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ORIGINAL ARTICLE

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Comparing intraoperative hemodynamics and medication use during cranial nerve monitoring with partial muscle relaxants versus without in cerebellopontine angle tumors: a randomized controlled trial

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Abstract

Background There are many methods used for cranial nerve monitoring in cerebellopontine angle (CPA) tumor excision with or without muscle relaxant which may affect hemodynamics and consumption of drug doses. The partial neuromuscular blockade, on the other hand, appears to be compatible with monitoring in some patients, according to clinical experience. In this study, we evaluated hemodynamic changes and drug consumption differences between partial and without muscle relaxants.

Forty patients ages ranging from 18 to 60 years old had CPA surgery and were given either a muscle relaxant to maintain neuromuscular blockade level train-of-four (TOF) count two (group A) or a placebo of normal saline to maintain train-of-four (TOF) count four (group B). Fentanyl was given to both groups. The dose of fentanyl was modified to 0.5–1 mcg\kg/h, while the dose of propofol was modified to have bi-spectral index between 40 and 60. The total amount of propofol and fentanyl, as well as mean blood pressure and heart rate, are all measured intraoperatively.

Results There was a statistically significant difference in propofol and fentanyl doses between both research groups ($p = 0.003$, $p = 0.002$) respectively during the intraoperative period. Furthermore, there is a difference in as there were significant differences between two groups in time between stop of anesthesia and eye opening which is shorter in group with partial muscle relaxant reflecting shorter duration of anesthesia and recovery time (stop anesthesia to eye opening time) ($p = 0.003$, $p > 0.001$) respectively. Also, there was no statistically significant difference in the incidence of nausea and vomiting, shivering, bradycardia, or hypotension between the two study groups.

Conclusions We demonstrated that partial muscle relaxant (train of four count 2) has benefits over no muscle relaxant (train of four count 4) for patients undergoing cerebellopontine angle tumor surgery because it can reduce anesthetic duration and generate rabid recovery. Furthermore, partial muscle relaxants exhibit the same hemodynamic stability, side effects, and surgical interruptions as group without muscle relaxants.

Keywords Hemodynamics, Propofol, Fentanyl, Cerebellopontine angle, Neuromuscular Nondepolarizing agents, Neurosurgery

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Background

The major goal of anesthetic care for patients having neurosurgical procedures is to provide anaesthesia that is smooth and maintain hemodynamically stability and good intra-operative circumstances, as well as speedy smooth recovery which enables early neurological assessment (Chui et al. 2014). Facilitation of endotracheal intubation and improving surgical conditions during anesthesia need Neuromuscular blocking (NMB) agents' administration (Li et al. 2014).

As a result, the Association of Anesthetists of Great Britain and Ireland (AAGBI) recommendations say that when NMB agents are employed, a peripheral nerve stimulator is required for easy monitoring of NMB agent administration and recovery (Checketts et al. 2016). Kim et al. 2013 compared the effects of various degrees of muscle relaxant in brain tumor patients, cerebral aneurysms, and spinal procedures. It also prefers a count-two train-of-four (TOF) because it provides a greater degree of muscle relaxation for neurophysiology.

Intraoperative neurophysiological monitoring is one technique to improve surgical outcomes while reducing morbidity. During posterior-fossa and brainstem surgery, this allows for easier identification and preservation of the cranial nerves, their motor nuclei, and corticobulbar networks (Hernández-Palazón et al. 2015, Sloan et al. 2008). The reduction of blood pressure and bradycardia are common side effects of drugs used in complete intravenous anesthetic like propofol, and without the use of a muscle relaxant, propofol consumption is expected to increase, as well as the side effects on hemodynamics. (Sloan et al. 2008).

The purpose of this study is to assess the effects of partial muscle relaxation on hemodynamics and medication intake during cranial nerve monitoring in cerebellopontine angle tumor surgery.

Methods

From October 2019 to November 2021, all patients scheduled for cerebellopontine angle tumors were enrolled in this prospective randomized double-blind trial after receiving approval from the research ethical committee (D-4–2019) and clinical trial registration (NCT04148534).

Patients with an American Society of Anesthesiologists (ASA) score of I–II were included in the study. They ranged in age from 18 to 60 years old. Subjects were removed from the study if they refused to participate, had a GCS of lower than 15, were hemodynamically unstable, had a disease that affected neuromuscular transmission, or had arrhythmia or convulsions.

The enrolled patients were assigned randomly to one of two clusters using computer-generated random sampling techniques and an opaque and secured envelope, which is opened only after the participants have been transferred to the preoperative holding area. Group I ($n = 20$) receive rocuronium infusion as a muscle relaxant. Group II ($n = 20$) get regular saline instead of rocuronium injection. the anesthesiologist who administered the muscle relaxant medicines and the investigator who recorded the observations were not aware of the patients' randomization numbers and were excluded from the trial. The surgeon and anesthesiologist were unaware of the research groups when they administered muscle relaxant infusions.

For blinding to be effective, the syringes in both groups were identical in every way. Furthermore, the anesthesiologist in charge of the patients was dealing with quantities rather than dosages. as we computed the dosage per milliliter and requested the number of milliliters per hour.

Patients were assessed the day before surgery by collecting a full medical history, a physical and neurological examination, and regular investigations (CBC, PT, PC, INR, ALT, AST, electrolyte, urea, and creatinine).

The patient's demographic data (age, sex), as well as operation data (type and size of the tumor), was recorded when they arrived at the preoperative holding area and a fasting time of 6 h was confirmed. Intravenous cannula 22 was placed in this location. As premedication, all patients received intravenous 0.15 mg/kg ondansetron, intravenous 0.1 mg/kg metoclopramide, and intravenous 1 mg midazolam.

The patients were transferred to the operating room, where standard monitoring techniques (electrocardiography, non-invasive blood pressure, pulse oximeter, and temperature) were used, as well as BIS (Covidien, Mansfield, Massachusetts, USA), Entropy (GE Healthcare, Helsinki, Finland) to assess anesthesia depth and peripheral nerve stimulators (PNS) (GE Healthcare, Helsinki, Finland) to monitor the level of neuromuscular blockade.

Neurophysiology performed cranial nerve monitoring in the form of facial nerve motor evoked potentials and electromyography intraoperative monitoring on all patients. Five rectangular pulses ranging from 200 to 600 V (mean, 380 V) were used to stimulate the contralateral of affected side, with a pulse duration of 50 s and an ISI of 2 ms. To obtain waveforms, bandpass filters (150–3000 Hz) were used. In response to MEP responses from the face and hands, the number of pulses and intensity of the stimulus were increased. During continuous electromyography (EMG) monitoring, a train of 5 pulses was used.

Patients were given a standardized anesthetic induction with 1–2 mg/kg propofol and 2–3 mcg\kg fentanyl until the eyelash reflex was gone. By using rocuronium 0.6 mg/

kg as induction dose, intubation was facilitated with only a tiny, single, intermediate-acting dosage of muscle relaxant. Then, to get the greatest response (control response) from the adductor pollicis muscle, the maximal electromyographic amplitude of T1 before rocuronium infusion delivery (Tc), prior to rocuronium infusion, a baseline twitch response was generated using a neuromuscular nerve stimulator.

Reaction of adductor policies brevis muscle to train-of-four (TOF) and ulnar nerve stimulation was assessed every 2 min to determine the level of relaxation according to grouping, and the rocuronium infusion was changed according to the partial NMB group's aim, group I ($n=20$) = train of four count 2 and group II ($n=20$) = train of four count 4.

In the prone position, the patient's eyes were taped shut and padded to protect them from harm. A urinary catheter was inserted, an arterial line and central line were placed, two large-bore IV lines were inserted, one for muscle relaxation infusion and the other for the administration of total intravenous anesthesia (TIVA) protocol and fluids, and a temperature probe was inserted, and to protect the contents of the oral cavity, appropriately sized bite blocks were wedged between the molars, and a temperature probe was inserted.

The bi-spectral index, or entropy, was used to determine the level of anesthesia during surgery. To accurately monitor intraoperative blood loss, all sponges were weighed, and saline washes were measured. We did arterial blood gas analyses and hemoglobin estimations as needed.

For the duration of anesthesia, propofol and fentanyl infusions were administered via syringe pump. And to keep up a BIS value between 40 and 60 during surgery, fentanyl was incremented at 0.5–1 g/kg/h while propofol dose was administered at a range of 6–10 mg/kg/h. The patient was then randomly assigned to one of two groups and given rocuronium doses that were modified according to the group's NMB aim.

The following were the objectives for the groups taking partial NMB: To sustain train-of-Four (TOF) 2 twitches, group I ($n=20$) receive rocuronium infusion as a muscle relaxant at a dose range of 5 mcg\kg/min. Group II ($n=20$) get regular saline instead of rocuronium injection in the same volume per kilogram.

Invasive arterial measurement was used to track mean arterial pressure throughout surgery, which was collected every 30 min and compared across groups.

Hypotension was expressed when meaning arterial pressure dropped greater than 20% lower than the baseline preoperative levels or drop to 55-mm mercury or less, and it was generally treated with multiple 2.5 mg I.V. ephedrine bolus doses. If at least three ephedrine bolus doses were required, A vasopressor infusion (0.3 to 2 mcg/kg/min norepinephrine) was administered. If bradycardia of less than 60 beats per minute developed, 0.6 mg of atropine was administered.

All anesthetic medicines were stopped after the surgery, and the extubating criteria were as follows: When the patient breathes spontaneously, the TOF ratio was greater than 0.9, the BIS was greater than 70, the respiratory pattern was regular, the tidal volume was at least 5 ml/kg, and the SpO2 was greater than 95%, and Sugammadex (2 mg/kg) and atropine (0.02 mg/kg) were used to reverse the muscle relaxant effect.

Outcome assessment

The primary outcomes were the total volume of propofol and fentanyl injected. **The secondary outcomes** were the number of hypotension episodes and the use of vasopressors.

Statistical analysis

The statistical package for the social sciences (SPSS) version 26 was used to code and enter the data (IBM Corp., Armonk, NY, USA). In quantitative data, mean, standard deviation, median, minimum, and maximum were used, while categorical data were summarized using frequency (count) and relative frequency (%). For normally distributed quantitative variables, the unpaired t-test was employed, whereas, for non-normally distributed quantitative variables, the non-parametric Mann–Whitney test was utilized (Chan 2003a). The chi-square (2) test was used to compare categorical data. When the anticipated frequency is less than 5, the exact test was utilized instead (Chan 2003b). Statistical significance was defined as a P-value of less than 0.05. Using G-power software, we estimated our sample size. Our primary outcome was estimated using previous data with the SPSS program and was found to be a mean of 0.72 0.43 in a previous study. The number of patients in the sample was calculated to be 38. (19 in each group). We recruit 20 patients in each group to make up for dropouts.

Results

This trial enrolled 42 patients, 20 in each group but two were excluded: one due to exclusion criteria and hemodynamic instability, and the other due to an increased risk of arrhythmias. The remaining 40 patients were randomly distributed into two equal groups. Group I ($n=20$) receive rocuronium infusion as a muscle relaxant. Group II ($n=20$) get regular saline instead of rocuronium injection (Fig. 1). Patients in the group without muscle relaxants had considerably longer anesthetic duration than those in the group with muscle relaxants, but there was

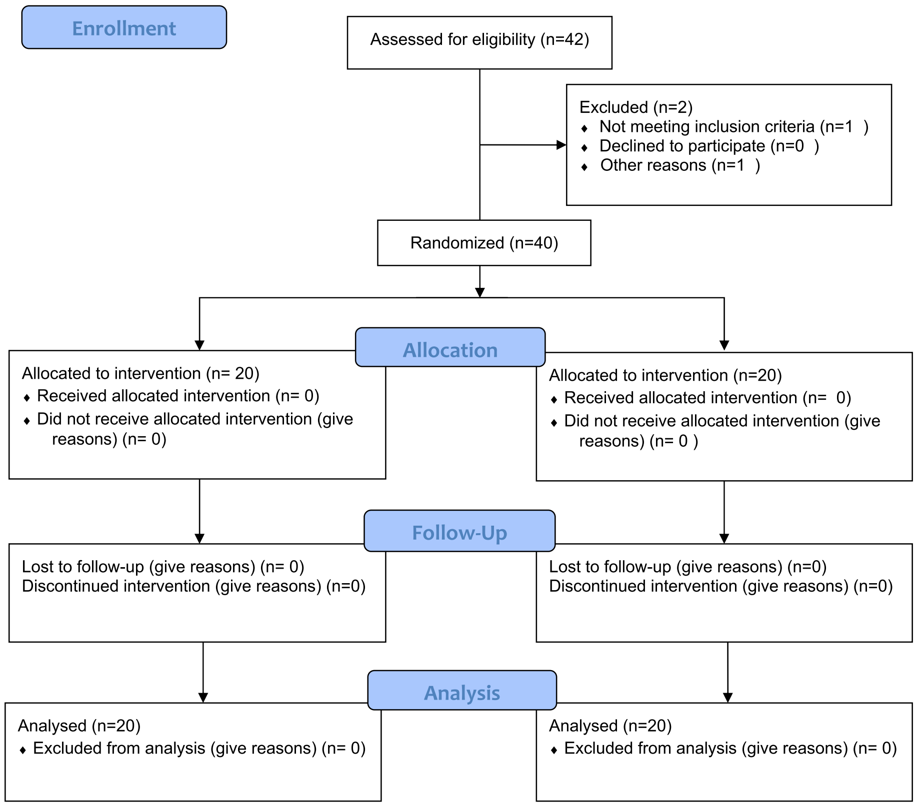

Fig. 1 CONSORT flow diagram

Table 1 Demographic data and duration of surgery (mean ± SD and the number of patients)

		Group				
		(Group I) with muscle relaxant		(Group II) without muscle relaxant		*P* value
		Mean	SD	Mean	SD	
Age (years)		32.95	8.34	38.45	14.44	0.221
Duration of surgery (h)		5.63	0.90	5.73	1.12	0.947
Duration of anesthesia (h)		6.60	1.06	8.17	1.76	0.003*
		Group				
		(Group I) With muscle relaxant		(Group II) Without muscle relaxant		*P* value
		Count	%	Count	%	
Type	Meningioma or epidermoid	3	15.0%	1	5.0%	0.286
	vestibular schwannoma	4	20.0%	8	40.0%	
	Acoustic neuroma	13	65.0%	11	55.0%	
Size	Small (1–10 mm)	9	45.0%	7	35.0%	0.641
	Intermediate (11–20 mm)	9	45.0%	9	45.0%	
	Large (> 20 mm)	2	10.0%	4	20.0%	
Sex	Male	10	50.0%	9	45.0%	0.752
	Female	10	50.0%	11	55.0%	

* Denotes statistically significant difference between two groups

no significant change in age, gender, type, size, or surgical time between both research groups (Table 1).

Throughout the trial, there were no significant changes between both research groups in terms of heart rate (HR) properties (Fig. 2). There was no significant change in blood pressure values during the intraoperative or postoperative periods (Fig. 3). In each occurrence of hypotension, incremental doses of ephedrine were delivered by the research protocol, and arterial blood pressure was restored in all cases.

During surgery or in the PACU, all the patients in both groups had SpO2 levels greater than 95% (Fig. 4).

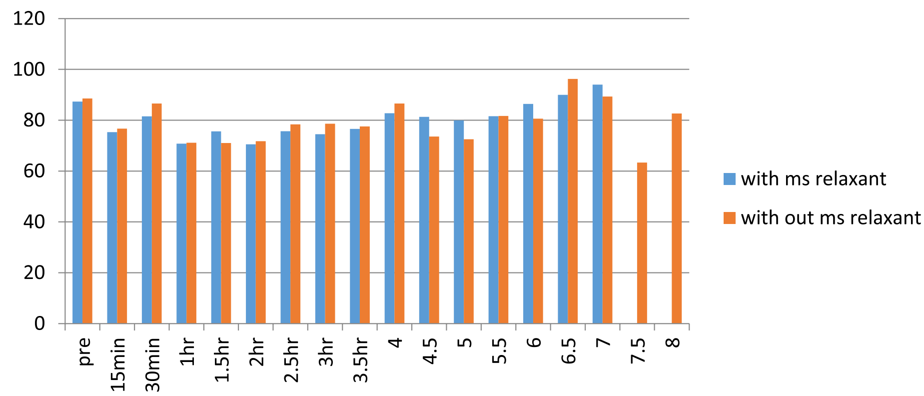

Fig. 2 Heart rate data

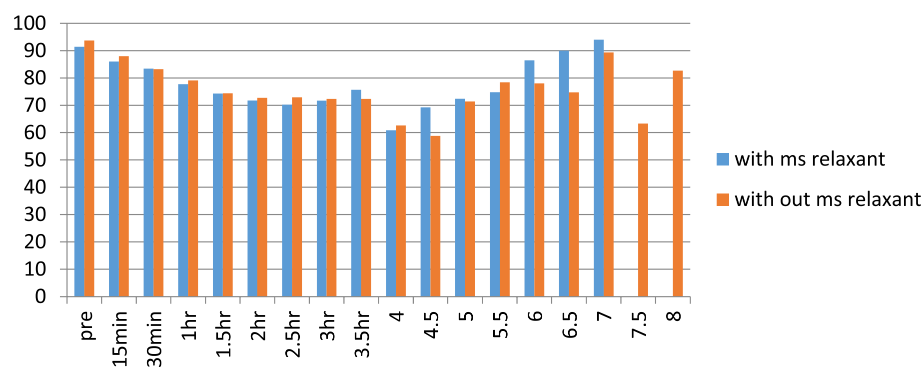

Fig. 3 Mean arterial blood pressure data

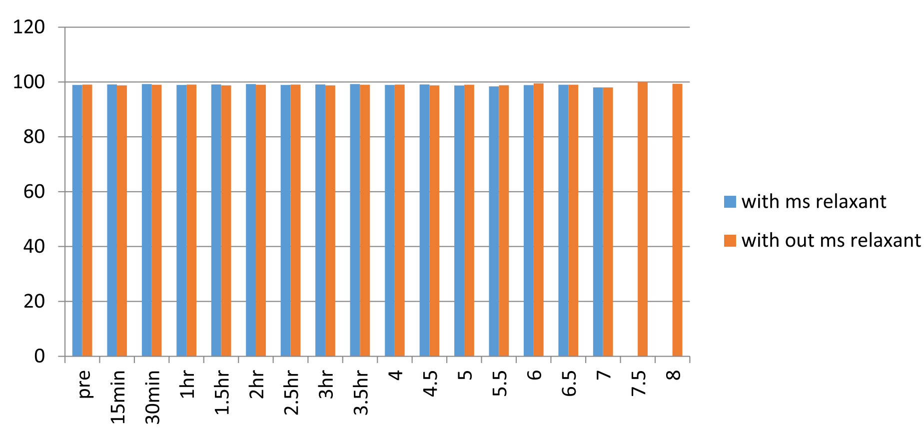

Fig. 4 Oxygen saturation data

During the intraoperative phase, there were significant changes in propofol and fentanyl doses between both research groups ($p=0.003$, $p=0.002$) respectively, but no significant difference in ephedrine and atropine (Table 2).

Although there was no significant change in the incidence of hypotension ($p=0.235$), bradycardia ($p=0.407$), and side effect as shivering and postoperative nausea and vomiting between the two study groups, otherwise clinically, there is a risk of being in both groups but more at that does not use a muscle relaxant (Table 3).

In terms of anesthesia duration and time from anesthetic withdrawal to eye-opening (recovery time), there was a significant difference between the two study groups ($p=0.003$, $p>0.001$) respectively (Tables 1 and 4). In terms of patient surgery duration, there were no significant differences between the two study groups (time from skin incision to skin closure) ($p=0.947$) (Figs. 5, 6, 7 and 8).

Table 2 Doses of drugs. Data are presented as mean and SD

	Group				
	(Group I) with muscle relaxant		(Group II) without muscle relaxant		*P* value
	Mean	SD	Mean	SD	
Propofol (μg ml^{-1})	4.22	1.39	6.03	1.76	0.003
Ephedrine (mg)	0.25	0.77	1.00	1.50	0.174
Fentanyl (μg)	337.50	66.64	405.00	45.60	0.002*
Atropine (mg)	0.04	0.12	0.10	0.18	0.429

* Denotes statistically significant difference between two groups

Table 4 Recovery profiles in post-anesthesia care unit. Data are presented as mean and SD

	Group				
	(Group I) with muscle relaxant		(Group II) without muscle relaxant		*P* value
	Mean	SD	Mean	SD	
Induction to stop anesthesia time (h)	5.38	0.84	5.20	0.97	0.355
Stop anesthesia to eye-opening (mins.) (recovery time)	59.25	18.94	145.5	58.62	< 0.001*

Group A partial neuromuscular blockade, *group B* free of neuromuscular blockade

The numbers are expressed as a percentage of the total number of patients

* Denotes statistically significant difference between two groups

Discussion

This study investigated the impact of partial NMB and no NMB on anesthesia during neurosurgical cerebellopontine angle surgery. Furthermore, during cranial nerve monitoring, there is no unanimity on the level of neuromuscular inhibition, and researchers discovered that the quality of cranial nerve monitoring was not impaired in any of the patients who had partial peripheral neuromuscular inhibition. In this study, partial NMB was found to have numerous advantages over no NMB in cerebellopontine angle surgery.

Although the significant proportion of institutions do not encourage partial NMB, some assume about using no NMB may create issues in the surgical field and an increased risk of unexpected patient movement. Thoughts on the necessity of NMB have not been thoroughly researched, they are critical to all neurosurgical anesthesiologists (Kim et al. 2013).

Table 3 Perioperative complications. Data are presented as the number of patients

		Group				
		(Group I) with muscle relaxant		(Group II) Without muscle relaxant		*P* value
		Count	%	Count	%	
Bradycardia (*n*) (%)	Not happened	18	90.0%	15	75.0%	0.407
	Once	2	10.0%	5	25.0%	
Low BP (*n*) (%)	No	18	90.0%	14	70.0%	0.235
	Once	2	10.0%	6	30.0%	
Shivering (*n*) (%)	No	18	90.0%	17	85.0%	1
	Once	2	10.0%	3	15.0%	
PONV (*n*) (%)	No	19	95.0%	19	95.0%	1
	Once	1	5.0%	1	5.0%	

Group A partial neuromuscular blockade, *group B* free of neuromuscular blockade

The numbers are expressed as a percentage of the total number of patients

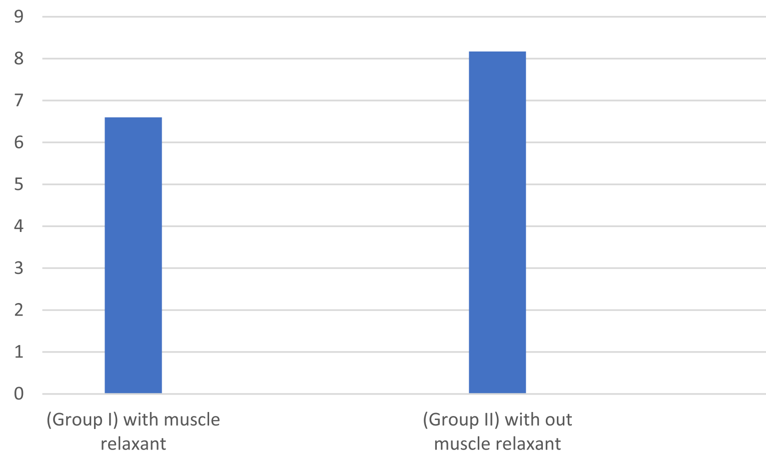

Fig. 5 Duration of anesthesia (h)

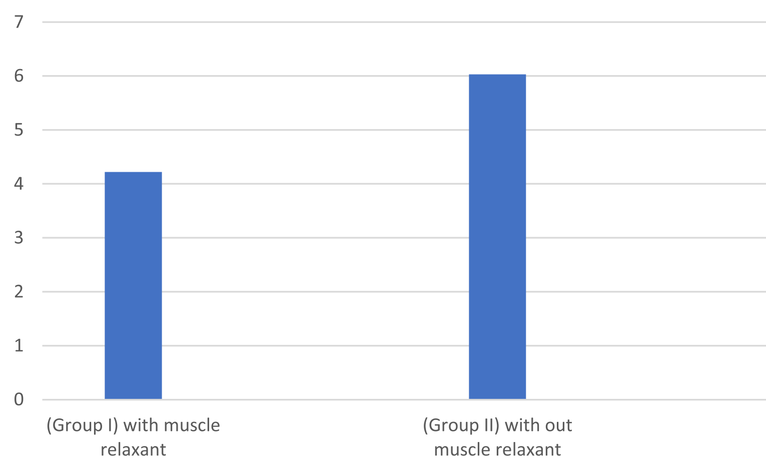

Fig. 6 Dose of propofol (μg ml[1])

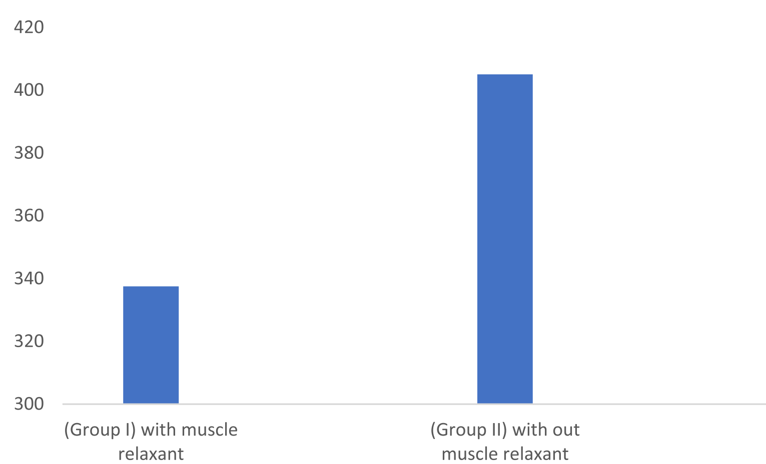

Fig. 7 Doses of fentanyl (μg)

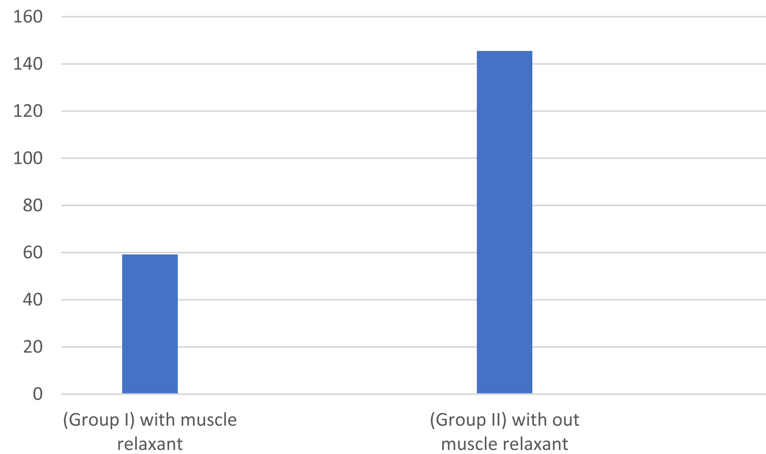

Fig. 8 Stop anesthesia to eye-opening (min) (recovery time)

Although there was no discrepancy in hemodynamics as well as intra-operative or post-intervention complication between the two methods, the benefits of partial NMB include a shorter duration of anaesthesia and a reduced level of propofol use.

Hypotension and bradycardia were more common with no muscle relaxant technique than with muscle relaxant technique in this trial, with no clinically meaningful difference between the two groups. Fentanyl 0.5–1 mcg\kg/h in combination with propofol by infusion either exhibited no hemodynamic effects or resulted in a when meaning arterial pressure drop greater than 20% lower than baseline preoperative levels or a drop to 55 mmHg or less, as seen in this study.

This study corroborates prior research that suggested partial NMB might be used as part of an anesthetic protocol for cranial nerve monitoring during CPA surgery.

Lennon et al. 1992 discovered that while maintaining face EMG monitoring, certain levels of partial NMB can be achieved. In a retrospective analysis of 69 individuals with NMB levels maintained at train-of-four (TOF) at count two. (Vega-Céliz et al. 2015) concluded that facial nerve monitoring under the neuromuscular blockade is viable and safe in patients without prior facial palsy. If the patient exhibited an electromyographic response after the tumor was removed and improved facial function in the postoperative period and after a year of observation.

Cranial nerve monitoring is a a reliable predictor of postoperative proper function (Akagami et al. 2005, Dong et al. 2005), When compared to people who do not use a muscle relaxant, adding a partial muscle relaxant can be accomplished and with reduced side effects. (Akagami et al. 2005).

Using an uninterrupted infusion of vecuronium bromide to establish a TOF value count 3, Zhang, Jun et al. determined that even various intraoperative groups underwent partial muscular relaxation under general anesthesia, it is possible to monitor the cranial nerves (Zhang et al. 2008).

The effects of vecuronium and cisatracurium on the efficacy of intraoperative MEP monitoring were studied by Hoon Chung, Yang, and colleagues. The partial NMB aim for proper maintenance was T1/Tc 50%, with no discernible difference between the two (Chung et al. 2017).

When comparing four groups of people who received partial NMB and had varying levels of relaxation, it was observed that if NMB is given during MEP intra-operative monitoring technique, A T2/Tc goal of 0.5 is recommended (Kim et al. 2013).

Intraoperative monitoring is achievable with partial neuromuscular blocking with T1 of 10–20% or TOF with 2 responses out of 4 as evaluated at the ulnar nerve (Sloan 2013).

No muscle relaxation is strongly preferred over partial NMB during Neurophysiological monitoring in neurosurgery, according to Kim et al. 2013 despite preferring a T2/Tc target of 0.5, during neurophysiological monitoring, if NMB is employed.

However, the consequence of this work revealed that there was a statistically significant difference between both research groups in terms of propofol and fentanyl consumption, as well as the duration of anesthesia. Additionally, there was no statistically significant difference in hemodynamics or complications postoperative between the partial muscle relaxation and the no muscle relaxant groups.

There is generally no literature which already have investigated the influence of several degrees of muscle relaxation during CPA surgery on intra-operative and post-operative outcomes. Given all the previous scientific research, the present study may be the first randomized controlled trial to investigate the impact of a partial muscle relaxation on hemodynamics during cranial nerve monitoring.

The limitation is the need of comparing different level muscle relaxant levels and different degrees of relaxation. Furthermore, we were unable to quantify the blood loss that occurred intraoperatively, because it was a visual and rough calculation.

Conclusions

We demonstrated that partial muscle relaxant (train of four count 2) has benefits over no muscle relaxant (train of four count 4) for patients undergoing cerebellopontine angle tumor surgery because it can reduce anesthetic duration and generate rabid recovery. Furthermore, partial muscle relaxants exhibit the same hemodynamic stability, side effects, and surgical interruptions as group without muscle relaxants.

Abbreviations

CPA	Cerebellopontine angle
TOF	Train-of-four
NMB	Neuromuscular blockade
ASA	American Society of Anesthesiologists
GCS	Glascow Coma Scale
CBC	Complete blood count
PT	Prothrombin time
PC	Prothrombin concentration
INR	International normalized ratio
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
BIS	Bi-spectral index
PNS	Peripheral nerve stimulators
Tc	T(control)
TIVA	Total intravenous anesthesia
SpO2	Oxygen saturation
mcg	Microgram
mg	Milligram
ml	Milliliter
kg	Kilogram
min	Minute
HR	Heart rate
PACU	Post-anesthesia care unit
MEP	Motor evoked potential
PONV	Post-operative nausea and vomiting

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Authors' contributions
MMG: concepts, data acquisition, statistical analysis, manuscript editing and manuscript review. SH: definition of intellectual content, literature search, data analysis, manuscript preparation and manuscript review. MM and HA: design, clinical studies, experimental studies, data acquisition, manuscript review and guarantor. NF helps with the anesthesia procedure, writing the manuscript, the data collection, and editing of the manuscript. The authors read and approved the final manuscript.

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Availability of data and materials
The data and the material sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Approval was obtained from the Research Ethics Committee of the Faculty of Medicine, Cairo University (D-4–2019), and written informed consent was obtained from the patients. The trial was registered on clinical trial.gov (NCT04148534). Every patient signed a written informed consent before inclusion after a complete presentation of the goal of the research with full details of the study.

Consent for publication
Not applicable (no individual data included).

Competing interests
The authors declare that they have no competing interests.

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