T_{in}, entry to postanesthesia care unit; T_{out}, departure from postanesthesia care unit.

* Significantly different from control group ($P < .05$).

disturbance (sleep was graded as "worst" for ≥2 days), severe pain from wounds (pain score, >5), headache, nausea and vomiting, and excessive sputum, were similar between the 2 groups ($P > .05$; Table 4).

Postoperative complications are listed in Table 5. There were no differences between the 2 groups for hypotension, bradycardia, vascular crisis of the flap, postoperative infection, and medical complications such as respiratory failure ($P > .05$). The revision surgery and flap failure rates also were similar between the 2 groups ($P > .05$).

Discussion

This prospective, double-blinded, comparative study primarily investigated the effect of dexmedetomidine on decreasing agitation in patients after free flap surgery during their recovery in the PACU. The results showed that the overall incidence of agitation was similar between the treatment and control groups. However, when the influence of patient shifting was excluded, the incidence of agitation was lower in the dexmedetomidine group than in the control group (10.3% [4 of 39] vs 30% [12 of 40], respectively; $P = .029$). The data suggest that dexmedetomidine is effective in decreasing agitation after admission to the PACU.

The characteristics of recovery from general anesthesia and the management of agitation after flap surgery are seldom described in the literature. In the authors' unit, patients are usually breathing spontaneously and intubated when entering the PACU. During the course of PACU admission, patients are moved into PACU beds, checked for bed sores, and have their tracheas suctioned by nurses. These procedures are strong stimuli for patients and can cause agitation in some less sedated patients. Several methods were used in this study to increase the level of sedation, including the maintenance of sevoflurane inhalation, low doses of sufentanil given before procedures were completed, and a loading dose of dexmedetomidine administered intraoperatively. However, patients' responses to stimuli could not be completely suppressed. Moreover, residual anesthesia and inadequate analgesia also can induce agitation in some patients. Thus, factors associated with PACU transfer made the overall incidence of agitation complicated and similar between the 2 groups.

After admission, patients no longer received such strong stimuli during their care, and the effect of dexmedetomidine became more apparent. Dexmedetomidine activates α_2-adrenergic receptors in the central nervous system, inhibits the release of norepinephrine, and produces sedation, anxiolysis, and analgesia through net pathways.[16] The efficacy of dexmedetomidine in decreasing agitation after PACU admission

Table 3. VARIABLES DURING PATIENTS' STAY IN THE PACU

Variable	Experimental Group (n = 39)	Control Group (n = 40)	*P* Value
Overall agitation	15 (38.5)	18 (45)	.556
Agitation after admission	4 (10.3)	12 (30)	.029
Sufentanil use in PACU	21 (53.8)	25 (62.5)	.436
Sufentanil dosage (μg)	5.1 ± 6.3	6.5 ± 6.8	.337
Midazolam use in PACU	5 (12.8)	8 (20)	.390
Midazolam dosage (mg)	0.3 ± 0.8	0.6 ± 1.5	.221
Overall sleep score	5.0 (3.0-7.0)	5.0 (3.0-7.5)	.507
Pain score	4.0 (2.0-5.0)	4.0 (0.3-5.0)	.534
Overall comfort score	5.0 (4.0-8.0)	5.0 (3.0-7.0)	.484

Note: Data are presented as mean ± standard deviation, number (percentage), or median (interquartile range).
Abbreviation: PACU, postanesthesia care unit.

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observed in this trial is similar to the results of previous ICU studies.[10,17]

Patients' HR and SBP were lower in the dexmedetomidine group than in the control group. This is in accordance with previous studies of dexmedetomidine[18,19] and is caused by the inhibitory effect of dexmedetomidine on the sympathetic nervous system.[16] The hemodynamic data also prove that dexmedetomidine was effective in this study.

It is interesting to note that, although dexmedetomidine decreased agitation after PACU admission, the overall sleep, pain, and comfort scores were similar between groups. One explanation is that patients in the 2 groups received equal overall sedation and analgesia, resulting in similar comfort levels. Although saline was infused instead of dexmedetomidine in the control group, patients were not without any treatment. Their pain, anxiety, and sleeplessness also were treated by sufentanil and midazolam as described earlier. Another explanation could be related to the sleep characteristics associated with dexmedetomidine. Oto et al[20] found that dexmedetomidine induced non-physiologic sleep, which is constituted primarily of non-rapid eye movement (NREM) sleep without evidence of slow wave sleep or REM. This could be because dexmedetomidine binds to α_2 receptors in the locus ceruleus and inhibits the release of norepinephrine, which is important for NREM sleep.[21] Similarly, Stephanie et al[19] found that dexmedetomidine does not improve patient satisfaction, although it is clinically effective.

The incidence of delirium within 5 days postoperatively was the second endpoint of the study. It has been unknown whether continuous dexmedetomidine sedation in the PACU influences delirium after discharge. The present results showed no difference in postoperative delirium between groups. This can be explained in part by the short elimination half-life of dexmedetomidine, which is approximately 2 hours.

Table 4. DELIRIUM AND PATIENTS' MAIN COMPLAINTS WITHIN 5 DAYS POSTOPERATIVELY

Variable	Experimental Group	Control Group	*P* Value
Delirium	2 (5.1)	5 (12.5)	.432
Severe sleep disturbance	2 (5.1)	7 (17.5)	.154
Severe pain from wounds	18 (46.2)	11 (27.5)	.085
Excessive sputum	28 (71.8)	28 (70)	.861
Lower back pain	8 (20.5)	9 (22.5)	.830
Headache	18 (46.2)	19 (47.5)	.905
Nausea and vomiting	5 (12.8)	6 (15.0)	.780

Note: Data are presented as number (percentage).

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Table 5. POSTOPERATIVE COMPLICATIONS

Variable	Experimental Group	Control Group	*P* Value
Hypotension in PACU	0 (0)	1 (2.5)	1
Bradycardia in PACU	1 (2.6)	0 (0)	.494
Vascular crisis of flap	2 (5.1)	2 (5.0)	1
Revision surgery	3 (7.7)	3 (7.5)	1
Failure of flap	0 (0)	1 (2.5)	1
Postoperative infection	1 (2.6)	0 (0)	.494
Respiratory failure	1 (2.6)	0 (0)	.494

Note: Data are presented as number (percentage).
Abbreviation: PACU, postanesthesia care unit.

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The effect of dexmedetomidine on delirium can decrease with time, even with continuous infusion in the PACU. In addition, there are multiple risk factors for postoperative delirium, including age, pain, and sleep disturbances, among others[22]; because the major complaints within 5 days postoperatively were similar between the treatment and control groups, it is reasonable to believe there was a similar incidence of delirium between these groups. This result is in agreement with a previous cardiac ICU study,[11] which also did not find a preventive effect by dexmedetomidine on postoperative delirium. As indicated by the 2013 guidelines for the management of pain, agitation, and delirium in the adult ICU published by the Society of Critical Care Medicine, there remains a lack of evidence for the prophylactic use of dexmedetomidine to prevent delirium.[23]

It should be noted that agitation and delirium were evaluated separately in this study. Agitation is defined as a state characterized by increased irritability and tension that can lead to confusion, excessive psychomotor activity, and hostility.[24] It is generally diagnosed using the SAS and the RASS.[23] Delirium is a syndrome characterized by the acute onset of cerebral dysfunction; the CAM-ICU and the Intensive Care Delirium Screening Checklist are the most reliable monitoring tools.[23] When agitation lasts for hours, changes in consciousness can produce delirium. The 2 mental states are sometimes difficult to distinguish clinically; however, in trials focusing on postoperative recovery during short periods, agitation has usually been studied,[7,25] whereas in studies looking at patients receiving days of treatment in the ICU, delirium has usually been investigated.[11,17,23] Because the present patients stayed in the PACU for only 1 night, agitation was measured by the SAS during this time, and delirium was assessed by the CAM-ICU for 5 days after the operation.

There are several limitations to this study. First, it is a single-center study with a small sample. The sample size was determined according to agitation during the PACU stay; thus, it might not provide enough power to detect differences in delirium for 5 days after the operation. Second, the protocol was designed to mimic everyday practice in the authors' unit, which could be different from the protocols used in other centers. In the authors' unit, all patients are breathing spontaneously when transferred into the PACU, so less sedation is needed compared with patients receiving mechanical ventilation. Differences in patient management can make the results less comparable to some studies.

In conclusion, dexmedetomidine sedation in the PACU does not change the overall incidence of agitation after free flap surgery, but does decrease the incidence of agitation after PACU admission. As shown by the study, it does not prevent delirium within 5 days after a free flap operation. Dexmedetomidine appears to be beneficial for patient sedation in the PACU after free flap surgery. However, more effort should be made to decrease agitation during patient shifting at PACU admission.

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