Comparison Between Sevoflurane and Propofol With Remifentanil Anesthesia Avoid Neuromuscular Blocking Agent After Intubation in Thyroid Operation

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Research Article

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Abstract

Background: The goal of the study is to compare sevoflurane and propofol with remifentanil anesthesia avoid neuromuscular blocking agent after intubation in thyroid operation with intra-operative neuromonitoring.

Methods: 80 patients scheduled to receive thyroid operation were randomly assigned to sevoflurane

or propofol anesthesia maintained group. The time of rocuronium recovery profile were monitored. Adverse events such as sinus bradycardia, tachycardia, hypertension, hypotension and movement were recorded. Analyze the time from anesthetic stop to the extubation time and operation time. Record the incidence rate of sore throat, drowsiness, agitation, nausea and vomiting after extubation. Record the first neuromonitoring time and the number of successful neuromonitoring.

Results: There were significant differences in the recovery profile of rocuronium between sevoflurane and propofol group(P<0.05). The incidence of hypotension was similar between sevoflurane and propofol group. There was no significant difference of sinus braducardia between the two groups. The incidence of movement was less in sevoflurane compared to propofol(12.% vs. 47.5%, P=0.002). The propofol group had longer extubation time than sevoflurane group(13.10±1.52 vs. 8.07±1.07 min, P=0.001).The incidence of sore throat, drowsiness, agitation, nausea and vomiting in the two groups was similar during the recovery period, and the difference was not statistically significant. There was no significant difference of neuromonitoring between the two groups.

Conclusion: Sevoflurane has advantage with less movement adverse effects in thyroid surgery with intra-operative neuromonitoring compared to propofol when associated with remifentanil 0.1μg/kg/min in general anesthesia.

Trial registration: Chinese Clinical Trial Registry (ChiCTR1800017166, 15 July 2018)

Introduction

One of the most serious complications of thyroid gland surgery is injury to the recurrent laryngeal nerve resulting in temporary or permanent paresis. Loss of recurrent laryngeal nerve function may be life-threatening especially for the patients had already lateral recurrent laryngeal nerve injury in previous.[1] Intra-operative neuromonitoring during thyroid and parathyroid operation has gained increased popularity to assist in nerve identification and dissection, detection of lesion site, and prediction of postoperative vocal cord function.[2] General anesthesia is commonly used in thyroid gland surgery, neuromuscular blocking agents are administered to provide non-spontaneous breath state and a muscle relaxant condition in the clinical practice. A controversial question is whether relaxant-free anesthesia is mandatory for intra-operative intra-operative neuromonitoring of the recurrent laryngeal nerve.

The duration of neuromuscular blockade is of great importance in intra-operative neuromonitoring. If high-dose neuromuscular blocking agent chosen, its action long and inhibit neuromuscular transmission diminishes electromyographic signals and motor-evoked potentials and consequently interferes with interpreting neuromonitoring recordings. On the other hand, if low-dose adopted, the patient may swallow or move during operation period which is severe problem for patient and surgeon. Rocuronium, a monoquaternary, amino steroid, non-depolarizing neuromuscular blocking agent, has fewer adverse effects and recommend used in the general anesthesia recently years.[3] Rocuronium one ED95(0.3 mg/kg) was suggested during the anesthesia induction in thyroid and parathyroid operation with intra-operative neuromonitoring.[4,5] However, the narcotics have influence on the neuromuscular blocking agent, especially the sedative agents no matter inhalant or intravenous anesthetics.[6–9] The aim of the present study was to compare the two commonly used anesthetics (sevoflurane and propofol) during thyroid gland surgery and to find a relatively optimal anesthesia project in the surgery with intra-operative neuromonitoring.

Materials And Methods

Patients

This study was registered prior to patient enrollment in the Chinese Clinical Trial Registry (http://www.chictr.org.cn, identifier: ChiCTR1800017166). The study was approved by the ethics committee of Henan Cancer Hospital. All patients were informed of the intent to use this monitoring system to potentially aid surgeons in the localization and identification of the recurrent laryngeal nerves and for the assessment of their function during operation and written informed consent was obtained from each patient. We recruited 80 consecutive adult patients (including 40 men and 40 women; age range, 22-45 years) scheduled to receive a thyroid operation with intra-operative neuromonitoring. Inclusion criteria included ASA□□□, BMI between 18.5 and 27 kg/m^2, Exclusion criteria were intolerance to the medications employed in the study, Mallampati classification grade III/IV or ones who were expected difficulties during intubation, regular medication which may interfere with muscle relaxants, neurological or neuromuscular disease, and hepatic or renal insufficiency. Using a sealed envelope method, Patients were allocated to a sevoflurane (S) or propofol group (P) by table of random numbers.

Anesthesia technique and measurements

Midazolam (0.05 mg/kg) and penehyclidine hydrochloride (0.01mg/kg) were injected intravenous 30 minutes prior to the induction of anesthesia. After arrival in the operating room, the patients were monitored using an electrocardiograph, non-invasive blood pressure monitor, and pulse oximeter. A BIS sensor (BIS Complete Monitoring System, Covidien IIc, USA) was attached and measurements were taken when the signal quality index was above 95. Muscle relaxation was monitored using an electrical stimulator (Veryark-TOF, VERYARK Co., Ltd) by applying train of four (TOF) on the wrist's ulnar nerve and measuring the contraction of the adductor pollicis muscle. The TOF were calibrated above 95%. Body

temperature was maintained by a heating blanket (Type SIIWT-B, Haiming Co., Ltd, Tianjin, China). Skin temperature was measured under thenar eminence and maintained above 35.5 °C.

After preoxygenation, anesthesia was induced with 2.0 mg/kg propofol, 0.3–0.5 μg/kg sufentanil and 0.3 mg/kg rocuronium was administrated to facilitate electromyographic endotracheal tube (Medtronic Xomed, Inc., Jacksonville, FL, U.S.A.) insertion when we confirmed the loss of consciousness after administration of propofol by checking the eyelash reflex and BIS under 60. If the patients would be still awake at 2 min after administration of propofol, additional propofol 0.5 mg/kg would be given. Tracheal intubation was performed using visual laryngoscopy at 180s after administration of rocuronium. Immediately after intubation, the assistant checked the intra-operative neuromonitoring signal assure the electromyographic endotracheal tube were placed in the right depth and location. Anesthesia were maintained by 1.5–3.0 vol.% sevoflurane or 4.0–6.0 mg/kg/h propofol associated with 0.1 μg/kg/min remifentanil, respectively.

Neuromuscular monitoring

Neuromuscular function was assessed using acceleromyography of the adductor pollicis muscle (Veryark-TOF, VERYARK Co., Ltd) according to the guidelines of manufacture. After loss of consciousness (BIS value < 60), neuromuscular monitoring began immediately with TOF stimulation (0.2 ms duration, frequency 2 Hz, 2s duration with supramaximal current, repeated every 20s), record the time between rocuronium administrated and the TOF decreased to 75 %(T1), 50 %(T2)and 0(T3). The time required for the TOF reappearance to counts of 4(T4), TOF ratio to recover to 50 %(T5) and 75%(T6) also recorded.

All patients were treated by the same surgeon team and the NIM-Response 3.0 machine (Medtronic Xomed, Inc., Jacksonville, Florida, U.S.A.) was used for intermittent RLN monitoring in all patients. Sinus bradycardia and tachycardia were treated with atropine and esmolo, respectively. Hypertension and hypotension were corrected by symptomatic treatment. If swallow or body movement happened, additional intravenous anesthetics propofol (0.5 mg/kg) is used to prevent further patient movement. All the adverse responses were recorded. Record the time form operation start (incision) and intubation to the time recurrent laryngeal nerve neuromonitoring. All patients were delivery to postanesthesia care unit with electromyographic endotracheal tube. Record the respiratory complication and delayed recovery.

Statistical analysis

SigmaPlot 12.5 software (Systat Software, Inc., Point Richmond, CA) was used for sample size calculation and statistical analyses. Sample size was calculated to achieve a power of 0.9 for the first time TOF recovery profile T4. The minimum sample size turned out to be 37 in 0.1μg/kg/min remifentanil treatment base on a pilot study so the study was done using 40 subjects in each group. The Shapiro-Wilk test was used for testing data for normality. We report data as means and standard deviations (SD) or median and interquartile range (IQR, 25^{th} to 75^{th} percentile) and depict data as line plots on data distribution. Quantitative variables were compared by *t*-test/Mann–Whitney test (for nonparametric data).

Comparisons of frequency distributions were performed using the Chi-squared test/ Fisher's exact test. *P* < 0.05 was defined as statistically significant.

Results

Descriptive analysis

80 patients were recruited into the trial. Demographic characteristics are summarized in Table 1. There was no difference between sevoflurane and propofol group in age, weight and BMI.

Table 1
Demographic data for the study patients, Data are expressed as mean ± SD

n = 40(M:F = 1:1)	S	P	*P*-value
yr	34.3 ± 6.7	34.7 ± 6.6	0.826
weight	65.7 ± 8.0	66.2 ± 7.2	0.759
BMI	23.56 ± 0.41	23.80 ± 1.89	0.645

Tof Recording And Adverse Events During Operation

There was no difference in the time course from intubation to maximum neuromuscular blockade T1,T2 and T3 either sevoflurane or propofol anesthesia(*P* > 0.05). There were significant differences between the two groups for the time course for increases in the TOF value in both groups. In the treatment groups, the time T4, T5 and T6 was longer in sevoflurane group than propofol group (median 869.5 (IQR 655.0-1202.0)s) vs median 492.5(IQR 463.0-551.25)s, *P* = < 0.001), (median 2209.0 (IQR 1912.5-2699.5)s) vs median 1363.5 (IQR 1091.25-1740.5)s, *P* = < 0.001) and (median 3590.0 (IQR 3479.5-3740.5)s) vs median 2050.0(IQR 1872.75–2343.0)s, *P* = < 0.001), respectively.(Fig. 1).

The Incidence of movement were lower in sevoflurane anesthesia groups compared with the propofol (12.5% vs. 47.5%; *P* = 0.002). There were no differences between the groups with regard to hypotension and sinus braducardia (Table 2).

Table 2
Comparison of adverse events during operation. Values are percentage (number of patients)

n = 40	S	P	*P*-value
Hypotension	2.5%(40)	0(40)	1.000
Sinus braducardia	2.5%(40)	0(40)	1.000
Movement	12.5%(40)	47.5%(40) [a]	0.002
[a] *P* < 0.05 Propofol vs sevoflurane group			

Neuromuscular Monitoring And Adverse Events After Operation

The time of extubation was shorter in sevoflurane group than propofol group(8.07 ± 1.07 vs. 13.10 ± 1.52 min; *P* = 0.001). The incidence of sore throat, drowsiness, agitation, nausea and vomiting in the two groups was similar during the recovery period, and the difference was not statistically significant. Significant respiratory complications including hypoventilation and delayed recovery did not occur in any of the patients and all were discharged from the PACU without any adverse event (Table 3 & Table 4).

Table 3
Postoperative Complications in Two Groups

n = 40	S	P	*P*-value
sore throat throat	5	7	0.754
drowsiness	0	0	-
agitation	1	2	1
nausea and vomiting	5	3	0.712
Time of extubation (min)	8.07 ± 1.07	13.10 ± 1.52 [a]	0.001
[a] *P* < 0.05 Propofol vs sevoflurane group			

Table 4
Intraoperative Conditions in Two Groups

n = 40	S	P	*P*-value
Operation time(min)	126.72 ± 11.37	123.67 ± 10.56	0.217
first neuromonitoring time (min)	75.34 ± 5.37	73.45 ± 7.16	0.186
Number of cases in which neuromonitoring signal was initially observed	40	40	-

Discussion

In this study, we found anesthetics both sevoflurane and propofol with remifentanil could provide a condition free of neuromuscular blocking agent, which required for recurrent laryngeal nerve monitoring during operation, however, sevoflurane provide a long neuromuscular recovery duration and avoid movement adverse effect without diminished electromyographic signals. The incidence of movement was main adverse in propofol group. The patients in sevoflurane group showed a shorter extubation time than propofol group. So sevoflurane has an advantage compared to propofol in thyroid surgery with intra-operative neuromonitoring.

Recurrent laryngeal nerve injury is an main adverse event of thyroid surgery.[10] The patients who had already lateral recurrent laryngeal nerve paresis should be caution in the second time operation, bilateral loss of recurrent laryngeal nerve function may be life-threatening because apnea.[1] Intra-operative neuromonitoring of the recurrent laryngeal nerve is commonly used in thyroid operations to prevent recurrent laryngeal nerve damage. Standard general anesthesia with endotracheal tube commonly includes opioids, intravenous anesthetics, neuromuscular blocking agents for anesthesia induction, and inhalational anesthetics for anesthesia maintenance. The use of neuromuscular blocking agent has been well-known to diminish the evoked potential, reduce sensitivity of a positive signal, and interfere with data interpretation during intra-operative neuromonitoring. To obtain adequate relaxation for surgery and to obtain minimal variations in electromyographic signals and motor-evoked potentials during neuromonitoring, it is summon on to administer neuromuscular blockade drugs to wear off and a full return of muscular activity as soon as possible after the intubation, or at least have no influence on the electromyographic signal when neuromonitoring. The proper anesthesia project is using muscle relaxants only in induction, avoid muscle relaxation during operation. If endotracheal intubation without neuromuscular blocking agent is required, the suggested approach is using induction agents propofol and remifentanil, remifentanil depress spontaneous breathing and movement during operation in the absence of neuromuscular blockade in dose-depend,[11,12] To achieve operating conditions, narcotic sedation agents and remifentanil could be qualified. In this study, the effect of rocuronium muscle relaxation wear off longer in sevofluane group than profol group either with remifentanil 0.1μg/kg/min(Fig. 1), however, the intra-operative neuromonitoring signal had no disturbance in sevofluane group. The reason is related to sevofluane enhanced the effect of rocuronium,[13] inhalant

anesthetics have synergistic effect with rocuronium. It reported 1.3 MAC sevoflurane and desflurane inhaling for 40 min significantly reduces ED(50) and ED(95) of rocuronium, prolongs the onset time and action time of rocuronium in children. Sevoflurane can significantly prolong the recovery characteristics of rocuronium,[14] it reduced rocuronium concentration in effect compartment producing 50% inhibition of both T1 and T4 response and significantly delayed not only T1, but also T4 recovery.[15] Remifentanil might also have synergistic effect with rocuronium when inhale sevoflurane. These evidences also explain the incidence of movement was greater in propofol group.

Preventing nerve damage is currently standard practice in operations on the thyroid gland, a total of 1 ED(95) of rocuronium (0.3 mg/kg) is an optimal dose for intra-operative neuromonitoring during thyroid surgery. It reported that 44 minutes after administration of single dose (0.5 mg/kg) of rocuronium is adequate for eliciting an electromyographic signal from the vagus never.[16] In our study, there was no difference in the time from rocuronium injection to the total neuromuscular blockade (Fig. 1, T1, T2 and T3). This was in consisitent to Sangseo research, the type of anesthetic (sevoflurane and propofol) does not significantly influence the time to maximum block by rocuronium. Both anesthesia regimens could provide a good intubation condition.[17] The neuromuscular block recovery time were different from TOF counts 4(T4) to TOF 75%(T6), we therefore proposed that the type of anesthetic could influence the recovery from neuromuscular block. Interaction of rocuronium and volatile anaesthetics resulted in augmentation of the intensity of neuromuscular block but did not result in significant effects on duration of recovery from block.[18] The laryngeal muscles exhibited a shorter response time than the adductor pollicis and recovered more quickly,[19] Meistelman found response times of 1.4 min and 2.4 min, respectively, for the laryngeal adductors and the adductor pollicis after application of rocuronium 500 μg/kg with a maximum blockade of 77(5)% and 98(1)%, respectively.[20] This complicated effect could not only explain the effect of delayed recovery in sevoflurane group but also prohibit movement, which is main adverse event in propofol group (Table 2). So we recommend sevoflurane as anesthesia maintained anesthetics. There are some flaws in the research: we did not measure the strength of neuromonitor signal. A neuromuscular blocking agent may diminish the evoked potential, delay a positive signal, and interfere with data interpretation during intra-operative neuromonitoring.[21]It is feasible avoiding neuromuscular blocking agents after intubation in the thyroid operation with intra-operative neuromonitoring.

Conclusion

Compared to propofol, sevoflurane has advantage with less movement adverse effects in the thyroid surgery with intra-operative neuromonitoring when associated with remifentanil.

Abbreviations

ED95
95% effective dose; TOF:train of four.

Declarations

Ethics approval and consent to participate

This study was approved by the ethics committee of Henan Cancer Hospital (approval number 2018104, dated 4 May 2018) and conducted in accordance with the ethical standards of the 1964 Helsinki declaration and it's later amendments. Informed consent was obtained from all patients prior to inclusion in the study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analyzed during the current study are available from the Chinese Clinical Trial Registry (ChiCTR1800017166) or corresponding author on reasonable request.

Competing interests

None.

Funding

None

Authors' contributions

CY had design the study and prepared the manuscript. J analyzed the date. XH and C had carried out the treatment. All authors have read and approved the manuscript

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Figures

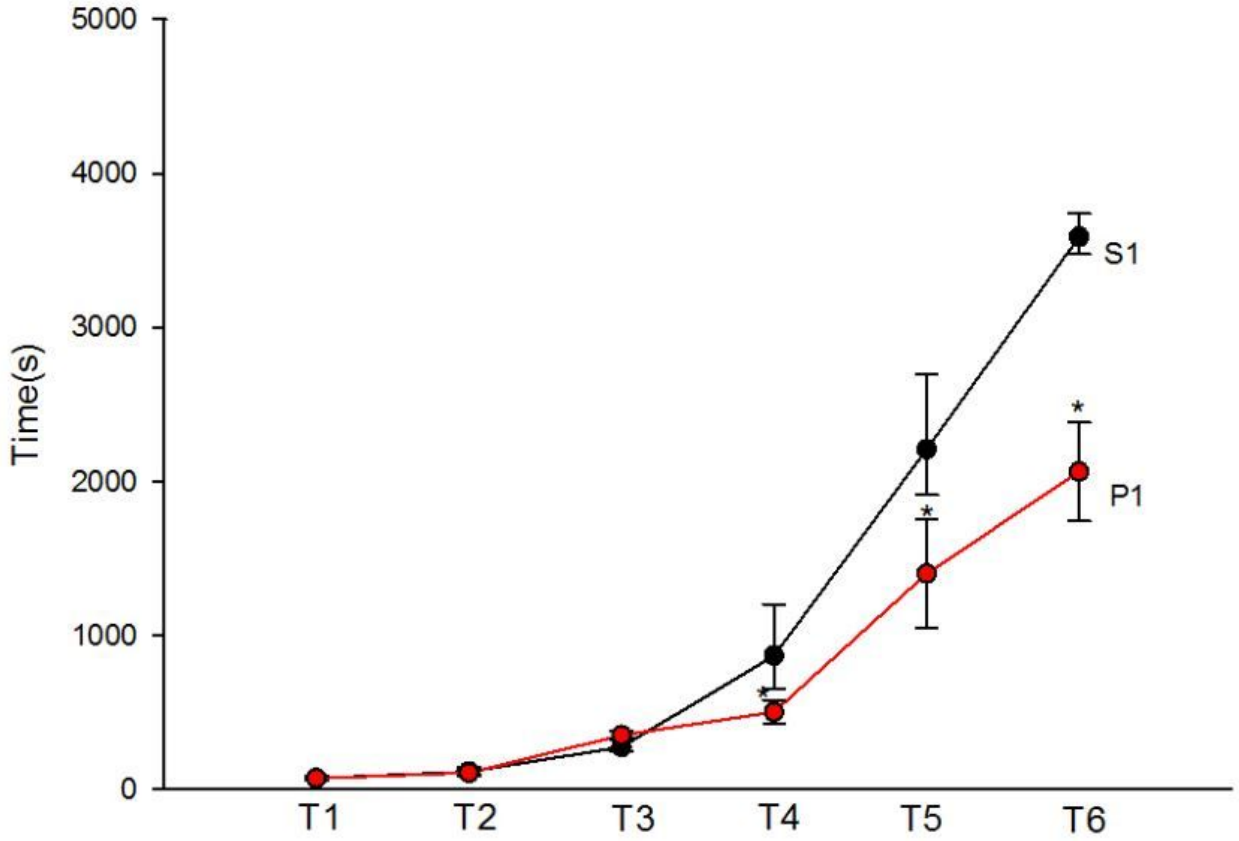

Figure 1

The TOF profile of rocuronium when sevoflurane and propofol with 0.1 μg/kg/min remifentanil anesthesia. Data are expressed as median(IQR), S= sevoflurane group, P=Propofol group, * P=<0.001.