MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2020; 26: e926452
DOI: 10.12659/MSM.926452

Received: 2020.05.30
Accepted: 2020.06.17
Available online: 2020.07.15
Published: 2020.09.16

Efficacy and Safety of Neuromuscular Blockade in Overweight Patients Undergoing Nasopharyngeal Surgery

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Statistical Analysis C
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Source of support: This work was supported by Wu Jieping medical fund (320.6750.18186)

Background: Adequate muscle relaxation and rapid recovery of neuromuscular function are essential in the perioperative period. We therefore compared various anesthetic regimens of neuromuscular blockers and antagonists administered to overweight patients undergoing nasopharyngeal surgery.

Material/Methods: This prospective, randomized, double-blind study was conducted in overweight patients undergoing nasopharyngeal surgery. We randomly assigned 102 patients into 3 groups (each n=34) treated with various muscle relaxant agents and antagonists: rocuronium and sugammadex (Group RS), rocuronium and neostigmine (Group RN), and cisatracurium and neostigmine (Group CN). Then, we compared the efficacy and safety indexes of the 3 groups.

Results: Onset times of muscular relaxation in Group RS and Group RN (110 s and 120 s) were shorter than in Group CN (183 s). Time from administration of antagonist to recovery of the TOF ratio to 0.9 was shorter in Group RS (3.3 min) than in other groups (20.7 min and 19.1 min, respectively). The incidence of postoperative residual curarization (PORC) was significantly lower in Group RS (5.9%) than in the other 2 groups (both 41.2%). The hemodynamic parameter changes before extubation were significantly higher in Group RN and Group CN than in Group RS. The postoperative pain scores were lowest in Group RS.

Conclusions: For overweight patients undergoing nasopharyngeal surgery, the use of rocuronium with sugammadex had the shortest onset time of neuromuscular relaxation, accelerated the reversion of neuromuscular blockade, effectively reduced the occurrence of PORC, relieved postoperative pain, and maintained hemodynamic stability before extubation. The combination of rocuronium and sugammadex may be the best anesthetic regimen for overweight patients undergoing nasopharyngeal surgery.

MeSH Keywords: **Cholinergic Antagonists • Neuromuscular Nondepolarizing Agents • Overweight**

Abbreviations: **ANOVA** – analysis of variance; **ASA** – American Society of Anesthesiologists; **CRE** – critical respiratory events; **DBP** – diastolic blood pressure; **HR** – heart rate; **MAP** – mean arterial pressure; **NMT** – neuromuscular transmission; **NMB** – neuromuscular blockade; **nNMBA** – non-depolarizing neuromuscular block agent; **PACU** – post-anesthesia care unit; **PONV** – postoperative nausea and vomiting; **PORC** – postoperative residual curarization; **PTC** – post-tetanic count; **SBP** – systolic blood pressure; **SD** – standard deviation; **SpO_2** – pulse oximeter saturation; **TOF** – train-of-four; **VAS** – visual analog scale

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/926452

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Background

Nasopharyngeal surgery is usually a relatively quick operation. As the surgical area is rich in nerves, blood vessels and muscles, any minor trauma during surgery can lead to catastrophic outcomes. Therefore, deep neuromuscular blockade (NMB) is crucial to improve conditions for some surgical procedures and to prevent surgical trauma resulting from patients' body movements or incompletely paralyzed vocal cords [1]. Nondepolarizing neuromuscular block agents (nNMBAs), including rocuronium and cisatracurium, are usually used to facilitate airway management, decrease the risk of laryngeal injury during intubations, and reduce hoarseness secondary to intubation by decreasing the incidence of vocal cord injuries [2]. However, when deep NMB is required, complete and quick recovery of neuromuscular function is crucial to reduce the perioperative time, allow a more rapid and clear-headed recovery, and fast-track discharge from the operating room [3]. However, overweight and obese patients are more susceptible to postoperative respiratory complications, longer recovery time, and postoperative residual curarization (PORC) [4–6]. In China, overweight and obesity are highly prevalent, and overweight patients account for almost one-third of the total population (with a prevalence of 28.1%) [7]. Therefore, anesthesiologists should pay more attention to choosing the most effective muscle relaxants and antagonists with the least complications for overweight patients undergoing nasopharyngeal surgery.

PORC is the most common complication in NMB. A train-of-four (TOF) ratio ≥0.7 was previously considered sufficient to exclude PORC, but now it is thought the TOF ratio should be ≥0.9 [8,9]. Even during minimal NMB (TOF ratio 0.8), impaired inspiratory flow and upper-airway obstruction frequently occur, and extubation may put the patient at risk [10]. The functions of the larynx and pharynx muscles are the last to be restored after NMB [11]. Even small degrees of PORC increase the incidence of critical respiratory events (CREs) in the post-anesthesia care unit (PACU) [12,13]. PORC also increases the risk of many other outcomes, including delayed PACU discharge [14], cardiac arrest [15], and even aspiration of the lungs due to depressed reflexes from the larynx and pharynx [16].

Some PORC cases could be avoided if neuromuscular function were measured routinely during anesthesia [17]; however, it cannot speed the recovery of neuromuscular function and is not frequently applied as a standard monitor in daily clinical practice. To date, there have been no ideal muscle relaxants with rapid onset time and minimal adverse effects [18]. All of these facts indicate the need to find an optimal anesthetic regimen of muscle relaxants and antagonists for overweight patients undergoing brief nasopharyngeal surgery.

This randomized, double-blind, controlled trial evaluated and compared 3 anesthetic regimens of nNMBAs and antagonists: rocuronium-sugammadex (Group RS), rocuronium-neostigmine (Group RN), and cisatracurium-neostigmine (Group CN). We propose an optimal anesthetic regimen with better efficacy and safety for overweight patients undergoing nasopharyngeal surgery.

Material and Methods

Study design

This randomized, double-blind, parallel-group, clinical trial was approved by the China Ethics Committee of Registering Clinical Trials, Hong Kong, China (No. ChiECRCT-20180028). The study was registered at the China Clinical Trial Registration Center (No. ChiCTR1800015044). The trial was carried out at Wuhan Union Hospital (Wuhan, China) between September 2019 and December 2019. All participants gave written informed consent.

Participants

We recruited participants at the surgical ward on the preoperative day. The inclusion criteria were age 18–75 years, body mass index (BMI) >25 kg/m^2, American Society of Anesthesiologists (ASA) physical status I or II, and scheduled for selective nasopharyngeal surgery under general anesthesia, for which the type of nasopharyngeal surgery is benign neoplasms resection of the nasopharynx. The exclusion criteria were: predicted difficult airway, contraindications for the use of neostigmine, neuromuscular disease, minor arthritis, history of malignant hyperthermia, serious hepatic or renal dysfunction, history of allergy to NMBAs, cerebral infarction, diabetes, heart disease, mental illness, history of alcoholism or drug abuse, preoperative acid and base balance disorders, and use of preoperative medications that interact with NMBAs (e.g., aminoglycosides, carbamazepine).

Randomization and blinding

An independent statistician randomized the recruited patients in a 1: 1: 1 ratio to receive various anesthetic regimens of nNMBAs and antagonists (Groups RS, RN, and CN). Randomization was based on the patient's enrollment order and the random code generated in SAS statistical software (version 9.4, SAS Institute, Cary, NC, USA) using simple randomization.

After patient enrollments by anesthesiologists and random assignment by the statistician, the allocation sequence was concealed until the end of the study to maintain blinding in patients and outcome assessors. Group allocation occurred before anesthesia using sealed, number-coded envelopes. The

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size and color of the syringes used in the 3 groups were identical. Anesthesiologist could not be blinded to the treatment assignments given the nature of the interventions (they prepared the anesthetic), but most outcome indicators were assessed by the independent outcome assessors.

Sample size

To detect a difference of 5 min or greater between groups for recovery time of neuromuscular function, assuming a standard deviation (SD) of 1.5 min in the sugammadex group and SD of 7.0 min in the neostigmine group, 30 subjects in each group would be needed to reach a power of 95% at α=0.05. Assuming a 10% dropout rate, we included 34 patients in each group [19].

Interventions and neuromuscular monitoring

In the operating room, the venous channel was opened, and lactated Ringer's solution was infused. Neuromuscular monitoring was carried out using the neuromuscular transmission (NMT) module of the Anesthesia Monitor (Mindray, Shenzhen, China). The NMT monitoring system was connected to the patient before induction of anesthesia. The piezoelectric probe of the acceleromyograph was attached to the tip of the thumb. The forearm and the fingers were immobilized, and skin surface electrodes were placed over the ulnar nerve proximal to the wrist. The skin temperature was maintained at above 32°C throughout the study period.

After 3 min of oxygen supplied via the mask, intravenous general anesthesia was induced with fentanyl (3–4 ug/kg) and propofol (2.5–3.0 mg/kg). After induction of anesthesia and before administration of NMBs, the NMT monitor was calibrated using the automatic start-up procedure until the signal was stable. We used TOF assessed at 12-s intervals by stimulation of the ulnar nerve with 4 rectangular impulses at 2 Hz, duration 0.2 ms, and 25 mA. Once the neuromuscular recording was stable, intravenous rocuronium 0.9 mg/kg (3×ED95 of rocuronium) or cisatracurium 0.15 mg/kg (3×ED95 of cisatracurium) was given for NMB [20]. Tracheal intubation was performed when the TOF showed that the ratio of T1 to baseline data was less than 5%. Additional and intermittent doses of i.v. rocuronium 0.1–0.2 mg/kg or cisatracurium 0.03 mg/kg were permitted during the surgery as required to keep post-tetanic count (PTC) less than 2. Propofol (5–10 mg/kg/h) combined with remifentanil (0.2–0.4 ug/kg/min) was used throughout the operation. Liquid infusion rate and anesthetic medicine infusion rate were adjusted according to hemodynamic changes during the operation. Mechanical ventilation was used during the surgery and was adjusted to maintain an end-tidal carbon dioxide concentration of 35–45 mmHg.

After the operation, NMB was reversed with sugammadex 2 mg/kg or neostigmine 0.04 mg/kg together with atropine 0.015 mg/kg at reappearance of a TOF score of 2. After extubation, the patient was transferred to the PACU. Vital signs continued to be monitored in the PACU and neuromuscular monitoring was resumed without calibration of the device. If the patient had dyspnea, muscle weakness, or a serious respiratory or circulatory event, symptomatic treatment was initiated immediately.

Outcome measures

The independent outcome assessors recorded the perioperative indicators of each group, which were classified as safety indicators and effective indicators. The effective indicators include the onset time of neuromuscular relaxation, the time of intubation, intubation conditions, and the recovery time of neuromuscular function. The onset time of nNMBAs was the time from the end of its injection to disappearance of all 4 twitches of the TOF. All endotracheal intubation was performed by an experienced anesthesiologist and the conditions of intubation were graded according to Cooper's criteria [21]. The intubation time was defined as the time from the beginning of tracheal intubation with laryngoscope to completed intubation. The recovery time of neuromuscular function was defined as the time from the administration of antagonist to the recovery of TOF to 0.9.

The safety indicators included the incidence of PORC, hemodynamic stability, postoperative pain, postoperative nausea and vomiting (PONV), postoperative arrhythmia, and postoperative respiratory events. PORC was defined as 3 consecutive reappearances of TOF ratios less than 0.9 after extubation. Postoperative pain and PONV were evaluated by visual analog score (VAS). Postoperative arrhythmia was defined as a heart rate of less than 50 or more than 100 beats per minute. The CREs that occurred in the PACU included hypoxemia (SpO_2 less than or equal to 90%), airway obstruction, and reflux aspiration. Hemodynamic stability was defined as the change in hemodynamic index after administration of nNMBAs or antagonist. Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR) were assessed at the time of giving the nNMBAs (T0), 1 min after injecting nNMBAs (T1), 5 min after injecting nNMBAs (T2), 10 min after injecting nNMBAs (T3), the time of giving the antagonist (T4), and before extubation (T5). The absolute values of hemodynamic changes of nNMBAs were C1 (T0 to T1), C2 (T0 to T2), and C3 (T0 to T3). The absolute values of hemodynamic changes of muscle relaxant antagonist from administration to extubation were C4 (T4 to T5).

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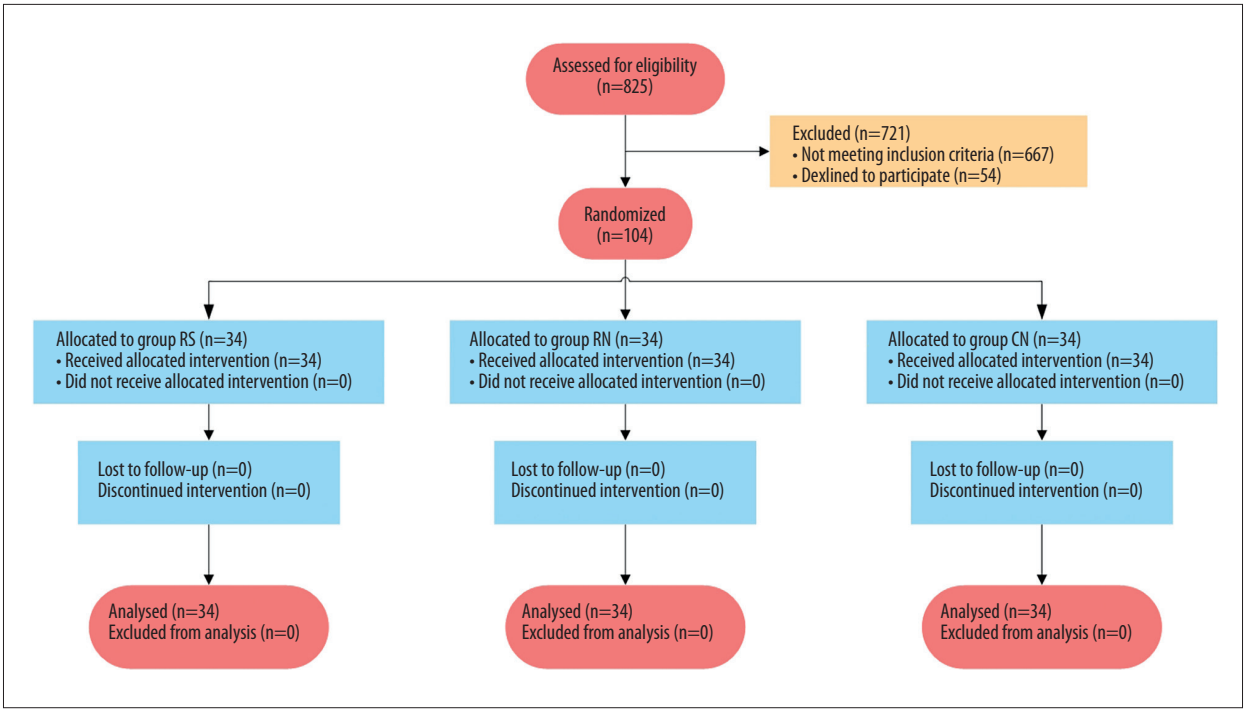

Figure 1. Flow diagram of the study design.

Statistical analysis

All data were analyzed using SPSS, version 25.0 (IBM SPSS, Chicago, IL). Continuous data were described as "mean (SD)" and were assessed for general distribution, normality, and equality of variance with a Shapiro-Wilk test and F test. Then, the variables were tested by analysis of variance (ANOVA) or Kruskal-Wallis test, as appropriate. Categorical variables were described as the number of patients and percentage and were compared using the chi-square or Fisher exact test in the presence of expected cell frequencies less than 5. Statistically significant differences were further analyzed by Tukey post hoc analyses. P-value <0.05 was considered statistically significant. All data were analyzed using SPSS statistical software (version 22.0, IBM, New York, USA).

Results

In the present study, 102 patients were enrolled and randomized to Group RS (n=34), Group RN (n=34), and Group CN (n=34) (Figure 1). The data of all participant characteristics showed no statistically significant difference among the 3 groups in age, sex, ASA physical status, weight, height, BMI, history of surgery, or smoking status (P>0.05; Table 1). The mean BMIs among the 3 groups were 27.4~27.7 kg/m^2. All patients had ASA physical status I~II. Their Mallampati grades were I~II, and the mean thyromental distances were all >8 cm. The surgery duration, anesthesia duration, and the total dose of propofol and remifentanil were not statistically different among groups. The baseline data of all participant were well balanced among the 3 groups.

Table 2 compares the effective indicators among the 3 groups. The mean onset time of nNMBAs in Group CN (183 s) was longer than in Group RS (110 s) and Group RN (120 s). The intubation conditions of our study participants were all classified as class I or II (excellent or good), and the intubation condition class I rate and intubation time showed no statistically significant differences among the 3 groups. The recovery time of neuromuscular function was shorter in Group RS (3.3 min) than in Group RN (20.7 min) and Group CN (19.1 min). These results showed that rocuronium had a shorter onset time and similar intubation conditions compared with cisatracurium, and sugammadex produced a shorter recovery time of neuromuscular function than did neostigmine.

Table 3 reveals the changes in hemodynamic variables among the 3 groups. Results of ANOVA showed that there were nearly no statistically significant between-group differences in SBP, DBP, MAP, or HR after the use of nNMBAs (P<0.05). By contrast, for the absolute values of hemodynamic changes of muscle relaxant antagonist from administration to extubation, Groups RN and CN showed higher absolute change values for SBP, DBP, MAP, and HR than in Group RS (P<0.05).

Figure 2 shows the trend of hemodynamic variables after the administration of muscle relaxant agent and antagonist. After

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Table 1. Baseline characteristics of the participants.

	Group RS (n=34)	Group RN (n=34)	Group CN (n=34)	*P*
Age (yr)	47 (10)	46 (11)	43 (10)	0.314
Height (cm)	168.8 (7.5)	168.0 (7.2)	169.4 (6.5)	0.723
Weight (kg)	78.2 (9.7)	78.2 (9.6)	79.7 (10.4)	0.781
BMI (kg/m^2)	27.37 (1.97)	27.61 (2.03)	27.66 (2.21)	0.690
Male (%)	25 (73.5)	24 (70.6)	26 (76.5)	0.860
Mallampati grade I (%)	18 (52.9)	16 (47.1)	16 (47.1)	0.855
Thyromental distance (cm)	8.6 (0.8)	8.2 (0.8)	8.3 (0.7)	0.145
ASA status I (%)	28 (82.4)	22 (64.7)	26 (82.4)	0.236
History of surgical (%)	16 (47.1)	22 (64.7)	20 (58.8)	0.327
History of smoking (%)	12 (35.3)	10 (29.4)	11 (32.4)	0.610
Propofol total dose (mg)	576 (249)	611 (200)	511 (194)	0.158
Remifentanil total dose (mg)	0.88 (0.48)	0.94 (0.39)	0.74 (0.37)	0.119
Surgery duration (min)	37 (16)	41 (15)	34 (15)	0.190
Anesthesia duration (min)	55 (24)	61 (20)	53 (20)	0.250

Data are presented as mean (SD) or number (%); P was used to indicate differences among the 3 groups. BMI – body mass index; ASA – American Society of Anesthesiologists.

Table 2. Effective indicators of the participants among the 3 groups.

	Group RS (n=34)	Group RN (n=34)	Group CN (n=34)	*P*
Onset time (s)	110 (25)**	120 (33)***	183 (30)	0.00
Recovery time (min)	3.3 (0.8)*,**	20.7 (6.0)	19.1 (4.8)	0.00
Intubation time (s)	48 (4)	50 (5)	50 (4)	0.22
Intubating conditions I (%)	33 (97.1)	34 (100)	33 (97.1)	0.60

Multiple comparisons using Tukey honest significant difference test. *P* was used to indicate the difference between the 3 groups; * statistically significant difference between Group RS and Group RN (P-value <0.05); ** statistically significant difference between Group RS and Group CN (P-value <0.05); *** statistically significant difference between Group RN and Group CN (P-value <0.05).

the use of nNMBAs, SBP, DBP, and MAP increased and HR decreased until T3 recovered to a stable level. After administration of nNMBAs antagonist and before extubation, SBP, DBP, MAP, and HR increased significantly in Groups RN and CN, but not in Group RS.

The comparisons of other safety indexes except hemodynamic stability are summarized in Table 4. After extubation, the incidence rate of PORC was significantly lower in Group RS (2/34) than in the other 2 groups (14/34 in both Group RN and CN). The postoperative VAS for pain was lowest in Group RS (0.7 in Group RS *vs.* 2.9 in Group RN and 3.0 in Group CN). The VAS for PONV, incidence of CREs, and arrhythmia were low in all 3 groups, with no significant differences among the 3 groups. The between-group differences of the VAS for pain and incidence of CREs are displayed in Figure 3.

Discussion

Overall findings

Our randomized, double-blind, parallel-group study demonstrated that the combination of rocuronium and sugammadex is better than other regimens in various effectiveness and safety indexes. To the best of our knowledge, this is the first comparative study to propose the best anesthetic regimen of nNMBAs and nNMB antagonist for use in overweight patients undergoing nasopharyngeal surgery.

Effectiveness indexes

The intraoperative efficacy indexes, including onset time of neuromuscular relaxation, the time of intubation, and

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Table 3. Changes in hemodynamic variables among the 3 groups.

Change	Group RS (n=34)	Group RN (n=34)	Group CN (n=34)	*P*
C1	19 (12)	14 (12)	20 (12)	0.09
C2	20 (14)	20 (13)	18 (13)	0.70
C3	15 (12)	16 (10)	12 (9)	0.21
C4	8 (6)*,**	19 (15)	20 (15)	0.00
C1	13 (9)	10 (7)***	16 (9)	0.01
C2	14 (11)	14 (11)	12 (9)	0.61
C3	13 (8)	12 (7)	10 (7)	0.19
C4	8 (5)**	10 (10)	13 (10)	0.04
C1	15 (9)	11 (8)	17 (10)	0.02
C2	16 (11)	15 (12)	14 (10)	0.72
C3	13 (8)	12 (8)	10 (7)	0.16
C4	6 (5)*,**	13 (11)	15 (11)	0.00
C1	10 (8)	9 (7)	9 (7)	0.72
C2	11 (7)	10 (7)	13 (10)	0.37
C3	5 (4)	6 (6)	7 (9)	0.51
C4	7 (7)*,**	14 (11)	19 (11)	0.00

Multiple comparisons using Tukey honest significant difference test. *P* was used to indicate the difference between the 3 groups; * statistically significant difference between Group RS and Group RN (P-value <0.05); ** statistically significant difference between Group RS and Group CN (P-value <0.05); *** statistically significant difference between Group RN and Group CN (P-value <0.05). The absolute values of hemodynamic changes of nNMBAs after 1 min, 5 min, and 10 min of administration were C1, C2, and C3, respectively. The absolute values of hemodynamic changes of muscle relaxant antagonist from administration to extubation were C4; SBP – systolic blood pressure; DBP – diastolic blood pressure; MAP – mean arterial pressure; HR – heart rate.

intubation conditions, mainly depend on the kind of nNMBAs used. Compared with cisatracurium, the use of rocuronium in our study showed comparable intubation condition and intubation time. However, the onset time of rocuronium was significantly shorter than the time of cisatracurium. As early as the 1990s, there was evidence that rocuronium can produce a more rapid onset of muscle relaxation than cisatracurium with equipotent intubating doses [22]. Other studies also showed that rocuronium provides shorter onset time [23–26], and priming with rocuronium significantly accelerated onset of cisatracurium [27]. Previous studies have also compared cisatracurium with rocuronium in tracheal intubation condition. A study evaluated the condition of tracheal intubation at 60 s following the administration of cisatracurium versus rocuronium. Compared with cisatracurium, the administration of 2 ED95 rocuronium brought about better intubating conditions, although it was associated with high incidence of pain on injection in most patients [28]. Another study used 3 ED95 muscle relaxant agents, showing that cisatracurium provided very good intubating conditions [23]. Therefore, the intubation conditions are related to both the dose and type of muscle relaxants. Moreover, patient physiological differences such as body shape, BMI, and airway conditions may also be related to the intubation conditions; the proficiency of the intubation operation of the anesthesiologist and the rating criteria of the intubation conditions may also affect the results. Nowadays, after improving the onset time of nNMBAs, they can basically achieve good tracheal intubation conditions. Our study revealed that there were no statistically significant differences in intubating conditions among overweight patients.

In recovery of neuromuscular function, Group RS was faster than Groups RN and CN in reversing moderate NMB (at the reappearance of T2), and Group RN and Group CN showed no statistically significant difference. A randomized controlled study conducted by Choi et al. also showed that there was no significant difference in the recovery time of neostigmine between a rocuronium group and cisatracurium group [29]. A recent Cochrane System review showed the time to reversal of NMB (from T2 to a TOF ratio >0.9) with neostigmine 0.05 mg·kg^{-1} was 6.6 times that of sugammadex 2 mg·kg^{-1} (12.87 *vs.* 1.96 min) [30], and the difference in recovery time was comparable with our results in overweight patients.

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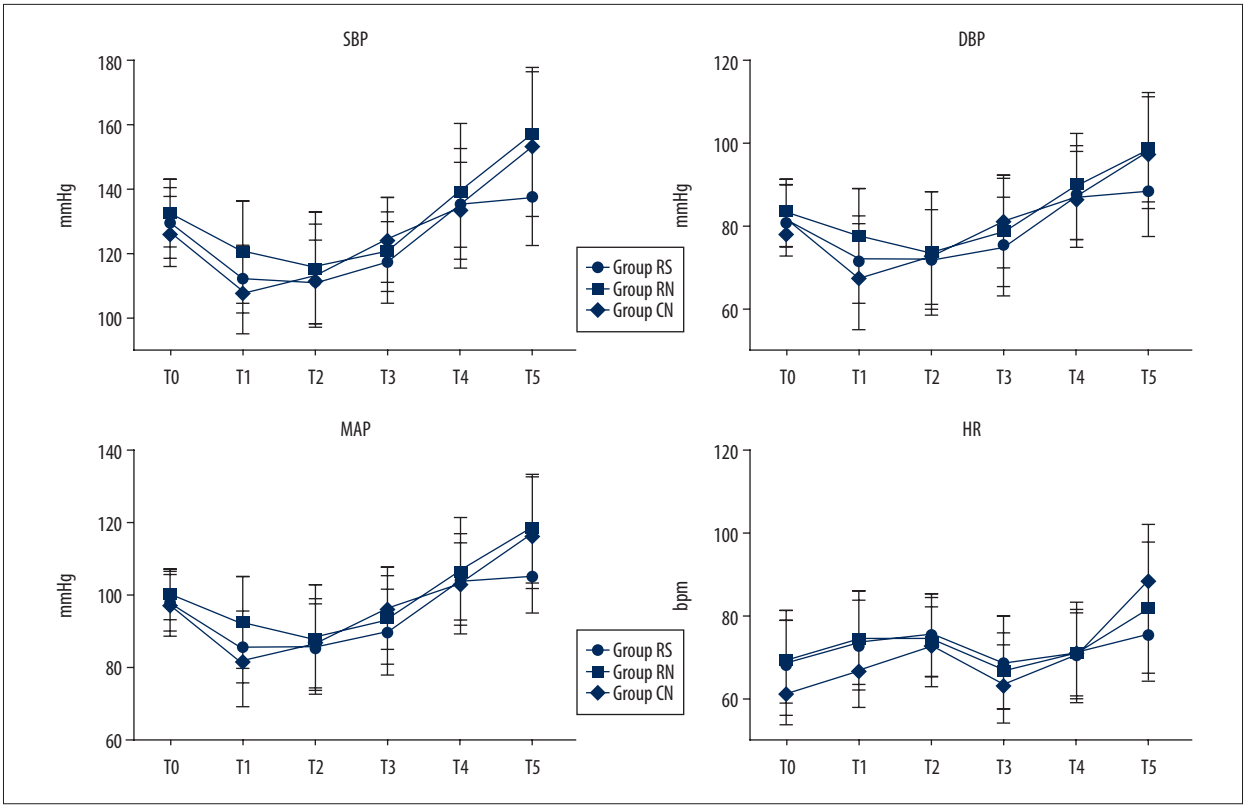

Figure 2. Hemodynamic indexes (SBP/DBP/MAP/HR) on T0 T1 T2 T3 T4 T5 of each group. SBP – systolic blood pressure, DBP – diastolic blood pressure, MAP – mean arterial pressure, HR: heart rate. T0: the time of giving the nNMBAs, T1: 1 min after injecting nNMBAs, T2: 5 min after injecting nNMBAs, T3: 10 min after injecting nNMBAs, T4: the time of giving the antagonist, T5: before extubation.

Table 4. Comparison of PORC incidence (A) and VAS pain scores (B) in each group.

	Group RS (n=34)	Group RN (n=34)	Group CN (n=34)	*P*
PORC (%)	2 (5.9)*,**	14 (41.2)	14 (41.2)	0.00
VAS for pain	0.7 (0.8) *,**	2.9 (1.6)	3.0 (1.7)	0.00
VAS for PONV	0	0.3 (0.9)	0.5 (1.6)	0.14
Arrhythmia (%)	0	2 (5.9)	0	0.33
CREs (%)	0	2 (5.9)	4 (11.8)	0.16

Multiple comparisons using Tukey honest significant difference test. *P* was used to indicate the difference among the 3 groups; * statistically significant difference between Group RS and Group RN (P-value <0.05); ** statistically significant difference between Group RS and Group CN (P-value <0.05). PORC – postoperative residual curarization; VAS – visual analog scale; PONV – postoperative nausea and vomiting; CRE – critical respiratory events.

Safety indexes

PORC was the primary outcome of our study. The most important complication of NMB is PORC, which is associated with a variety of major and minor adverse events [31]. Previous studies have demonstrated that the use of rocuronium-sugammadex significantly reduced the incidence of PORC compared with cisatracurium-neostigmine under general anesthesia [32,33]. The type of surgery, duration of anesthesia and operation, and patient physiological conditions can affect the NMB and NMB-related complications. Therefore, we concentrated on overweight patients undergoing nasopharyngeal surgery who needed deep NMB and were vulnerable to PORC [5]. We found that rocuronium-sugammadex significantly reduced the incidence of PORC among overweight patients undergoing nasopharyngeal surgery. Furthermore,

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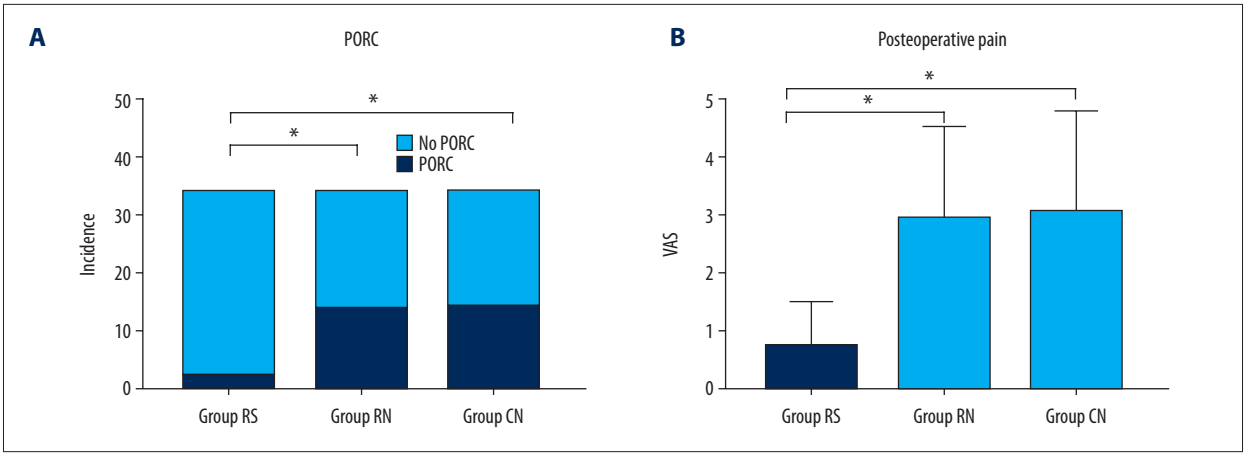

Figure 3. Comparison of PORC incidence (**A**) and VAS pain scores (**B**) in each group. PORC – postoperative residual curarization; VAS – visual analog scale.

this combination may be suitable for use in other surgeries requiring deep NMB levels.

Stability of hemodynamics is an important issue in the whole perioperative period. This study evaluated and compared changes in hemodynamics after the use of muscle relaxant agents and antagonists. One randomized-cohort study showed that rocuronium could increase HR and decrease MAP significantly in 1 min after administration, while it provided a better, reasonably cardio-stable alternative to vecuronium for short surgical procedures [34]. Under laboratory animal experimental conditions, cisatracurium produced more stable hemodynamic levels compared with pancuronium [35]. In clinical application, rocuronium and cisatracurium rarely affect hemodynamic levels, but their cardiac effects cannot be ignored [36]. There are few comparative studies on the hemodynamic effects between rocuronium and cisatracurium, especially for overweight patients. For muscle relaxant antagonists, it has been proved that sugammadex provides more hemodynamic stability than neostigmine in cardiac patients whose hemodynamics are unstable [37]. For pediatric patients, there are also randomized controlled trials showing that sugammadex provides more stable hemodynamic levels than neostigmine [38]. Few studies have explored the stability of hemodynamics in overweight patients receiving various anesthetic regimens of NMB. Our study collected hemodynamic data at several time points, showing the more stable hemodynamic condition in Group RS compared with the other 2 groups, especially from the administration of muscle relaxant antagonist to extubation.

It also should be noted that we found the VAS score for pain was statistically significantly lower in Group RS than in the other 2 groups. Our findings are in line with those of Castro et al. [39], who reported less immediate acute postoperative pain in sugammadex-treated morbid obese patients than in neostigmine-treated patients, perhaps because the sugammadex-treated patients are calmer and can be extubated faster and more smoothly, so as they reported less pain. Castro et al. also found less PONV in patients treated by sugammadex, which is consistent with our results [39]. There are also some other findings about the relationship between muscle relaxant antagonist and postoperative pain that conflict with our results [40]. This potential "opioid-sparing" effect of nNMBAs antagonist has rarely been studied in previous research. For overweight patients, our results revealed that the rocuronium-sugammadex regimen can relieve pain and make patients more comfortable after surgery.

For other safety indexes of NMB such as arrhythmia and CREs in PACU among the overweight patients, our results found no adverse events in Group RS, and few in Group RN and Group CN. These incidences of outcome events were too low to be assessed for significant differences, even by Fisher exact test. For adverse events with low incidence, such as CREs or postoperative death, a larger-sample prospective or retrospective observational study is needed to explore the risk differences among NMB regimens. One prospective observational study enrolled 3000 patients and found that 0.06 mg/kg neostigmine can increase postoperative respiratory events [41]. A recent retrospective cohort study that observed 65 702 patients suggested that 90-day mortality after non-cardiac surgery was lower in the rocuronium-sugammadex group compared to the rocuronium-neostigmine group [42]. Therefore, the optimal regimen of muscle relaxants and antagonists may reduce the risk of short-term or long-term postoperative adverse events, but more observational studies are needed.

Limitations and strengths

Compared with previous studies, the present study has some strengths and limitations. The first limitation is that this was a single-center study, and multi-center studies are needed

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to determine the best choice of nNMBAs and antagonists. Second, we focused on overweight patients because overweight is more prevalent than obesity; however, further studies are needed that assess separate groups of overweight and obese patients. Nevertheless, the present findings evaluated appropriate combinations of nNMBAs and antagonists in patients, with comprehensive consideration of all aspects in the perioperative period. Notably, we concentrated on management of NMB in patients and surgery that are more challenging for anesthesiologists.

Conclusions

Our results contribute to determining clinically effective and safe combinations of nNMBAs and antagonists for use in overweight patients undergoing nasopharyngeal surgery, as well as other surgeries that require deep NMB. We suggest that the rocuronium-sugammadex regimen should be used for NMB in overweight patients.

Acknowledgements

We are indebted to Ms. Juan Xu for providing random codes and to Ms. Leiming Xia for assistance in patient recruitment. We are very grateful to the operating room and PACU staff in Wuhan Union Hospital for their support in conducting the study.

Availability of data and materials

The datasets analyzed here are not publicly available because they contain information that could compromise research participant privacy, but they are available from the corresponding author on reasonable request.

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