

PREVENTION OF SUCCINYLCHOLINE INDUCED MUSCULAR EFFECTS BY PRETREATMENT WITH ROCURONIUM

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ABSTRACT:

We have studied in 60 patients undergoing minor muscle cutting surgeries under general anesthesia, the effectiveness and sequelae of pretreatment with rocuronium for reducing muscular side effects after succinylcholine as well as the muscular effects of rocuronium alone for intubation. Patients were randomly allocated to one of the two groups; group A received rocuronium for intubation and group B received succinylcholine for intubation 5 minutes after pretreatment with rocuronium. The group receiving rocuronium had significantly less muscular effects. At the same time the group receiving succinylcholine with rocuronium pretreatment, experienced a significant reduction in muscular side effects.

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

INTRODUCTION

Despite the recent introduction of short acting non depolarizing neuromuscular blockers, succinylcholine, with its rapid onset of action, short duration of effect, complete and predictable paralysis remains unsurpassed in providing ideal intubating conditions for tracheal intubation (Mirsad *et al.*, 2010). However since its introduction into clinical practice it has been recognized that fasciculations, myalgia, rise in biochemical markers including serum creatine kinase and potassium occurs frequently with its use (Wong and Chung, 2000). Non depolarizing agents circumvent most of these problems, but none has the same pharmacokinetic profile as succinylcholine. Rocuronium and the newer rapacurium come closer, but both have longer lasting effects than succinylcholine and so they too could not replace it. Several strategies have been advocated to decrease the incidence of these adverse effects, one of the most successful being the administration of small doses of nondepolarizing neuromuscular

blocking agents before administration of succinylcholine (Abbas *et al.*, 2009). Various factors influence the efficacy of pretreatment, including the choice of nondepolarizing agent, degree of prejunctional receptor block, interval between administration of pretreatment agent and succinylcholine and speed of onset of nondepolarizing agent (Erkola, 1990). Rocuronium, which has more rapid onset of action compared with the established nondepolarizing agents, provides good intubating conditions. As the optimum interval for pretreatment with pre-existing is approximately 3 minutes, this property of rocuronium may be relevant to its use in prophylaxis of muscular side effects after succinylcholine pretreatment on frequency of post operative muscular effects (Motamed *et al.*, 1997).

MATERIAL AND METHOD

After approval by the ethical Committee and completion of written informed consent, we studied 60 patients, aged 18-65 years, ASA

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I and II. All patients were undergoing minor muscle cutting surgeries under general anesthesia necessitating tracheal intubation. We excluded patients who were assessed as possibly posing difficulty with tracheal intubation. All patients were premedicated with pethidine 1 mg/kg I/V just prior to surgery. They were pre-oxygenated with 100 percent oxygen for 3-5 minutes. Patients were induced with thiopentone 5 mg/kg I/V. They were randomly divided into two groups A and B of 30 patients each. Group A received I/V injection rocuronium 0.5 mg/kg body weight for intubation. Group B received injection rocuronium 0.1 mg/kg body weight followed by succinylcholine in a dose of 1.5 mg/kg body weight I/V after 5 minutes 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 according to a system described in table 1 (Yun *et al.*, 2010). Anesthesia was maintained with the maintenance doses of the volatile anesthetic agent isoflurane and 60 percent nitrous oxide in oxygen (Santra and Das, 2009). At the end of the procedure, isoflurane was discontinued; neuromuscular blocking

agents were pharmacologically reversed with the standard reversal doses of neostigmine bromide 0.05 mg/kg in atropine sulphate 0.02 mg/kg (Sen *et al.*, 2003). The patients were given 100 percent oxygen till the consciousness was regained and the patients started following verbal commands. At that point endotracheal tubes were removed after gentle suction of secretions through the tube. The patients were fully recovered in the recovery room and thereafter were shifted to the respective wards (Lee *et al.*, 2010). 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 myalgia was scored as no muscle pain or stiffness, nil=0; muscle pain or stiffness at one site but not causing disability or limiting activities, mild=1; muscle pain or stiffness noticed spontaneously by the patient, possibly requiring analgesic therapy, moderate = 2; and generalized, severe or incapacitating discomfort, severe = 3. No I/M injection was

Table 1
Grading and scoring system for fasciculations

Nil	No visible fasciculations	0
Mild	Very fine fingertip or facial muscle movements	1
Moderate	Minimal fasciculations on trunk and extremities	2
Severe	Vigorous fasciculations on trunk and extremities	3

(Yun *et al.*, 2010)

Table 2
Grading and scoring system for postoperative myalgia

Nil	No muscle pain or stiffness	0
Mild	Muscle pain or stiffness at one site but not causing disability or limiting activities	1
Moderate	Muscle pain or stiffness noticed spontaneously by the patient, possibly requiring analgesic therapy	2
Severe	Generalized, severe or incapacitating discomfort	3

(Harvey *et al.*, 1998; Korula *et al.*, 2010)

administered during the perioperative period. Postoperative care was standardized for all patients. Pain related to surgical intervention was treated with ketorolac 30 mg I/V as required (Yun *et al.*, 2010).

Venous blood samples were obtained before induction of anesthesia at 0 hours for the measurement of serum K⁺ and CK. The second sample was drawn five minutes after the administration of the drug for intubation for the measurement of serum K⁺ (Yun *et al.*, 2010). The serum K⁺ was estimated using ion selective electrode method at AFIP. A two millilitres blood sample was drawn 24 hours postoperatively for estimation of serum CK (Ozlu *et al.*, 2002). The serum CK was estimated using ultraviolet (UV) – Kinetic method at AFIP. CK measurement in serum has remained the best overall marker for detection and monitoring of skeletal muscle diseases and damage (Simpson *et al.*, 2002). The estimation of serum K⁺ was done by ion selective electrode method at AFIP (Cammann *et al.*, 1991). Data was analyzed using SPSS version 16.

RESULTS AND DISCUSSION

There were no significant differences in patient's characteristics or operative details between the two groups. In group A, no fasciculations were observed in any patient. In

group B, mild fasciculations were observed in 7 (23.3 percent) patients while no fasciculations were observed in 23 (76.7 percent) patients. In group A fasciculations scored 0 however in group B it scored 7. The difference in fasciculations was highly significant ($p < 0.001$) between the two groups.

In group A, 18 (60 percent) patients had moderate myalgia while no myalgia was observed in 12 (40 percent) patients. In group B, 16 (53.3 percent) patients had mild myalgia; moderate myalgia was observed in 3 (10 percent) patients while no myalgia was observed in 11 (36.7 percent) patients. In group A, myalgia scored 18 however in group B it scored 22. The difference in myalgia was highly significant ($p = 0.001$) between the groups.

In group A there was slight increase in serum K⁺ level from the start of the study to five minutes after intubation however this increase was insignificant ($p = 0.717$). In group B average increase in serum K⁺ level from start of the study to five minutes was significant ($p = 0.001$) (Table 3). Average increase in serum CK level in group A was 23.93 ± 4.615 IU/L and in group B it was 22.30 ± 3.903 IU/L. The change in serum CK level was insignificant between group A and group B ($p = 0.999$) (Table 4).

Table 3
Initial and final levels of serum potassium (K⁺) in all the groups

	Group A (n= 30)	Group B (n= 30)
At 0 hours	4.02 ± 0.059 mmol/L	4.08 ± 0.072mmol/L
After 5 min	4.03 ± 0.054 ^{NS} mmol/L	4.32 ± 0.074*mmol/L

Table 4
Comparison of serum creatine kinase (CK) between group A and group B

	Group A (n= 30)	Group B (n= 30)
At 0 hours	84.80 ± 5.749 ^{NS} IU/L	78.40 ± 6.669 ^{NS} IU/L
After 24 hours	108.73 ± 7.149*IU/L	100.70 ± 6.383*IU/L
Difference of Mean ± S.E.M	+23.93 + 4.615	+22.30 + 3.903

NS=Not Significant, *= $p < 0.05$, S.E.M=Standard Error of Mean, += An increase in the average after 24 hours

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, myalgia and increased muscle enzymes like creatine kinase (CK) in the serum (Wong and Chung, 2000; Yun *et al.*, 2010). Moreover, the subsequent rise in serum potassium (K^+) as a result of its depolarizing mechanism of action, can clinically manifest as cardiac arrest in the susceptible individuals (Donati and Bevan, 2009). These muscular unwanted effects of succinylcholine have limited its usefulness and present distressing consequences for the patients after minor surgeries (Spence *et al.*, 2002). On the other hand the nondepolarizing muscle relaxant-rocuronium circumvent most of these adverse effects but the high cost and the universal non availability makes it less of a choice for intubation.

In group A of our study there was significantly lower incidence of fasciculations. It was expected in this group, pertaining to the pharmacodynamic properties of rocuronium. However in group B where succinylcholine was given for intubation with rocuronium as pretreatment, 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.

In our study the statistical analysis showed that fasciculations in group B were significantly less as compared to the previously observed high incidence of fasciculations with succinylcholine alone, 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).

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 in our study. Similar doses were used by Tsui *et al* in their study (Tsui *et al.*, 1998). Smaller doses have been used by other researchers. 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). 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 by Abbas *et al* that pretreatment had no effect on the intubating conditions (Abbas *et al.*, 2009).

The incidence of myalgia with succinylcholine varies from 20 to 80 percent (Abraham *et al.*, 2009). 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). Although pretreatment with nondepolarizing muscle

relaxants seems to be effective in decreasing muscle fasciculations, 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 nondepolarizing 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).

Our results were in the support of most of the studies which were proving the efficacy of pretreatment in preventing postoperative myalgia. In our group A, 60 percent patients had mild myalgia and the score in this group was 18. This appeared to be attributed to the tissue trauma related to surgery. 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 myalgia was somewhat similar to group A. Here again since the studies with succinylcholine previously done have shown a much higher incidence of myalgia, proved the pretreatment to be effective in this regard.

In our study the rise in serum CK level was statistically insignificant between group A and group B. Although our study demonstrated an average increase in serum CK in the group B however this increase was within the normal range, signifying the effectiveness of precurarization with rocuronium. For the prevention of this adverse effect on muscles, different studies have been carried out. Ozlu established the efficacy of rocuronium pretreatment at 30 minutes, six hours and 24 hours in preventing the succinylcholine associated rise in muscle derived enzymes (Ozlu *et al.*, 2002).

Our results have evaluated rocuronium pretreatment in group B to be effective in preventing succinylcholine-induced rise in

serum K^+ . In 2001 Theroux concluded the significance of mivacurium before administration of succinylcholine in reducing the increase in serum K^+ at five minutes (Theroux *et al.*, 2001). In 2004 precurarization with rocuronium 90 seconds before succinylcholine administration prevented increase in serum K^+ and myoglobin concentrations (Hernandez-Palazon *et al.*, 2004).

CONCLUSION

Though rocuronium has very less muscular side effects as compared to succinylcholine but the high cost of this drug makes it less of a use for a developing country like ours. The cost of this drug in the market presently is 11 times more than that of succinylcholine. As an intubating drug, it is not used routinely and 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 on one hand and on the other hand it will cut the cost of intubation on each patient to one fourth as compared to rocuronium alone. This study has statistically proven the effectiveness of precurarization with rocuronium in reducing the postoperative myalgia, the 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 (Abbas *et al.*, 2009). It is therefore concluded that the technique of precurarization will not only help in reducing the muscular adverse effects of succinylcholine but also prevent the significant rise in serum K^+ leading to adverse complications such as cardiac arrest, in susceptible individuals, making it a safe drug for use in the clinical settings.

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