Faculty of Medicine, Cairo University Postgraduate Research Program Template

1. Proposed Study Title

Intra operative motor evoked potential monitoring of facial nerve in patients undergoing cerbellopontine angle tumor resection using partial versus no neuromuscular block.

Degree : M.D

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4. Background and Rationale:

The well-accepted goals for the anaesthetic management of patients undergoing neurosurgical procedures include the delivery of smooth and hemodynamically stable anaesthesia with provision of good operating conditions and a smooth but rapid emergence that allows for early neurological assessment.(1)

Muscle relaxation is considered as elements of general anaesthesia. Neuromuscular blocking agents (NMBAs) are usually administered during anaesthesia to facilitate endotracheal intubation and/or to improve surgical conditions.

The use of NMDs for general anaesthesia may cause many side effects, which cannot be ignored, such as residual paralysis, delayed recovery from general anaesthesia, recurarization, anaphylactic or anaphylactoid reactions, histamine release, all of which need to be reversed. At last but not least it interferes with the neurophysiologic

monitoring of these patients. (2)

Now we can use nerve stimulator device for easily monitoring of administration of and recovery from neuromuscular blocking agents (NMBAs) whenever possible is recommended.

We agree with the guidelines issued by the Association of Anaesthetists of Great Britain and Ireland (AAGBI) statements that a peripheral nerve stimulator is mandatory when NMBAs are used (3).

Intraoperative neurophysiological monitoring has been established as one of the paths by which modern neurosurgery can improve surgical results while minimizing morbidity. This proceeding consists of the monitoring of functional integrity of the neural pathways and mapping of techniques for identification and preservation of the cranial nerves, their motor nuclei, and corticospinal or corticobulbar pathways during posterior-fossa and brainstem surgery.(4)

During these surgical procedures, small injuries can produce significant neurological deficits, and therefore global integrity of the brainstem must be monitored through transcranial electric motor-evoked potentials (TceMEPs). (5,6)

Preservation of facial nerve (FN) function is a well-recognized goal of tumor excision at the cerebellopontine angle (CPA). Especially in cases of vestibular schwannoma excision, postoperative facial paresis and paralysis may occur despite efforts to avoid injury and maintain anatomic integrity of the nerve during dissection.(9)

Motor-evoked potential monitoring of the FN using transcranial stimulation of the motor cortex (TceMEP) yields information regarding the full facial nerve pathway without requiring direct nerve stimulation.(9)

Direct electrical stimulation can be used intermittently to assist with identification and mapping of the facial nerve location during tumor resection However, This method can be of limited utility when the nerve course and/or its emergence from the brainstem is inaccessible or obscured by tumor bulk at the CPA.(9)

Current standard of anesthesia in Motor Evoked Potential (MEP) monitored neurosurgeries is TIVA (total intravenous anaesthesia) without muscle relaxant or with shallow NMB because deep NMB prevents monitoring of MEPs during surgery.

To the best of our knowledge, there are no direct comparative studies involving partial versus no neuromuscular blocker effect in facial nerve monitoring of TceMEPs during the surgery of brainstem lesions but rarly there is studies which compare the effect of muscle relaxant in brain tumers ,cerebral aneurysm and spinal surgeries(4).

The use of TceMEP monitoring during surgery for intraparenchymal and extraparenchymal brainstem lesions has become a safe, reliable, and sensitive method to detect and reduce injury to the brainstem, allowing an early intervention to avoid permanent impairment(7).

The effects of muscle relaxation on TceMEPs are an important consideration in intraoperative neurological monitoring during surgery for intraparenchymal and extraparenchymal brainstem lesions for easily and early detection (8).

5. Objectives:

This study is designed to compare the operating condition of two different levels of muscle relaxation on facial nerve monitoring using transcranial motor evocked potential in CPA surgery at KasrAlainy University Hospitals.

- To Estimate End to start facial nerve MEP amplitude ratio
- To determine the effect of neuromuscular relaxant degrees on recovery and hemodynamics.
- To compare doses of hypnotics given at different level of muscle relaxant.
- Assessment of propofol doses needed for enhancement of early recovery and ambulation.

6. Study Design :

A comparative study will be used in this trial

7. **Ethical committee approval** (was it ethically approved by the department)

Yes
No
N/A

8. Study Methods

Population of study & disease condition:

40 Patients aged from 18-60 years old, scheduled for Cerebellopontine angle surgery will be included in the study. Patients will be randomly allocated using concealed closed envelope method into one of two groups: Induction will be accomplished with fentanyl, propofol, and a single dose of a neuromuscular blockade. Following intubation, general anesthesia was maintained with a continuous infusion of propofol and fentanyl.

Group A (n=20): will receive Rocronium as muscle relaxant, maintain partial NMB T2\TC 0.5 or TOF count 2 (10) and targeting BIS = (40-60)

Group B (n=20): will not receive muscle relaxant, targeting BIS = 25-35 after ending of monitoring of neurophysiology propofol dose will be dropped to 4–6 mg\kg\hr. targeting Bispecteral index 40- 60.

Inclusion criteria:

1. Patients age between >18 and<60.
2. Patients scheduled for neurosurgical CPA surgeries
3. Ability to sign the consent
4. ASA classification I, II

Exclusion criteria:

1. ASA > II
2. Hemodynamically unstable
3. Disease affecting neuromuscular transmission (myasthenia gravies ...etc.)
4. GCS < 15.
5. Any cardiac patient (ischemic heart disease – cardiomyopathy...etc.)

Methodology in details :

Before induction of anaesthesia and Before Rocronium administration, the baseline twitch response will be established with a neuromuscular nerve stimulator (NMT mechanosensor, GE healthcare, Helsinki, Finland) to achieve the maximum response of the adductor pollicise muscle.

The maximum electromyography amplitude of T1 before Rocronium administration will be considered to be the control response (Tc). The response of the adductor pollicise brevis muscle to TOF stimulation of the ulnar nerve will be monitored every 5 min and will be recorded every 30 min, and the infusion dose of Rocronium will be adjusted according to the target of the partial NMB group.

Anaesthesia will be induced by I.V. propofol (1.5-2 mg\kg) with fentanyl (2–4 mcg\kg) through syringe infusion pump. After induction, tracheal intubation will be facilitated with Rocronium (0.6 mg kg).

Anaesthesia will be maintained by propofol and fentanyl infusions through the pump. Subjects will be randomly allocated into one of the two groups:

Group A (n=20): will receive Rocronium as muscle relaxant, maintain partial NMB T2\TC 0.5 or TOF count 2 (10) , Fentanyl will be infused at a dose range of 0.5–1mcg\kg\hr. to control the haemodynamic response to the surgical procedure within a 20% range of its preoperative value, and propofol will be infused at a dose range of 6–8 mg\kg\hr. to targeting Bispectral index at 40 -60.(11)

Group B (n=20): will not receive muscle relaxant, Fentanyl will be infused at a dose range of 0.5–1mcg\kg\hr. to control the haemodynamic response to the surgical procedure within a 20% range of its preoperative value, and

propofol will be infused at a dose range of 8–12 mg\kg\hr. to targeting Bispectral index at 25-35, after ending of monitoring of neurophysiology propofol dose will be dropped to 4–6 mg\kg\hr. targeting Bispecteral index 40- 60.(11)

The mean arterial pressure during the surgery will be monitored every 5 min and will be recorded every 30 min and will be compared between the groups. Hypotension will be defined as a decrease in the mean arterial pressure of more than 20% of the preoperative value or below 55 mm Hg and will be treated by repeated 5 mg I.V. ephedrine bolus doses. Vasopressor infusion (norepinephrine in starting dose of 0.3 up to 2 mcg/kg/min) will be given if three or more ephedrine bolus doses is required. If bradycardia (60 beats min) developed, 0.6 mg of atropine will be administered.

Intraoperative monitoring included continuous ECG, pulse oximetry, arterial pressure (via arterial line and non-invasive arterial pressure cuff) ,temperature to avoid hypothermia ,The monitoring of transcranial electrophysiology for surgery will be performed by recording MEP, bispectral index (Covidien, Aspect medical systems, inc, Norwood, USA) and train of four.

TCMEP monitoring of the facial nerve will be performed using two stimulant corkscrew scalp electrodes (NIM Eclipse,Midtronic) placed at positions C3 and C4 (International 10–20 EEG electrode system) Potentials will be recorded from paired sub dermal needle electrodes placed in the orbicularis oris and oculi . intraoperative monitoring for all patient will be performed by a same operator .

TCMEP recording will begin (1) prior to skin incision as baseline amplitude before muscle relaxant be taken for intubation (2) at Dural closure and end \start amplitude ratio will be calculated.

After the end of surgery, anaesthetic drugs will be stopped The extubation criteria are as follows: TOF ratio > 0.9, BIS > 70, regular respiratory pattern, tidal volume of at least 5 ml/kg and SpO2 > 95% when the patient breathes spontaneously.

The patient will be sent to the PACU while the neurosurgeons will assess appearance of neurological dysfunction.

Measurement tools

1- Duration of the surgery from skin incision till skin closure will be recorded. And duration of anaesthesia from intubation till closure of anaesthetic agent.

2- TOFr and BIS will be monitored continuously every 5 min and will be recorded at baseline, at intubation, at skin incision, 30 and 60 minutes after skin incision, every 30min and 1 hr after extubation.

3- Intraoperative mean blood pressure and heart rate will be monitored every 5 min and will recorded in all groups immediately after induction, at surgical incision and every 30 minutes till the end of procedure.

4- Total amount of intraoperative propofol, fentanyl, ephedrine and norepinephrine consumption will be recorded

5- Number of hypotensive episodes, and required doses of ephedrine and vasopressors (norepinephrine in starting dose of 0.3 up to 2 mcg/kg/min)

6- The eye-opening time (defined as the period from the cessation of propofol-fentanyl administration to when the patient opened his/her eyes on command)

7- Facial nerve function will be evaluated pre-operatively, immediately postoperatively.

8- Ratio of end operative to start-operative FMEP amplitude will be monitored .

Possible Risk (mention if there is any risk or not):

No possible risk.

Primary outcomes (Most important outcomes to be assessed)

1- End to start facial nerve MEP amplitude ratio.

Secondary outcome parameters (other outcomes to be assessed)

1- Recovery profile ((time to eye opening, extubation, orientation, obeying commands, and an Aldrete score >9)) , [Time Frame: every 10 min for 1 hour at PACU.]
2- Total volume of propofol infused
3- BP , number of hypotension episodes and use of vasopressors

Sample size (number of participants included)

We calculated our sample size using G-power software Our primary outcome is end to start facial nerve MEP ratio was derived from a previous study to be mean 0.72 ± 0.43 calculated by using previous results (12) with SPSS program . We assumed that ratio will decrease 50%. Considering a study power of 80% and a p-value of 0.05 to be significant, the sample size was calculated to be 38 patients (19 in each group). To compensate for drop-out we will recruit 20 patients in each group.

Statistical analysis:

Data will be coded and entered using the statistical package SPSS version 24. Data will be summarized using mean and standard deviation for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups will be done using unpaired t test when comparing 2 groups and analysis of variance (ANOVA) with multiple comparisons post hoc test when comparing more than 2 groups (13). For comparing categorical data, Chi square (χ 2) test will be performed. Exact test will be used instead when the expected frequency is less than 5 (14). Correlations between quantitative variables will be done using Pearson correlation coefficient (15). P-values less than 0.05 will be considered as statistically significant.

Source of funding (is there any source of funds or not)
No source of fund.

9. Time plan (when to start/ when expected to finish/ when to publish)

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