Electromyographic Response of Facial Nerve Stimulation Under Partial Neuromuscular Blockade During Resection of Vestibular Schwannoma

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■ OBJECTIVE: To evaluate whether use of partial nondepolarizing neuromuscular blocking agents, at a train-of-four level 1, compromise facial nerve monitoring during vestibular schwannoma (VS) resection.

■ METHODS: Sixty consecutive patients undergoing VS resection were enrolled into a partial peripheral neuromuscular blockade group or free of neuromuscular blockade group. Stimulation threshold to elicit an electromyographic response amplitude of at least 100 μV was recorded at the proximal and distal facial nerve after VS removal. The proximal-to-distal ratio of amplitude of the orbicularis oculi and oris muscles was calculated.

■ RESULTS: All patients successfully passed the electromyography monitoring test. Mean electrical stimulation thresholds were higher in the peripheral neuromuscular blockade group than in the free of neuromuscular blockade group (0.12 mA vs. 0.06 mA at proximal site, $P = 0.001$; 0.08 mA vs. 0.03 mA at distal site, $P = 0.0002$). The differences in median proximal-to-distal amplitude ratios were not statistically significant in both groups. There was a trend toward more patients needing phenylephrine. Recovery profiles were comparable in the 2 groups.

■ CONCLUSIONS: Although mean stimulation threshold to elicit a response amplitude was higher in the peripheral neuromuscular blockade group than in the free of neuromuscular blockade group at the proximal site, the stimulation thresholds in both groups were sufficient for facial nerve monitoring in VS surgery, indicating no clinical difference in both groups.

INTRODUCTION

The facial nerve is vulnerable during microsurgical resection of vestibular schwannoma (VS). Introduction of routine intraoperative facial nerve monitoring has reduced the incidence of facial nerve paresis.[1-3] However, this monitoring technique can pose a challenge for the anesthesiologist because neuromuscular blocking agents (NMBAs) can render the facial muscles unresponsive to electrical and mechanical stimulation in neurosurgery. Hence some electrophysiologists request that, with the exception of succinylcholine for intubation, no muscle relaxants be given.[4,5]

Absolute immobility of the patient during delicate microsurgical resection of VS can be achieved by using large doses of narcotics and volatile anesthetic agents without the administration of a muscle relaxant.[6] For example, remifentanil and propofol total intravenous anesthesia (TIVA) produces excellent results with no effect on evoked electromyography (EMG) or twitch tension.[7] However, the clinical necessity for this pure state has not been documented.[5] Furthermore, this anesthetic technique may lead to cardiovascular depression, especially in vulnerable patients with hemodynamic instability.[4]

Maintaining a balance between absolute immobility and hemodynamic stability is essential, while preserving an optimal condition for facial EMG monitoring. Some centers are satisfied with a continuous infusion of NMBAs to maintain a constant

level of modest twitch suppression, which protects patients from the cardiovascular depression that results from high-dose anesthesia while keeping patients immobilized.[7-10] Although some studies have found that even under moderate to profound partial levels of peripheral neuromuscular blockade it was possible to evoke facial muscle electromyographic responses by stimulation of the facial nerve,[8-10] the weakness of these studies include an observational study design with a small sample size[8,10] and patients undergoing middle ear surgery.[9] Therefore, we carried out a prospective, randomized, controlled study to investigate the effectiveness of facial nerve monitoring in patients with partial level of peripheral neuromuscular blockade during resection of VS.

MATERIALS AND METHODS

This study was registered in the Chinese Clinical Trial Registry (ChiCTR1800016702). The Institutional Review Board at Shanghai Eye, Ear, Nose, and Throat Hospital affiliated with Fudan University approved the study procedures, and each enrolled patient provided written informed consent. Sixty adult patients undergoing VS resection via the retrosigmoid approach were recruited. Patients were randomly assigned to the partial peripheral neuromuscular blockade group (P group) or free of neuromuscular blockade group (F group) by computer-generated allocation. All patients involved in the study had normal or near-normal facial nerve function, grades I and II as rated by the House-Brackmann (HB) system.[11] Tumor size was recorded as the largest tumor diameter measured in the axial, coronal, or sagittal views within the cerebellopontine angle. Patients with a tumor size >3 cm diameter were excluded.

No premedication was given. On arrival to the operating room, invasive monitoring of arterial blood pressure, pulse oximetry, electrocardiography, and bispectral index monitoring (BIS VISTA Monitoring System; Aspect Medical Systems, Inc., Norwood, Massachusetts, USA) was established. For TIVA, propofol and remifentanil were administered concurrently by intravenous infusion using a target-controlled infusion system (Orchestra Base Primea; Fresenius Vial S.A.S., Brezins, France) for anesthesia induction and maintenance. Effect-site concentrations of propofol and remifentanil were kept within the ranges of 2–5 μg/mL and 2.5–10 ng/mL, respectively. Depth of anesthesia was titrated to maintain a bispectral index range of 40–60. Remifentanil was titrated to maintain the mean arterial blood pressure within ± 20% change of the preinduction value. During the procedure, the surgeon and the electrophysiologists were blinded to the patients' assignment.

After loss of consciousness and TOF-Watch (Organon Ireland Ltd., Dublin, Ireland) calibration, 0.15 mg/kg cisatracurium besylate was administered as a muscle relaxant. The degree of peripheral neuromuscular blockade by cisatracurium besylate was determined directly from the train-of-four (TOF) response at the adductor pollicis of the thumb.[12] In the P group, adjustments to the cisatracurium besylate infusion rate were made as necessary to maintain TOF level 1 during the operation until the completion of tumor resection and facial EMG monitoring. In the F group, no additional cisatracurium besylate was administered after anesthesia induction.

Patients were placed in a 20° head-up position. All surgical procedures were performed by the same neuro-otology team with standard facial EMG monitoring. During surgery, 4-channel facial EMG monitoring was performed with a NIM-Response 3.0 system (Medtronic Xomed, Jacksonville, Florida, USA) in all patients. Two bipolar-paired subdermal needle electrodes were placed subdermally to monitor the orbicularis oculi and orbicularis oris muscles. EMG for the orbicularis oculi and orbicularis oris muscles was recorded on separate channels. Facial EMG generated was used as a guide for further dissection and as a gauge of intraoperative preservation of facial nerve function. If at any time the electromyographer determined that the quality of monitoring was compromised, the infusion of cisatracurium besylate would be decreased or terminated as needed. Ventilation was controlled with a frequency of 12–15 cycles/minute to maintain an end-tidal carbon dioxide between 3.5% and 4% with 50% oxygen in air. The patient's core temperature (bladder temperature) was maintained at 36.5°C–37°C during the procedure by using a forced-air warming system.
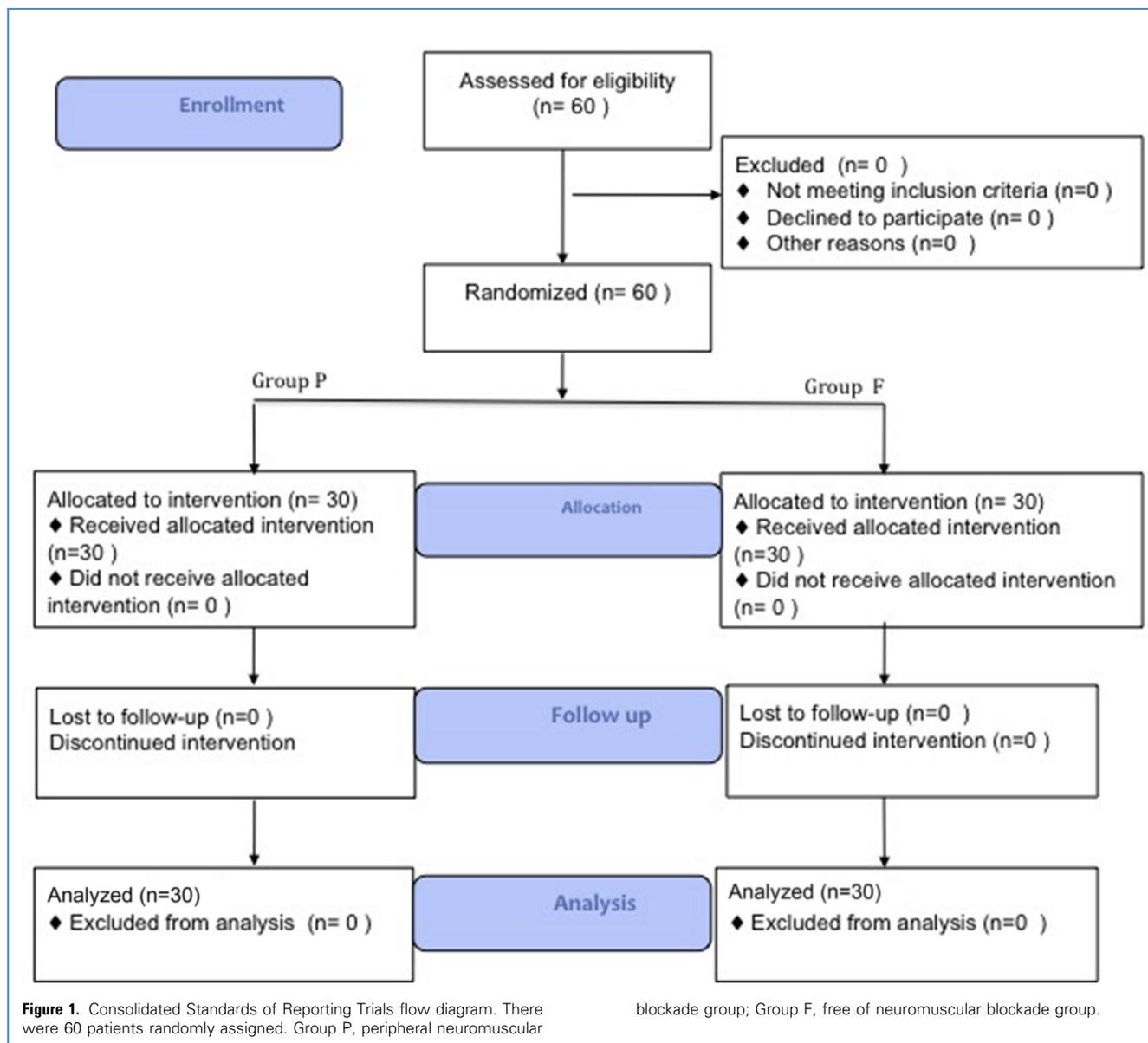
After resection of the VS was complete, a monopolar probe with a 0.5-mm tip was used to elicit the stimulation threshold of the facial nerve at the proximal site (near the brainstem) and the distal site (in the fundus). For each stimulation, the stimulation threshold that elicited a response >100 μV on at least 1 channel was determined, and the lowest stimulation threshold among the 3 parts was recorded. The range of stimulation intensities was 0.01–3 mA, with increments of 0.01 mA between 0.01 and 0.1 mA and increments of 0.05 mA between 0.1 and 3 mA. Extubation of the trachea was performed when the patient was awake and following commands and neuromuscular blockade had been effectively antagonized. Postoperatively, immediate facial function was evaluated by the neurosurgeon using the HB classification.

Statistical Analyses

The primary outcome was the stimulation threshold to elicit facial nerve response at the proximal site. Secondary outcomes were stimulation threshold to elicit facial nerve response at the distal site, use of vasopressors, requirement for anesthetics, and recovery profiles. Based on a previous study,[9] the mean ± SD threshold of electrical stimulation was 0.31 ± 0.10 mA at a TOF level 1 to elicit a response amplitude ≥100 μV. On the basis of an estimate of 60% decrease in stimulation threshold and potential 20% patient drop-off, we calculated that at least 25 patients were required in each group to give the study a statistical power of 90% at a 5% level of significance. Proximal-to-distal amplitude ratio was expressed as the median (first/third quartiles) and was analyzed using a Mann-Whitney rank sum test. Other continuous variables are expressed as mean ± SD and were analyzed using Student t tests. Categorical data were analyzed using χ^2 tests or Fisher exact tests. Statistical significance was set at $P < 0.05$.

RESULTS

There were 60 patients enrolled, and all completed the study (group P, n = 30; group F, n = 30) (**Figure 1**). Patient characteristics were examined (**Table 1**). Demographic data, duration of anesthesia and surgery, preoperative hemodynamic

Figure 1. Consolidated Standards of Reporting Trials flow diagram. There were 60 patients randomly assigned. Group P, peripheral neuromuscular blockade group; Group F, free of neuromuscular blockade group.

files, baseline bispectral index value, and average diameter size of the tumor were similar in both groups (Table 1). All patients had a total resection of VS, and anatomic preservation of the facial nerve integrity was possible in all patients.

No patient receiving partial peripheral neuromuscular blockade experienced compromised EMG monitoring quality. The mean stimulation thresholds at the proximal site were 0.12 mA in the P group and 0.06 mA in the F group; the difference was statistically significant (P = 0.001). The mean stimulation thresholds at the distal site were 0.08 mA in the P group and 0.03 mA in the F group; the difference was statistically significant (P = 0.0002). Proximal-to-distal amplitude ratios were 1.17 in the P group and 0.84 in the F group at the orbicularis

oculi muscles; the difference was not statistically significant (P = 0.085). The ratio was 1.15 in the P group and 0.78 in the F group at the orbicularis oris muscles; the difference was not statistically significant (P = 0.11).Two female patients (average age 63.5 years old) in the P group needed phenylephrine to maintain stable mean blood pressure, and 8 patients (average age 47.8 years) in the F group needed phenylephrine (Table 2).

Patients in both groups had similar recovery times (Table 3). In particular, the time from discontinuation of anesthetics to response to verbal command, extubation, ability to state correct birth date, and return to orientation were not significantly different (P > 0.05). In addition, no patients presented with severe facial nerve deficit (i.e., HB grade ≥3).

Table 1. Demographic Characteristics

	Group P (n = 30)	Group F (n = 30)	P Value
Age, years	47.4 ± 11.8	46.6 ± 8.8	0.76
Sex, male/female	16/14	11/19	0.30
Weight, kg	64.7 ± 10.6	46.6 ± 8.8	0.91
Height, cm	165.5 ± 8.4	164.7 ± 9.2	0.71
Tumor diameter, cm	1.86 ± 0.85	2.03 ± 0.64	0.38
Side distribution, right/left	16/14	18/12	0.79
HR, beats/minute	75.6 ± 6.3	74.7 ± 9.5	0.66
MAP, mm Hg	95.7 ± 12.8	92.2 ± 9.0	0.24
Baseline BIS	96.4 ± 2.0	95.6 ± 3.5	0.28
Anesthesia duration, minutes	384.9 ± 90.1	372.5 ± 65.1	0.54
Surgery duration, minutes	328.5 ± 88.9	301.6 ± 71.8	0.20

Data are expressed as mean ± SD or number of patients.
Group P, peripheral neuromuscular blockade group; Group F, free of neuromuscular blockade group; HR, heart rate; MAP, mean blood pressure; BIS, bispectral index.

DISCUSSION

In our study, we found that the stimulation thresholds to elicit an amplitude of 100 μV were <0.2 mA at the proximal site in both groups, whereas the stimuli threshold in the F group was lower

Table 2. Electromyographic Monitoring Values and Intraoperative Profiles

	Group P (n = 30)	Group F (n = 30)	P Value
Stimulation threshold, mA			
At the proximal site	0.12 ± 0.09	0.06 ± 0.05	0.001
At the distal site	0.08 ± 0.07	0.03 ± 0.02	0.0002
Proximal-to-distal amplitude ratio*			
Orbicularis oculi muscles	1.17 (0.55, 2.34)	0.84 (0.44, 1.27)	0.085
Orbicularis oris muscles	1.15 (0.71, 1.79)	0.78 (0.56, 1.32)	0.11
MAP, mm Hg	76.9 ± 9.1	80.2 ± 11.6	0.23
HR, beats/minute	63.7 ± 8.3	61.2 ± 8.1	0.25
Average BIS value	46.8 ± 6.3	49.0 ± 6.0	0.17
TOF level at extubation, %	102.2 ± 3.9	104.1 ± 6.4	0.16
Use of phenylephrine	2	8	0.08
Remifentanil dose, μg	4535.0 ± 1111.2	4489.0 ± 1029.8	0.87
Propofol dose, mg	2713.5 ± 961.6	2942 ± 931.7	0.35

Data are expressed as mean ± SD or number of patients.
P group, peripheral neuromuscular blockade group; F group, free of neuromuscular blockade group; MAP, mean blood pressure; HR, heart rate; BIS, bispectral index; TOF, train-of-four.
*Data are expressed as median (interquartile range).

Table 3. Recovery Profiles in Postanesthesia Care Unit

	Group P (n = 30)	Group F (n = 30)	P Value
Response to verbal command, minutes	10.0 ± 4.9	8.8 ± 3.2	0.26
Extubation, minutes	13.0 ± 6.1	11.2 ± 5.6	0.23
Stating birth date, minutes	17.97± 11.0	17.4 ± 12.2	0.93
Return to orientation, minutes	38.4 ± 14.9	42.7 ± 18.6	0.33
Immediate HB grade, I/II	19/11	17/13	1
Shiver	2	2	1
PONV	1	2	1

Data are expressed as mean ± SD or number of patients.
P group, peripheral neuromuscular blockade group; F group, free of neuromuscular blockade group; HB, House-Brackmann; PONV, postoperative nausea and vomiting.

than that in the P group. More remifentanil was needed in the F group. No patient demonstrated an unexpected severe facial nerve deficit postoperatively.

There is no consensus regarding the use of NMBAs or level of neuromuscular blockade during facial nerve monitoring. Owen et al.[13] suggested that when mechanically elicited EMG was recorded, it was necessary for the patient to demonstrate at least TOF level 2. However, Lennon et al.[8] found that moderate degrees of peripheral neuromuscular blockade can be achieved without compromising facial EMG monitoring. In the current study, we found that partial peripheral neuromuscular blockade with TOF level 1 did not compromise facial EMG monitoring. This confirmed previous findings[8-10] that intraoperative use of NMBAs did not compromise EMG monitoring during VS resection.

Several authors have examined parameters of facial EMG and their capacity to predict facial nerve outcomes. The ability to stimulate the facial nerve at the brainstem with ≤0.2 mA was correlated with a higher percentage (90%) of HB grade I or II facial nerve function at 180 days postoperatively.[14-16] Yokoyama et al.[17] showed that a response amplitude of ≥100 μV could predict HB grade I facial nerve outcome 85% of the time, whereas amplitudes of <100 μV were unable to predict facial nerve outcome. In our study, the stimulation threshold 0.12 mA was able to elicit a response amplitude of 100 μV at the proximal site in patients with partial peripheral neuromuscular blockade. In patients free of NMBAs, the stimuli threshold was 0.06 mA. In addition, we found that the stimuli thresholds at the distal sites were 0.08 mA in group F and 0.03 mA in group P. The above-mentioned findings supported the point that NMBA use does increase the stimulation threshold during facial EMG. In terms of the stimulation threshold 0.2 mA proposed by other researchers,[15,16] we may consider the difference was not clinically significant.

Goldbrunner et al.[18] demonstrated that a response amplitude recorded from stimulating the facial nerve both proximal and distal to the tumor dissection could be used to prognosticate

facial nerve function at 6 months after surgery. They showed that a proximal-to-distal amplitude ratio of ≤0.1 correlated with a poor facial nerve function in 75% of patients at 6 months. In the current study, we found that median ratios of the orbicularis oculi muscles were 1.17 in the P group and 0.84 in the F group. The median ratios of the orbicularis oris muscles were 1.15 in the P group and 0.78 in the F group. These findings further confirmed that partial peripheral neuromuscular blockade, with a TOF level 1, did not compromise facial EMG monitoring during VS surgery.

Owing to its potential to reduce intracranial pressure and rapid emergence, total intravenous anesthesia using propofol and remifentanil is considered the anesthetic technique of choice in neurosurgical patients.[19,20] However, propofol possesses a potent circulatory depressant effect, and meticulous care should be taken, especially for elderly patients and patients who are hemodynamically unstable. In cases where NMBAs are not used, intraoperative anesthetic management of patients undergoing VS resection is made more difficult by the need to maintain a balance between hemodynamic stability and absolute immobility, while providing optimal conditions for facial EMG monitoring. In our study, to maintain stable arterial mean blood pressure, compared with the P group, more patients in the F group needed phenylephrine, although the difference was not statistically significant.

Our study has several limitations. First, patients with a tumor size >3 cm diameter were excluded. Tumor size has been found to have a large impact on facial nerve outcomes.[21] Second, all patients underwent VS resection via the retrosigmoid approach. The surgeon in our institution preferred the retrosigmoid approach. Advantages of the retrosigmoid approach include short operative time, immediate and accurate identification of the tumor, better visualization of the brainstem structures, and better facial nerve preservation.[22-24] Third, we measured the immediate outcome of facial nerve function rather than long-term facial nerve function postoperatively. Follow-up should be carried out to investigate the effect of intraoperative NMBA use on long-term facial nerve function. Fourth, propofol and remifentanil TIVA technique was applied in the current study; in cases where inhalational anesthesia was applied, partial levels of peripheral neuromuscular blockade might have compromised facial EMG monitoring.

CONCLUSIONS

NMBA use, producing a TOF level 1 in the adductor pollicis, is sufficient for facial nerve monitoring in patients during VS resection.

ACKNOWLEDGMENTS

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