COMPARISON OF PRECURARISATION WITH ROCURONIUM BROMIDE AND VECURONIUM BROMIDE FOR SUCCINYLCHOLINE HYDROCHLORIDE INDUCED POST OPERATIVE MYALGIA

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INTRODUCTION:
Succinylcholine hydrochloride with its rapid onset of action, ultra short duration of effect, complete and predictable paralysis remains the best drug in providing ideal condition for tracheal intubation. However its use is limited by frequent occurrence of post-operative myalgia. Waters and Mapleson postulated that the pain is secondary to damage produced in muscles by the unsynchronized contractions of adjacent muscle fibers just before the onset of paralysis. This damage can be substantiated by measuring the elevation in serum creatinine kinase levels. Prior administration of a small dose of a non-depolarizing neuromuscular blocker prevents succinylcholine hydrochloride induced fasciculations.1 The factors which can affect the efficacy of pre treatment include the

ORIGINAL ARTICLE

ABSTRACT
BACKGROUND: The study was to compare the effectiveness of the pre-treatment with rocuronium bromide and vecuronium bromide for prevention of succinylcholine hydrochloride induced fasciculation and post operative myalgia, to evaluate intubating conditions and to assess any changes in serum potassium and serum creatinine phosphokinase level. MATERIAL AND METHODS: 120 patients were divided into 3 groups according to precurarisation in the form of either 0.06 mg/kg of Inj. rocuronium bromide or 0.01mg/kg of vecuronium bromide or 2 ml of normal saline intravenously. Induction was done with inj. thiopentone sodium 5mg/kg and inj. succinylcholine hydrochloride 1.5 mg/kg intravenously. Severity of muscle fasciculation was assessed by four point scale. After 60 seconds, laryngoscopy and intubation was done. The intubating condition was graded as excellent, good or poor. Blood sample was taken after 2 minutes of induction for serum K+ estimation and after 24 hours for serum creatinine phosphokinase estimation. Postoperatively on 1st, 2nd and 3rd day severity of myalgia was assessed and graded by using 4 point scale. Statistical analysis was done by using ANOVA, unpaired student’s t test and chi square test. RESULTS: Fasciculation was seen in 92.5% of saline group as compared to 22% and 32.5% in rocuronium bromide and vecuronium bromide group respectively. Myalgia was less with rocuronium bromide than with vecuronium bromide and saline group. Rise in serum potassium and creatinine phosphokinase was observed in saline group. CONCLUSION: The incidence and severity of fasciculations and post operative myalgia is greatly reduced by pretreatment with rocuronium bromide 0.06 mg/kg.

Key words: succinylcholine hydrochloride, rocuronium bromide, vecuronium bromide, myalgia

INTRODUCTION:

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choice of non depolarizing agents, degree of pre-junctional receptor block, interval between administration of pretreatment agent and succinylcholine hydrochloride and the speed of onset of the non depolarizer.

Rocuronium bromide has a more rapid onset of action compared with established non depolarizing agents and provides good intubating conditions within 60 seconds. So this study was undertaken to evaluate the effect of rocuronium bromide and vecuronium bromide for succinylcholine hydrochloride induced fasciculations, post-operative myalgia and any changes in serum potassium and serum creatinine phosphokinase levels.

**MATERIALS AND METHODS:**

Ethical committee approval was taken before the study was undertaken. After obtaining written and informed consent the study was carried out on 120 patients in the age groups 16 – 60 years, weighing 40 to 75 kgs with ASA physical status I or II, posted for different surgical procedures like general, gynecological, otorhinolaryngological, plastic surgery and urological surgery. The detailed history taking, airway and physical examination was done on the day before the surgery. Routine and specific investigations were checked. The nature of study and the procedure were explained to the patients. In the operating room, monitors in the form of ECG, NIBP, SpO\textsubscript{2}, and etco\textsubscript{2} were applied. Intravenous line was secured with wide bore cannula and blood sample was taken for serum potassium levels. Premedication in the form of inj. glycopyrrolate 4ug/kg, inj. ondansetron hydrochloride 0.15mg/kg and inj fentanyl citrate 1ug/kg intravenously were given. Pre-oxygenation was done with 100% O\textsubscript{2} for 3-5 minutes. According to precurarisation, patients were randomly divided into three groups.

**Group R** patients received 0.06 mg/kg of rocuronium bromide intravenously (in 2ml of saline).

**Group V** patients received 0.01 mg/kg of vecuronium bromide intravenously (in 2ml of saline).

**Group S** patients received 2 ml of normal saline

After 60 seconds of precurarisation induction was done with inj. thiopentone sodium 5mg/kg and tracheal intubation was facilitated by inj. succinylcholine hydrochloride 1.5mg/kg intravenously. All patients were observed for muscle fasciculations and its severity by assessing a four point scale. (Nil - no visible fasciculation, Mild - very fine finger tip or facial muscle movements, Moderate – minimum fasciculation on trunk and extremities, Severe - vigorous fasciculation on trunk and extremities)

After 60 seconds, laryngoscopy and intubation was done. The intubating condition was graded. (Excellent - Intubation easy, no reaction from the patient, Good - slight coughing or bucking, Poor - intubation possible, but resulting in marked patient’s response.) Blood sample was taken after 2 minutes of induction for estimation of serum K\textsuperscript{+} level. Anaesthesia was maintained with O\textsubscript{2} (50 %), N\textsubscript{2}O (50%) mixture with isoflurane / sevoflurane and inj. vecuronium bromide 0.025 mg/kg. intravenously. NIBP and heart rate were measured and recorded at 10 minutes of time intervals. Neuromuscular block was reversed with inj. glycopyrrolate 8 ug/ kg and inj. neostigmine methyl sulphate 0.05 mg/kg.

All patients were interviewed in by anesthesiologists on 1\textsuperscript{st}, 2\textsuperscript{nd} and 3\textsuperscript{rd} day of operation. Severity of myalgia was graded by using four point scales of (white 1962). (Nil - no muscle pain or stiffness, Mild - muscle pain or stiffness at one site but not causing disability or limiting activities, Moderate - muscle pains or stiffness at more than one site but not causing disability or limiting activities, Severe - muscle pains or stiffness at one or more sites and causing disability or limiting activities, e.g. difficulty in getting out of bed or turning head.) After 24 hours of administration of succinylcholine hydrochloride blood sample was taken for

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estimation of serum creatinine phosphokinase level. In our study statistical analysis for patient characteristic’s (age, weight), ASA grade, duration of surgery, fasciculation, intubating condition and hemodynamic parameters (Pulse, Systolic blood pressure and diastolic blood pressure) between three groups was carried out by ANOVA. A comparison between two groups was done by unpaired student’s t test. For categorical variables chi square test was used. The results were expressed as Mean±SD. A p<0.05 was considered as statistically significant.

RESULTS:

The three groups were comparable with regard to age, sex, weight, American society of anaesthesiologist physical status and duration of surgery. (Table 1)

Severe fasciculations were observed in 30% of patients in saline group as compared to 0% in rocuronium bromide and vecuronium bromide groups. Moderate and mild fasciculations were observed in 45% and 17.5% patients respectively of saline group, 5% and 17.5% patients respectively of rocuronium group and 12.5% and 20% patients respectively of vecuronium group. While 77.5% patients of rocuronium group and 67.5% of vecuronium group did not have any fasciculations. (Graph 1)

Myalgia was severe in saline group as compared to rocuronium bromide and vecuronium bromide group on day 1 and day 2 (P<0.05). There was no significant difference between vecuronium bromide and rocuronium bromide on all three days of observation (P>0.05). However, the mean value of myalgia was more in vecuronium bromide (0.35±0.62) as compared to rocuronium bromide (0.15±0.36) on day 1. (Table 2) (Graph 2)

In our study mild myalgia was present on 1st day in 25% of patients in saline group compared to 20% patients and 15% patients of vecuronium bromide and rocuronium bromide group respectively. On 2nd day it was observed in 25% patients of saline group compared to 10% and 7.5% patients of vecuronium bromide and rocuronium bromide group respectively. On 3rd day 5% of patients in saline group compared to 2.5% of vecuronium bromide group had myalgia.

No myalgia was observed in rocuronium bromide group. On the 1st and 2nd day moderate myalgia was observed in 12% and 2.5 % of patients in vecuronium bromide group respectively and 7.5% of patients in saline group. On the 1st day severe myalgia was observed in 7.5% of patients in saline group. But it was not observed on 2nd and 3rd day. (Table 3) (Graph 3)

The three groups were similar in serum potassium level at baseline (p>0.05). There was a significant increase in serum potassium level in saline group as compared to rocuronium bromide group and vecuronium bromide group 2 minutes after induction (P<0.05). (Graph 4) The serum creatinine phosphokinase level was significantly higher in saline group as compared to rocuronium bromide and vecuronium bromide group. (p<0.05) (Table 4) (Graph 5)

DISCUSSION:

Post succinylcholine hydrochloride pain and stiffness appear on the day following surgery may last 2-6 days and vary in intensity from mild malaise and tenderness to generalized and severe pain. This side effect of the drug is often considered as minor but it may be one of the most distressing consequences of minor surgery for the patient.

There has been much discussion about time interval between administration of pre-treatment agent and succinylcholine hydrochloride. Intervals of 2, 3 and 4 minutes or longer have been recommended but this type of lengthy intervals, required by slow onset drugs are impractical with busy operating list. Newer available non depolarizing muscle relaxant rocuronium bromide for its rapid onset of action, it would be effective at reducing myalgia when only a short interval was allowed appears to have been substantiated.

Table 1: Patient’s demographic data analysis. (Mean ± S.D) OR (n=no of pts)

<table>
<thead>
<tr>
<th></th>
<th>Group R (n=40)</th>
<th>Group V(n=40)</th>
<th>Group S(n=40)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>31.77±10.63</td>
<td>33.07±13.96</td>
<td>33.05±15.03</td>
<td>0.88</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>5/35</td>
<td>17/23</td>
<td>16/24</td>
<td></td>
</tr>
<tr>
<td>Weight (kgs)</td>
<td>48.77±8.07</td>
<td>57.12±11.87</td>
<td>52.27±9.86</td>
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<tr>
<td>ASA I or II</td>
<td>1.42±0.50</td>
<td>1.47±0.50</td>
<td>1.80±0.40</td>
<td>0.34</td>
</tr>
<tr>
<td>Duration of surgery (mins)</td>
<td>77.62±49.09</td>
<td>78.75±30.33</td>
<td>73.87±29.88</td>
<td>0.83</td>
</tr>
</tbody>
</table>

Table 2: Grading of Intubating conditions

<table>
<thead>
<tr>
<th>Grading of Intubating condition</th>
<th>Group R (n=40 pts)</th>
<th>Group V (n=40 pts)</th>
<th>Group S (n=40 pts)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent (grade 0)</td>
<td>34 (85%)</td>
<td>30 (75%)</td>
<td>35 (87.5%)</td>
</tr>
<tr>
<td>Good (grade 1)</td>
<td>06 (15%)</td>
<td>10 (25%)</td>
<td>05 (12.5%)</td>
</tr>
<tr>
<td>Poor (grade 2)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mean value</td>
<td>0.15±0.36*</td>
<td>0.25±0.43*</td>
<td>0.12±0.33*</td>
</tr>
</tbody>
</table>

*P=0.30 (Mean ± SD)

Graph 1: Fasciculation grading according to severity

Graph 2: Incidence and severity of myalgia
Table 3: Incidence and severity and myalgia

<table>
<thead>
<tr>
<th>Myalgia</th>
<th>Group R</th>
<th>Group V</th>
<th>Group S</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>0.15±0.36</td>
<td>0.35±0.62</td>
<td>0.72±0.96</td>
<td>0.001</td>
</tr>
<tr>
<td>Day 2</td>
<td>0.07±0.26</td>
<td>0.15±0.42</td>
<td>0.40±0.63</td>
<td>0.006</td>
</tr>
<tr>
<td>Day 3</td>
<td>0.00±0.00</td>
<td>0.02±0.15</td>
<td>0.05±0.22</td>
<td>0.36</td>
</tr>
</tbody>
</table>

Graph 3: Distribution of myalgia on 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> post operative day

Table 4: Serum creatinine phosphokinase levels after 24 hrs administration of suxamethonium

<table>
<thead>
<tr>
<th></th>
<th>Group R</th>
<th>Group V</th>
<th>Group S</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPK</td>
<td>196.17±108.20</td>
<td>226.77±105.83</td>
<td>365.45±105.83</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Graph 4: Changes of serum potassium level

Mean score of serum potassium

Baseline 2 min of induction
In our study we have kept 2 minutes of time interval. C motamed et al did the study with time interval of 1.5 minutes and 3 minutes and observed no significant difference in comparison of fasciculation. The probability of fasciculation decreases with longer time interval between pretreatment and succinylcholine hydrochloride administration. The speed of onset of action of non depolarizing muscle relaxant is inversely related to drug potency and this probably explains the effectiveness of rocuronium bromide.

Hartman et al demonstrated that fasciculations are caused by axonal depolarization initiated by action of succinylcholine hydrochloride on perijunctional nicotinic receptors at neuromuscular junction. Although study showed that rocuronium bromide effectively prevent fasciculations, its effect on the paralyzing action of succinylcholine hydrochloride was also considerable. Rocuronium bromide, at the dose administered in this study, delayed the onset of succinylcholine hydrochloride and shortened its duration. These findings suggest that rocuronium bromide is more likely than d-tubocurarine to interfere with the post-junctional (paralyzing) effects of succinylcholine hydrochloride.

In our study fasciculation was observed in 92.5% in saline group as compared to rocuronium bromide 22% and vecuronium bromide 32.5% (P<0.05). Study by V abraham and arti rajkumar mentioned that fasciculation in rocuronium bromide group 31.7% was significantly less (p<0.01) compared to vecuronium bromide group 51.6 %. G.p.findlay and J.spittal found that fasciculation was 84% in vecuronium bromide group compared to 4% in rocuronium bromide group. C.motamed and F.donati in their study mentioned that the incidence of fasciculations was lower in the ROC-3 min (9%) and ROC-1.5 min (30%) groups than in the without ROC group (83%; P < 0.00 I). The intensity of fasciculations was also less in both pre-treatment groups. J Demers and P Drolet did a study of 25 patients and observed fasciculations in all patients in saline group compared to 12 patients in rocuronium bromide group and 17 patients in d-tubocurarine group. R Martin and J Carrier compared rocuronium bromide with mivacurium, vecuronium hydrochloride, atracurium besylate and saline and noted that fasciculation was seen in 3 of the 20 patients in rocuronium bromide group compared to 19, 11, 7, 14, and 10 from 20 patients in saline, vecuronium bromide, atracurium besylate, mivacurium and d-tubocurarine respectively.

In our study no significant difference was observed in intubating condition among all three groups. Similar findings were observed in various studies. V Abraham and Arti rajkumar observed that intubating condition was significantly better with rocuronium bromide group than vecuronium bromide group. G.p.findlay and J.spittal and C.motamed and F.donati observed no significant difference in intubating condition between ROC-3min, ROC-1.5min and without ROC group. R Martin and J Carrier noted that intubating condition was better in saline group than...
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rocuronium bromide, mivacurium, vecuronium bromide and atracurium besylate group. Jae-Hawn Kim et al suggested that myalgia may be due to irreversible changes on muscle spindles. Unsynchronized contractions of muscle fibers resulting in shearing of connective tissues, electrolyte imbalance, and release of prostaglandins are among the various reasons proposed for post operative myalgia. Marianne Mikat-stevans and Radha Sukhani et al. observed myalgia in early ambulated patients. This is undoubtedly a reflection of the many factors which contribute in the effect of post operative myalgia e.g. choice of muscle relaxants, type and location of surgery, position during surgery, intubation, trauma, post operative ambulation, incidence and degree of post operative pain requiring analgesics and post operative rest. Most effective and widely used method is pre treatment with a small dose of non depolarizing neuromuscular blocking agent. In this respect vecuronium bromide was probably the best agent. V abraham and arti rajojumar and G.p.findlay and J. spittal observed rocuronium bromide was better non depolarizing muscle relaxant than vecuronium bromide in reducing myalgia and fasciculation. In our study mild myalgia was present on 1st day in 25% of patients in saline group compared to 20% and 15% patients of vecuronium bromide and rocuronium bromide group respectively. On 2nd day it was observed in 25% patients of saline group compared to 10% and 7.5% patients of vecuronium bromide and rocuronium bromide group respectively. On 3rd day 5% of patients in saline group compared to 2.5% of vecuronium bromide group and no myalgia was observed in rocuronium bromide group. V Abraham and arti rajojumar noted that there was no statistically significant difference between two groups regarding post operative myalgia on 1st and 3rd post operative day. G.p.findlay and J.spittal noted that incidence of myalgia 20% on 1st post operative day and 28.6% on day 4 in rocuronium bromide group compared with vecuronium bromide. This was significant on day 1st but not by day 4. This may be a reflection of the small sample size as a reduction in myalgia from 46.3% with vecuronium bromide compared to 28.6% with rocuronium bromide may be considered clinically significant. A larger sample size may clarify this issue. Demers and P Drolet observed severe myalgia in 8 patients of saline group compared to 1 and 2 patients in rocuronium bromide and d-tubocurarine group respectively at post operative 24 hours and 2 patients had severe myalgia in saline group compared to only 1 patient in both rocuronium bromide and d-tubocurarine group at post operative 48 hours. R Martin and J Carrier noted myalgia in 71% patients. Myalgia was not diminished by pre treatment with any non depolarizing muscle relaxant. It differs from other study. They mentioned that no advantage was observed with pre-treatment except that it prevented fasciculations.

In our study 2 minutes after induction there was a significant rise in serum potassium in saline group as compared to rocuronium bromide and vecuronium bromide group. The rise in serum potassium was significantly lower in rocuronium bromide as compared to vecuronium bromide group (p=0.02). V abraham and arti rajojumar also observed mild increase in potassium levels (4.6-5 meq/l) in 45% patients of vecuronium bromide group and 30% patients of rocuronium bromide group. In the pathogenesis of muscle cell injury produced in muscle by the unsynchronized contractions of adjacent muscle fibers just before the onset of paralysis is as follows. There is release of creatinine phosphokinase and myoglobin from muscle tissue by cell destruction and alterations in the permeability of the skeletal muscle cell membrane. Under normal conditions, the sodium potassium ATPase pump maintains very low intracellular sodium content. The intercellular sodium concentration is normally maintained at 10meq/L by a sodium-potassium adenosine triphosphatase (Na/K-ATPase) pump located in the sarcolemma. The sarcolemma, a thin membrane that encloses striated muscle fibers, contains numerous pumps that regulate cellular electrochemical gradients. A separate
Sodium-calcium channel then serves to pump additional sodium into the cell in exchange for calcium extrusion from the cell. In addition, most intracellular calcium is normally sequestered within organelles. Damage to muscle cells interferes with both mechanisms, leading to an increase in free ionized calcium in the cytoplasm. An increase in intracellular calcium levels results in hyperactivity of proteases and proteolytic enzymes and generation of free oxygen radicals. These enzymes and substances increasingly degrade myofilaments and injure membrane phospholipids with leakage of intracellular contents like potassium, phosphate, creatinine phosphokinase, urate and myoglobin into plasma. In our study serum creatinine phosphokinase level was higher in saline group as compared to rocuronium bromide and vecuronium bromide group (p<0.05). The vecuronium bromide group showed a significant increased values of creatinine phosphokinase as compared to rocuronium bromide group (p=0.02). V. Abraham and Arti Rajkumar found a significant rise in creatinine phosphokinase levels in both groups. In 1981 Charak DS and Dhar CL noted a significant increase in serum creatinine phosphokinase induced with succinylcholine hydrochloride. Jae-Hwan Kim et al did not find significant rise in creatinine phosphokinase level after 24 hour post-operatively. 

We observed that 0.06 mg/kg rocuronium bromide injected at 2 minutes before succinylcholine hydrochloride reduced the incidence of fasciculations with no difference in neuromuscular block and intubating conditions. However, such a study would require a large number of patients because the incidence of post operative myalgias is lower than the incidence of fasciculations.

**CONCLUSION:**
The incidence and severity of fasciculations and post-operative myalgia is greatly reduced by rocuronium bromide 0.06mg/kg as pre-treatment agent. Rocuronium bromide is better drug than vecuronium bromide in reducing succinylcholine hydrochloride induced fasciculations and post operative myalgia. Rocuronium bromide provides good intubating conditions and effective precurarisation within short interval. Rise of serum potassium and serum creatinine phosphokinase is also less with rocuronium bromide than vecuronium bromide.

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