COMPARATIVE STUDY OF SUCCINYLCHOLINE AND PRECURARIZATION WITH ROCURONIUM ON MUSCULAR EFFECTS IN PATIENTS UNDERGOING SURGERY UNDER GENERAL ANAESTHESIA

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ABSTRACT:
Succinylcholine remains the drug of choice in conditions where rapid paralysis and airway control are priorities. However it is associated with muscular side effects that have an overall incidence ranging from five to 83 percent. The administration of small doses of nondepolarizing muscle relaxants before the administration of succinylcholine has been shown to decrease the incidence and severity of muscular side effects experienced by the patients. This study was aimed at evaluating the efficacy of technique in reducing the muscular side effects of succinylcholine. Sixty healthy adults were enrolled in the study who were scheduled for minor muscle cutting surgeries under general anaesthesia. They were assigned at random to two groups of thirty patients each. They randomly received succinylcholine for intubation and a precurarization dose of rocuronium followed by succinylcholine for intubation. Intraoperative fasciculations and postoperative myalgia were graded and scored. There was a significantly increased incidence of fasciculations and myalgia in the succinylcholine group. In the precurarization group the incidence and severity of fasciculations and myalgia was significantly less as compared to the group which received succinylcholine alone. We found significant correlation between fasciculations and myalgia in the succinylcholine group. Present study concluded that precurarization with rocuronium was effective in reducing the succinylcholine-induced fasciculations and myalgia.

Keywords: Succinylcholine, Rocuronium, Fasciculations, Myalgia, Precurarization.

INTRODUCTION
Patients undergoing general anaesthesia usually need endotracheal intubation. Although many relaxing agents can be used for this purpose; Succinylcholine is still the most popularly used agent in our setup. Despite the recent introduction of short-acting, nondepolarizing neuromuscular blockers, succinylcholine with its rapid onset of action, short duration of effect, complete and predictable paralysis remains the best drug in providing ideal intubating condition for tracheal intubation (Kato et al., 2007). Succinylcholine is a depolarizing muscle relaxant, produces profound neuromuscular block with rapid onset but short duration. When used in a dose of 0.5 to 1.5 mg/kg, it produces excellent muscle relaxation in 30 seconds and its effects last for 3 to 5 minutes (Donati and Bevan, 2009). Its short half-life becomes life saving in the event of difficult intubation or failed intubation and rapid sequence induction in patients with full stomach. However the usefulness of succinylcholine is limited by few side effects such as muscle fasciculations; postoperative myalgia, increased serum levels of creatinine kinase and potassium, succinyl apnea, malignant hyperthermia, raised intraocular pressure, increased intraocular pressure, atrial fibrillation, and bradycardia. 

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pressure and intracranial pressure. The fasciculations are a benign side effect of the drug, but many anaesthetists prefer to prevent fasciculations. In this respect, a small dose of a nondepolarizing agent, given three to five minutes before succinylcholine is effective (Schreiber et al., 2005). When the drug was available, \(d\)-tubocurarine 0.05 mg/kg was used for this purpose. Rocuronium is an acceptable alternative, as long as appropriate doses 0.09 to 0.1 mg/kg, or 10 percent of the Effective Dose causing on average 95 percent suppression of neuromuscular response (ED_{95}) are given (Donati, 2006). Other drugs such as diazepam, lidocaine, fentanyl, calcium, vitamin C, magnesium and dantrolene have also been used to prevent fasciculations. The results are no better than with nondepolarizing relaxants and they may have undesirable effects of their own.

The postoperative myalgia are generalized aches and pains that commonly occur 24 to 48 hours after succinylcholine administration that mimic the muscular pains which usually follow violent exercise. It has been postulated that the muscle pain is secondary to the damage produced in the skeletal muscle by the unsynchronized contraction of adjacent muscle fibers just before paralysis occurs. Their incidence is variable (20 to 80 percent of patients receiving succinylcholine) and are more common in young, ambulatory patients (Mencke et al., 2002). The exact mechanism is not known but stimulation of presynaptic acetylcholine receptors and contraction of intrafusal fibers of muscle spindles may contribute. It has been suggested that the underlying mechanism of muscle damage associated with administration of succinylcholine may involve calcium-induced phospholipids degradation with release of damaging products of fatty acid metabolism (Mcloughin et al., 1988). The intensity of muscle pains is not always correlated with the intensity of fasciculations, but the methods that prevent fasciculations usually prevent muscle pains. For example, a precurarization dose of a nondepolarizing neuromuscular blocking agent is effective in preventing it (Subramaniam et al., 2002).

Rocuronium is a monoquaternary steroidal analogue of vecuronium. It has rapid to intermediate onset and intermediate duration of action (Bhatti and Parmer, 2009). It requires 0.45 to 0.9 mg/kg intravenously for intubation and 0.15 mg/kg boluses for maintenance. Rocuronium (0.1 mg/kg) has proved to be rapid (90 seconds) and a more effective agent (decreased fasciculations and postoperative myalgias) for precurarization prior to succinylcholine administration. Various factors influence the efficacy of pretreatment including the choice of nondepolarizing agents, degree of prejunctional receptor block, interval between administration of pretreatment agent and succinylcholine and the speed of onset of the nondepolarizing drug. Schrieber et al did a meta analysis of randomized trial on prevention of succinylcholine-induced fasciculations and myalgia and found that the best prevention of myalgia was with non-steroidal anti-inflammatory drugs and with rocuronium. This study was undertaken with the aim of comparing the efficacy of rocuronium and vecuronium for intubation, succinylcholine induced myalgia and the levels of creatine phosphokinase and urine myoglobin after the pretreatment with rocuronium. Our purpose of study was to assess the effects of rocuronium pretreatment on succinylcholine-induced fasciculations and postoperative myalgia.

**MATERIAL AND METHODS**

This study was conducted in the operation theatre of Combined Military Hospital, Rawalpindi from January 2010 to August 2010 after approval of the study project by research and ethics committee. Written informed consent was observed from all subjects. It was a prospective, single blind and randomized study including 60 patients who were allocated randomly to one of the two groups. Patients in group "A" received succinylcholine and group "B" received precurarization dose of
rocuronium followed by succinylcholine. There were 30 patients in each group. The two groups were comparable in respect to age, sex and weight. Patients of both sex aged from 18 to 65 years of ASA grade I and II, undergoing elective minor muscle cutting surgeries were included in this study. Patients with no proper medical history, intraocular hypertension, history of malignant hyperthermia, ASA status III and above, Diabetes mellitus, suspected difficult intubation patients and major muscle cutting surgeries were excluded from this study. Preoperative evaluation included detailed history, general physical, systemic and upper airway examination. Investigations including blood complete picture, urine routine examination, liver function tests, Hepatitis B surface Antigen, Anti Hepatitis C Virus, renal function tests and electrocardiogram (ECG). These were carried out to exclude liver disease, hepatitis B & C, renal disease and heart disease in study subjects. These all findings were recorded on a pre-clinical and clinical proforma. Routine monitoring was done after receiving the patient in theater. Standard anaesthesia technique was employed in all patients. Intravenous line was secured with 18g cannula. Patients were randomized and grouped in group "A" and group "B". Group "A" received succinylcholine 1 mg/kg body weight (Naguib et al., 2006). Group "B" received 0.1 mg/kg rocuronium followed by succinylcholine 1.5 mg/kg body weight for intubation (Donati and Bevan, 2009). These drugs were given by an investigator who was not included in rest of the study. Direct laryngoscopy was performed and the patients were intubated via oral route, 60 seconds after giving drugs for intubation. Following the administration of drugs of intubation, patients were observed for the presence and severity of fasciculations by the investigator and recorded on proforma. These fasciculations were graded and scored as a system described in table 1 (Yun et al., 2010). Anaesthesia was maintained with the maintenance doses of the volatile anaesthetic agent isoflurane and 60 percent nitrous oxide in oxygen. All the patients were visited 24 hours postoperatively in the respective wards and were asked about the presence and severity of myalgia in a non-leading manner by the investigator (Sen et al., 2003). A questionnaire was given to each and every patient to grade myalgia (Mikat-Steven et al., 2000) using a system described in table 2 (Harvey et al., 1998; Korula et al., 2010) and data was recorded on proforma. The data was entered in SPSS version 16.0 for analysis. Frequency along with percentage was used to describe qualitative variables like gender,

### Table 1

Grading and scoring system for fasciculations

<table>
<thead>
<tr>
<th>Nil</th>
<th>No visible fasciculations</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Very fine fingertip or facial muscle movements</td>
<td>1</td>
</tr>
<tr>
<td>Moderate</td>
<td>Minimal fasciculations on trunk and extremities</td>
<td>2</td>
</tr>
<tr>
<td>Severe</td>
<td>Vigorous fasciculations on trunk and extremities</td>
<td>3</td>
</tr>
</tbody>
</table>

(Yun et al., 2010)

### Table 2

Grading and scoring system for postoperative myalgia

<table>
<thead>
<tr>
<th>Nil</th>
<th>No muscle pain or stiffness</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Muscle pain or stiffness at one site but not causing disability or limiting activities</td>
<td>1</td>
</tr>
<tr>
<td>Moderate</td>
<td>Muscle pain or stiffness noticed spontaneously by the patient, possibly requiring analgesic therapy</td>
<td>2</td>
</tr>
<tr>
<td>Severe</td>
<td>Generalized, severe or incapacitating discomfort</td>
<td>3</td>
</tr>
</tbody>
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(Harvey et al., 1998; Korula et al., 2010)
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myalgia and fasciculations. Chi-square test was used to compare qualitative variables between the groups (Abbas et al., 2009). p value < 0.05 was considered as significant.

RESULTS

There was no significant difference in patient characteristics in the two groups and they were well matched for age, weight and sex. Each group had 30 patients (Group A: 17 males and 13 females and Group B: 16 males and 14 females). The mean age of Group A patients was 39.97 ± 1.833 years (range 18-65 years) and of Group B was 36.63± 1.791 (range 18- 65 years).

All patients in group "A" had moderate to severe (100%) fasciculations, compared to group B where only mild fasciculations were observed in 7 patients. On a four point scoring scale fasciculations in group A were 78 and in group B it was 7. In group "A" five patients suffered from mild, 22 from moderate and three from severe pain. In group B, 18 patients developed mild pain, at 24 hours after surgery. On a four point scoring scale myalgia in group A were 58 and in group B it was 22. The statistical analysis showed the frequency of fasciculations with rocuronium pretreatment (23.2%) to be significantly less than with no pretreatment (100%, p< 0.001). We observed a statistically significant reduction in frequency as well as intensity of fasciculations among group A and group B. The statistical analysis showed the frequency of postoperative myalgias with rocuronium pretreatment (63.3%) to be significantly less than with no pretreatment (100%, p<0.001) at 24 hours after surgery. We observed a statistically significant reduction in frequency as well as intensity of myalgia among group A and group B.

DISCUSSION

Succinylcholine is a popular drug due to the fact that it rapidly provides the ideal conditions for short procedures requiring endotracheal intubation (Abbas et al., 2009). Nevertheless, it is associated with muscular injury as it depolarizes the muscles prior to paralysis (Fukani and Ganzberg, 2004). This muscular injury is manifested in the form of fasciculations and postoperative myalgia. These muscular unwanted effects of succinylcholine have limited its usefulness and present distressing consequences for the patients after minor surgeries (Spence et al., 2002).

In our study, the frequency of fasciculations was 100 percent and 23 percent in the group A and B respectively. In group A, the intensity of fasciculations ranged from moderate to severe and scored 78 on a four point scoring scale (Yun et al., 2010). The same intensity of fasciculations with succinylcholine were observed in a group of 30 patients which received two milliliters of normal saline as pretreatment prior to succinylcholine (Abbas et al., 2009). These fasciculations are thought to be related to agonistic action of succinylcholine on prejunctional nicotinic receptors that results in rapid firing (Hartman et al., 1986). The incidence of succinylcholine-induced fasciculations in the general population varies between 78% and 95% (Schrieber et al., 2005). This wide range in the frequency may be associated with the different induction agents used before succinylcholine or perhaps due to inter-observer variations (Sen et al., 2003). However in group C where pretreatment with rocuronium was carried out, only mild fasciculations were observed and the score was 7. The significantly lower incidence of fasciculations in this group was pertaining to the fact that nondepolarizing muscle relaxant-rocuronium effectively prevented fasciculations, presumably by blocking presynaptic nicotinic receptors. Erkola showed that the ability of d-tubocurarine to induce a strong train of four fade, an indicator of prejunctional effects is correlated with its ability to prevent fasciculations (Erkola, 1988). In our study statistical analysis showed that fasciculations in Group B were significantly less when compared to Group A (23.3% vs 100%), depicting rocuronium to be
a potent defasciculant. The same benefit has been mentioned by Motamed et al in their study who concluded that the incidence and severity of succinylcholine-induced fasciculations can be reduced by giving rocuronium in a dose of 0.05 mg/kg 1.5 to three minutes before succinylcholine (Motamed et al., 1997). A study done in 2002 also proved the efficacy of a nondepolarizing neuromuscular blocking agent, cisatracurium in preventing succinylcholine-induced fasciculations (Mencke et al., 2002). Pretreatment with rocuronium and d-tubocurarine was found effective for prevention of succinylcholine-induced fasciculations (Steinberg, 2008). Both rocuronium and d-tubocurarine were found superior to cisatracurium in preventing succinylcholine-induced fasciculations (Joshi et al., 1999).

The reason for assessing the efficacy of rocuronium in the prevention of fasciculations caused by succinylcholine was because of the quicker onset of action of rocuronium, due to which it provides effective precurarization within a very short time interval (Motamed et al., 1997). Rocuronium was used in a dose of 0.1 mg/kg for this purpose. Smaller doses have been used by other researchers. Martin et al performed a study in 1998 using rocuronium 0.06 mg/kg 3 min before induction for prevention of fasciculations and postoperative myalgias. They found rocuronium to be the best among all that were compared in preventing succinylcholine-induced fasciculations (Martin et al., 1998). Motamed et al used rocuronium in the dose of 0.05 mg/kg 1.5 or 3 min before succinylcholine in their study (Motamed et al., 1997). The administration of this pretreatment agent has been recommended both on a weight related (Abbas et al., 2009) and fixed dose regimen basis (Donati, 2003). We selected the weight related dose of this nondepolarizing neuromuscular blocking agent for ease of routine administration. One of the main concerns related to this technique on the intubating conditions is that a larger dose of succinylcholine has to be given, as pretreatment with nondepolarizing neuromuscular blocking agents slows the onset time whereas decreases the duration of succinylcholine blockade (Mikat-Stevens et al., 2000). The dose of succinylcholine was increased to 1.5 mg/kg because of the possible antagonism between depolarizing and nondepolarizing drugs (Szalados et al., 1990) and we found that pretreatment had no effect on intubation conditions. It has also been mentioned earlier that pretreatment had no effect on the intubating conditions (Findlay and Spittal, 1996; Abbas et al., 2009).

There has been a great deal of argument about the interval between the administration of the nondepolarizing muscle relaxant pretreatment and the administration of succinylcholine for the intubation of trachea. Intervals of two, three and four minutes or even greater have been recommended (Horrow and Lambert, 1984). However, the data suggest that a three to five minute time interval can be safely applied for precurarization with nondepolarizing muscle relaxant to prevent succinylcholine-induced fasciculations and myalgia (Pinchak et al., 1994). These intervals are applied in view of the fact that shorter intervals do not inhibit fasciculations and longer intervals do not afford any additional advantages (Motamed et al., 1997). In our study, we gave the precurarization dose of rocuronium, five minutes before the administration of succinylcholine. This is supported by Tsui et al, who evaluated a rapid and time saving precurarization technique by using the rocuronium close to induction (Tsui et al., 1998).

In our study the frequency of myalgia in group A was 100 percent ranging from mild to severe. On a four point scoring scale the myalgia in this group scored 58. This high frequency and intensity of myalgia with succinylcholine has also been observed in some other studies too (Findlay and Spittal, 1996). The incidence of myalgia with succinylcholine varies from 20 percent to 80 percent (Abrahim et al., 2008). The most frequently quoted figure is 50 percent. This is
often listed as minor side effect of the drug but it may be one of the most distressing consequences of minor surgery for the patients. It occurs more commonly in females and resembles the aches experienced after unaccustomed exercise. The duration of this discomfort is highly variable. It generally lasts for two to three days but occasionally persists for even a week (Ali, 1989). This is certainly a reflection of various factors which influence the occurrence of pain (Findlay and Spittal, 1996). Amongst a variety of reasons proposed, postoperative myalgia has be related to irreversible changes on muscle spindles or unsynchronized contractions of muscle fibers resulting in shearing of connective tissues, electrolyte imbalance and release of prostaglandins (Hun cho et al., 1999). To assess the specific contribution of succinylcholine on postoperative myalgia in patients, we standardized the perioperative management, and the type of surgery was uniform. Thus anaesthesia and surgery related factors contributing to postoperative myalgia were controlled.

Although pretreatment with non-depolarizing muscle relaxants seems to be effective in decreasing muscle fasciculation, its effectiveness in reducing postoperative myalgia is controversial. Various attempts have been made to prevent the muscle pain caused after the administration of succinylcholine. One of the most useful is the administration of a small dose of nondepolarising neuromuscular blocking drug before administration of succinylcholine. However different studies came up with different outcomes. Generally this pretreatment is reported to reduce the incidence of postoperative myalgia caused by the administration of succinylcholine by 30 percent (Pace, 1990). A meta analysis concluded that pretreatment with nondepolarizing muscle relaxant, benzodiazepine or local anaesthetic decreased their incidence by about 30 percent (Schreiber et al., 2005). Thompson-Bell in 1996 found 0.03 mg/kg pretreatment dose of rocuronium effective in decreasing incidence and severity of postoperative myalgia. In that investigation, rocuronium, 0.03 mg/kg was compared with d-tubocurarine, 0.05 mg/kg, as a pretreatment two minutes before succinylcholine administration. Rocuronium’s faster onset than d-tubocurarine may have contributed to the findings of significantly less postoperative myalgia (Thompson-Bell et al., 1996). In another study, Findlay and Spittal found that rocuronium because of its rapid onset of action, was very efficient in reducing the postoperative myalgia when a short interval was allowed before administering succinylcholine for endotracheal intubation. They found that rocuronium pretreatment decreased the frequency of myalgias to 20% on first post operative day and to 28.6% by day 4 (Findlay and Spittal, 1996). In another study, the frequency of postsuccinylcholine myalgia in patients induced by propofol and succinylcholine and pretreated with 0.025 mg/kg atracurium was studied. The results showed that the frequency of myalgia were 24 percent without pretreatment and 1 percent in the patients who were pretreated with atracurium. It was thus concluded that atracurium reduces the incidence of myalgia. This study very considerably established the efficacy of non-depolarizing agents in this regard (Khan and Kamal, 1997). In a further study, Martin et al in 1998 compared the efficacy of d-tubocurarine, atracurium, mivacurium and rocuronium. They concluded that rocuronium in a dose of 0.06 mg/kg given three minutes before induction was the most effective agent to prevent fasciculations and postoperative myalgia caused by succinylcholine (Martin et al., 1998). However some of the studies could not establish the efficacy of pretreatment in decreasing the postoperative myalgia, as was observed in a study by Harvey et al in 1998, concluding rocuronium to be no better than normal saline in decreasing the incidence of postoperative myalgia (Harvey et al., 1998). Raman and San found out an overall incidence of myalgia with lidocaine pretreatment to be 22 percent and with atracurium to be 30 percent (Raman and Sen, 1997). Mencke in their study found rocuronium failing in decreasing the incidence
or severity of postoperative myalgia. This study was designed to compare myalgia after succinylcholine with and without pretreatment (Mencke et al., 2002). Spence concluded that lidocaine was significantly better than rocuronium at decreasing the severity of postoperative myalgia at 48 hours indicating that lidocaine provided better attenuation of postoperative myalgia (Spence, 2002).

Our results were in the support of most of the studies which were proving the efficacy of pretreatment with nondepolarizing agents in preventing postoperative myalgia. In group B, 63.3 percent patients had myalgia, the severity ranging from mild to moderate and scoring to 22, signifying that the frequency and intensity of myalgias had diminished in this group as compared to the group which received succinylcholine alone. We observed a statistically significant reduction in frequency as well as intensity of myalgia among group A and group B.

In conclusion, it is suggested that sincere efforts are required to find the efficacy of a technique which could significantly reduce the undesirable side effects of succinylcholine in order to curtail the valuable hospital cost being spent on the health of the patients in our poor country. This study has statistically proven the effectiveness of precurarization with rocuronium in reducing the fasciculations and postoperative myalgia. Thus decreasing the postoperative analgesic requirement associated with it, and most importantly the distress of the patients. This shall encourage the early ambulation of patients after minor surgeries, significantly reducing the time during busy operating lists. The resulting early mobility decreases the chances of deep vein thrombosis and also promises earlier restoration of gastrointestinal functions. This study was targeted at decreasing these side effects of succinylcholine by giving only one fifth of the dose of rocuronium. Rocuronium available in the market is very expensive as compared to succinylcholine. For using it as a pretreatment drug, patients will have to pay more. It would therefore be unfair to use the drug without documented evidence of the benefit of this technique. The implication of precurarization will decrease the side effects of succinylcholine effectively. The technique is cost effective as it cuts the cost of intubation on each patient to one fourth as compared to the newer nondepolarizing agents alone and reduced postoperative analgesic requirements resulting in decrease in burden on the hospitals.

REFERENCES


