



**COMPARISON OF BIOCHEMICAL CHANGES AND MYALGIA FOLLOWING ADMINISTRATION OF SUCCINYLCHOLINE WITH OR WITHOUT PRETREATMENT WITH ROCURONIUM IN PATIENTS UNDERGOING TYMPANOPLASTY**

### Anesthesiology

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### ABSTRACT

**Objective:** To study the biochemical changes and myalgia following the administration of succinylcholine (Sch) with or without pretreatment with rocuronium in patients undergoing tympanoplasty.

**Method:** The present prospective, double-blind, randomised clinical study was conducted after receiving clearance from the institutional ethical committee. Using a closed envelope technique, 80 American Society of Anaesthesiologists (ASA) grade I/II patients aged 20–40 years scheduled for tympanoplasty under general anaesthesia were randomly divided into two groups, Group R and Group C, with 40 patients in each group. Group R patients were administered Sch with rocuronium pretreatment, whereas Group C patients were administered Sch without rocuronium pretreatment. Venous samples were drawn for serum creatinine phosphokinase levels and serum potassium levels preoperatively, intraoperatively, and 24 h postoperatively between the two groups using the unpaired t-test. Sch-induced fasciculation and postoperative myalgia are known to be a well-recognised side effects of its administration.

**Results:** The mean creatinine kinase (IU/L) level 24 h postoperatively was significantly more among subjects in Group C than among those in Group R ( $P = 0.001$ ). The mean potassium level 24 h postoperatively was significantly more among subjects in Group C ( $5.03 \pm 0.90$ ) than among those in Group R ( $4.79 \pm 1.05$ ), ( $P = 0.045$ ).

**Conclusion:** Pretreatment with the nondepolarising muscle relaxant, rocuronium, prior to the administration of Sch significantly reduced the side effects of Sch.

### KEYWORDS

Myalgia, pretreatment, rocuronium, serum creatinine kinase, serum potassium level, succinylcholine

#### 1. INTRODUCTION

Succinylcholine (Sch) provides a prolonged ideal condition for both, regular and rapid sequence intubations. However, it produces undesirable side effects such as muscle fasciculation, postoperative myalgia, and increased serum levels of creatinine phosphokinase (CPK) and potassium (K<sup>+</sup>). Although these are minor side effects, they may be extremely distressing to the patient.<sup>1</sup>

Serum CPK measurement is the best overall marker for the detection and monitoring of skeletal muscle disease and damage.<sup>1</sup> Sch-induced fasciculation and postoperative myalgia are well-recognised side effects with a reported incidence of 95% and 50%, respectively.<sup>2</sup>

Attempts were made to decrease the incidence of muscular damage and biochemical changes using several drugs. One of the most useful methods is the administration of a small dose of a nondepolarising neuromuscular blocking drug before the administration of Sch.<sup>3</sup> True and Carter<sup>4</sup> compared various nondepolarising neuromuscular blocking drugs in the prevention and reduction of Sch-induced muscle fasciculation and found rocuronium to be a valid alternative. Rocuronium provides a more rapid onset of action, compared with other nondepolarising agents, and good intubating conditions within 60–90 s of administration.

#### 2. MATERIALS AND METHODS

The present prospective, double-blind, randomised clinical study was conducted after receiving clearance from the institutional ethical committee. The sample size was calculated using G\*Power, in which the mean prevalence was 50% and the incidence was reduced to 18% according to an article by Martin et al.<sup>5</sup> The sample size was calculated with 80% power and 5% significance level and was determined to be 80. Using the closed envelope technique, 80 American Society of Anaesthesiologists (ASA) grade I/II patients aged 20–40 years scheduled for tympanoplasty under general anaesthesia were randomly divided into two groups of 40 each. This surgical procedure was selected owing to the minimal risk of surgery-induced increase in CPK and K<sup>+</sup> levels because of minimal muscle handling. Thus, the rise in these levels was mainly due to Sch-induced fasciculation and

myalgia and not due to the surgery. The patients were divided into two groups:

Group R (rocuronium): Sch with rocuronium pretreatment  
Group C (control): Sch without rocuronium pretreatment

#### The exclusion criteria were as follows:

ASA grade III and IV, refusal for consent, coagulopathy or anticoagulation therapy, surgeries longer than 3 h in duration, surgeries involving extensive skeletal muscle handling, contraindications to the study drug, avoidance of any intramuscular injections during the perioperative period up to 24 h, myopathies, myasthenia gravis, hepatorenal dysfunction, pregnancy, burns, hyperkalaemia, malignant hyperthermia, suspected ocular injury, elevated intracranial pressure, intragastric pressure, and extensive muscle injuries such as crush injury.

Following a preanaesthetic checkup, an informed written consent was obtained from the study patients. Each patient was randomly assigned to one of the two groups, Group R or Group C. In the preoperative room, an intravenous (IV) line was secured to the patient and maintained with non-potassium containing IV fluids such as normal saline (0.9% sodium chloride). Preinduction (baseline) blood samples were taken. All patients were premedicated through the administration of glycopyrrolate (0.2 mg, IV) and midazolam (0.5–1 mg, IV) prior to the induction of anaesthesia. The heart rate, pulse oximetry, electrocardiograph (ECG), end-tidal carbon dioxide (ETCO<sub>2</sub>), noninvasive blood pressure (NIBP), and respiratory rate were monitored for all patients.

In the operation theatre, Group R patients were administered rocuronium (0.04 mg/kg, IV) for 30 s before induction as pretreatment, whereas Group C patients were administered same volume of normal saline as that of rocuronium. Following preoxygenation, anaesthesia was induced with 1% propofol (2.5 mg/kg, IV), followed by Sch (1.5 mg/kg). Oxygen was administered through a face mask during the introduction of Sch. After 60 s of administering Sch, laryngoscopy and intubation were performed using an appropriate-sized, disposable,

high-volume, low-pressure cuffed endotracheal tube. Anaesthesia was maintained with 66% nitrous oxide, 33% oxygen, 1%–2.5% isoflurane, a nondepolarising muscle relaxant using 0.06–0.12 mg/kg rocuronium. Patient oxygen saturation (SpO<sub>2</sub>) was maintained at 99%–100%, and ventilation adequacy was monitored clinically with ETCO<sub>2</sub>. At the end of the surgery, neuromuscular blockade was reversed with neostigmine (0.05 mg/kg, IV) and glycopyrrolate (0.008–0.01 mg/kg, IV). Drug adverse effects and anaesthesia-related problems were observed.

**2.1 Parameters assessed**

The heart rate, respiratory rate, NIBP, SpO<sub>2</sub>, ECG, and any adverse event were monitored in the preoperative room, every 5 min intraoperatively, and every 6 h postoperatively up to 24 h.

After 24 h, the patients were assessed for postoperative myalgia according to the the four-point scale, followed by postoperative blood sample collection.

**Grading system for postoperative myalgia (White)<sup>6</sup>**

1. **Nil:** No muscle pain or stiffness
2. **Mild:** Muscle pain or stiffness at one site but not causing disability or limiting activities
3. **Moderate:** Muscle pain or stiffness at more than one site but not causing disability or limiting activities
4. **Severe:** Muscle pain or stiffness at one or more sites and causing disability or limiting activities. For example, difficulty in getting out of bed or turning the head.

CPK and K<sup>+</sup> levels were obtained preoperatively, 5 minutes after intubation intraoperatively, and 24 h postoperatively in both the groups. The sites of the 24 h postoperative myalgia, namely shoulder, thorax, neck, back, calf, and thigh, were noted in both the groups.

**2.2 Statistical analysis**

The data were entered into Microsoft Excel, and the statistical analysis was performed using Statistical Package for the Social Sciences version 21.0 The student t test was used for comparing the mean values, whereas the chi-square test was applied for comparing the frequency between the two groups. The P value was considered significant when it was less than 0.05.

**3. RESULTS**

Patients in both the groups were comparable with respect to their demographic characteristics and the site and duration of surgery.

The mean CPK (IU/L) and K<sup>+</sup> levels were compared preoperatively, intraoperatively, and 24 h postoperatively between the two groups by using the unpaired t test. The mean CPK (IU/L) level 24 h postoperatively was significantly more among subjects in Group C compared with those in Group R (P = 0.001). The mean K<sup>+</sup> level 24 h postoperatively was significantly more among subjects in Group C (5.03 ± 0.90) compared with those in Group R (4.79 ± 1.05) (P = 0.045).

**Table 1: Comparison of the mean creatinine kinase (IU/L) levels preoperatively, intraoperatively, and 24 h postoperatively between subjects in Groups R and C**

Creatinine kinase (IU/L) level	Group R (with Rocuronium)		Group C (Without Rocuronium)		Mean Difference	t-test value	p-value
	Mean	SD	Mean	SD			
Pre-operatively	132.68	58.49	132.48	58.77	0.21	0.016	0.988
Intra-operatively	100.55	35.49	118.96	54.51	-18.41	-1.790	0.077
Post-operatively (24 hours)	210.65	59.30	304.39	127.09	-93.73	-4.227	0.001*

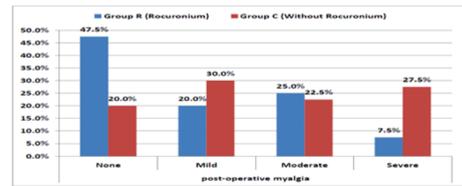
Unpaired t-test

\* Significant difference

**Table 2: Comparison of mean potassium levels preoperatively, intraoperatively, and 24 h postoperatively between subjects in Groups R and C**

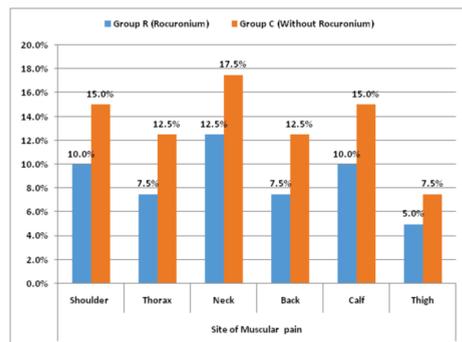
Potassium level	Group R (with rocuronium)		Group C (without rocuronium)		Mean Difference	t test value	P value
	Mean	SD	Mean	SD			
Preoperatively	4.42	1.08	4.53	0.90	-0.11	-0.482	0.631
Intraoperatively	5.43	1.05	5.53	0.90	-0.10	-0.444	0.659
Postoperatively (24 h)	4.79	1.05	5.03	0.90	-0.23	-2.015	0.045*

The distribution of postoperative myalgia was compared between the two groups by using the chi-square test. Severe postoperative myalgia was significantly more among subjects in Group C than among those in Group R (P = 0.019).



**Table 3: Comparison of the grading for postoperative myalgia between subjects in Groups R and C**

The sites of muscular pain differed significantly between the subjects of the two groups, but all sites were affected significantly more among subjects in Group C than among those in Group R.



**Table 4: Comparison of distribution of site of muscular pain between subjects in Groups R and C**

**4. DISCUSSION**

Sch causes depolarisation of the skeletal muscles resulting in the muscular damage of varying severity. Sch-induced fasciculations are involuntary skeletal muscle contractions occurring few seconds after drug administration, which are responsible for the efflux of the muscle enzyme CPK.<sup>7</sup> Abraham et al.<sup>8</sup> found a significant rise in CPK levels 24 h postoperatively in patients not receiving rocuronium as pretreatment.

The sustained depolarisation of acetylcholine receptors by Sch leads to hyperkalaemia in normal individuals. The rise in K<sup>+</sup> is observed more in patients experiencing myalgia.<sup>9,10</sup> Precurarisation with a nondepolarising muscle relaxant before the administration of Sch significantly reduced the incidence and severity of hyperkalaemia in their patients.<sup>8,11-14</sup>

The incidence of myalgia in the first 24 h after operation ranged from 41% to 92%.<sup>15</sup> The mechanism for the postoperative myalgia has not been completely elucidated yet. Proposed mechanisms include increased intracellular calcium concentrations, membrane phospholipid degradation, and release of free fatty acids and free radicals, which lead to increased membrane permeability.<sup>16-18</sup> The pain may occur due to muscle damage produced by shearing forces associated with the fasciculations at the onset of the phase one block.<sup>19</sup> The role of pretreatment with nondepolarising agents in postoperative myalgia prevention remains controversial. However, pretreatment is generally reported to reduce the incidence of myalgia by 30%.<sup>20</sup> The results of our study are similar to those of a study by Hernández-Palazón et al.,<sup>21</sup> in which the incidence of fasciculations was significantly lower (P < 0.001) and their severity was significantly less (P < 0.001) in patients who received rocuronium before the administration of Sch. Abraham et al.<sup>8</sup> reported that fasciculations in Group R were significantly less (P < 0.01) compared with those in Group V. Mencke et al.<sup>22</sup> stated that postoperative myalgia was more in the Sch without rocuronium group (39%) than in the Sch with rocuronium group (29%) (P = 0.25). Recent studies have revealed that pretreatment with a small dose of rocuronium is almost the gold standard in the prevention of Sch-induced muscular adverse effects.<sup>1</sup>

The shoulder, thorax, neck, back, calf, and thigh were the sites of muscular pain reported in the present study. All the sites were affected significantly more among subjects in Group R than among those in Group C (Table 4).

#### 4.1 Limitations of our study

1. The study was limited to only ASA I and II patients involving a single nondepolarising drug only for 24 h.
2. The study was also limited to a single surgery (tympanoplasty) involving extremely limited skeletal muscle with a short duration of surgery.
3. To make it more effective and reliable, the study needs to be conducted as a multicentre trial.

#### 5. CONCLUSION

The present study concluded that pretreatment with the nondepolarising muscle relaxant, rocuronium, prior to the administration of Sch significantly reduces Sch-induced fasciculations, which in turn are responsible for postoperative myalgia and rise in serum CPK and K<sup>+</sup> levels. Therefore, rocuronium pretreatment is recommended before Sch administration for an improved outcome.

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