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A COMPARATIVE STUDY OF ONSET TIME AND INTUBATING CONDITION FOR DIFFERENT DOSE OF ROCURONIUM IN BURN AND NON-BURN PATIENTS

Anesthesiology

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ABSTRACT

An aberrant pharmacodynamics responses to neuromuscular blocking drugs(NMBD)in burn patients increases the potential for lethal hyperkalemia with the administration of depolarizing muscle relaxant eg:succinylcholine and 2.5-5 folds increase in the dose of plasma concentration requirement for non-depolarizing muscle relaxants like :tubocurarine,metacurine,pancuronium,atracurium,vecuronium.Therefore Rocuronium may be the drug of choice in burn patients.This study was planned to assess the onset time and intubating conditions with two different doses of rocuronium in patients with thermal injury.It was concluded that in non-burn patient onset time(loss of response to TOF) was 85.5±4.8 sec with a dose of 0.9 mg/kg as compared to 1.2 mg/kg it was 60.55±70.4,while in burn patients (more than 30% burn area) these values were 120.83±6.81 sec and 86.16±5.2 respectively.

KEYWORDS

Burn patient(>30%),depolarising muscle relaxant (Succinylcholine), non-depolarising muscle relaxant (Rocuronium), Neuromuscular monitoring,hyperkalemia.

INTRODUCTION

Burn injury causes proliferation of acetylcholine receptors (AchR) on the muscle membrane located under burn site as well as site distant from the injury.Pathophysiological changes accompanying burn trauma can alter the pharmacodynanic and pharmacokinetic responses to neuromuscular relaxants. An increase in AchR number is usually associated with resistant to neuromuscular blocking effects of non-depolarising muscle relaxants and increased sensitivity to depolarising muscle relaxants.The magnitude of resistance is related to burn size and time after burn.

Rocuronium is the drug of choice in thermal injured patient because of rapid onset of paralysis and devoid of hyperkalaemic effect and fasciculation. Therefore this prospective study was planned to study onset time, intubating dose, and intubating conditions in burn patients as compared to non-burn patients.

MATERIAL And METHOD:

After approval from ethical committee of the institute this single blind study was conducted on the 120 adult patients(30 patients in each group) of either sex belonging to American society of anaesthesiology (ASA) physical status I & II,aged 18 to 60 years, requiring general anaesthesia and tracheal intubation for elective burn and non-burn surgery.after thorough preanaesthetic checkup. the patients were subjected for routine and special investigations(serum electrolyte Na,K) Patient with neuromuscular disease,difficult airways,pregnant women,total burn area ≤30%,emergency cases were excluded from the study.

The patients were randomly divided into four groups depending upon dose of rocuronium used for tracheal intubation as follows:

B1- Burn patients (0.9mg/kg Rocuronium)
B2- Burn patients (1.2 mg/kg Rocuronium)
N1- Non-burn patients (0.9mg/kg Rocuronium)
N2- Non-burn patients (1.2 mg/kg Rocuronium)

On arrival in the operation theatre, base line monitors were attached , an IV line secured in the arm. Peripheral nerve stimulator used for neuromuscular monitoring using the adductor pollicis muscle movement(train of four stimulation of ulnar nerve at wrist). All the selected patients were premedicated with atropine 0.01 mg/kg,midazolam 0.15mg/kg,fentanyl 1µg/kg iv 5 min prior to induction. After Induction with propofol 2mg/kg iv , Intubating dose of rocuronium was given as per group and TOF stimulation performed every 10sec. until maximum blockade (no twitch response)occurred.Laryngoscopy performed and intubating condition assessed.Ventilation was maintained by positive pressure ventilation using closed circuit.EtCo2 maintained at 35-40 mmHg. Repeat dose of rocuronium was given on appearance of 1st twitch of TOF stimulation. After completion of surgery the NMB was reversed with 50 µg/kg neostigmine and 5µg/kg glycopyrrolate. Following parameters were observed and recorded: NIBP, SpO2 & onset time and duration of block. Intubating conditions were graded as: EXCELLENT, GOOD and POOR.

EXCELLENT:Fully relaxed jaw with fully abducted vocal cords and no cough reflex.

GOOD: Partially relaxed jaw with partially abducted vocal cords and no cough reflex.

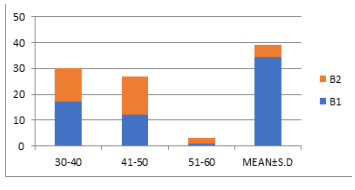
POOR:Partially relaxed jaw with partially abducted vocal cords and a cough reflex.

RESULTS:

In non-burn patients onset time (loss of response to TOF) was 85.5± 4.8 sec. with a dose of 0.9mg/kg as compared to 1.2 mg/kg where it was 60.55 ± 70.4 while in burn patients (more than 30% burn area) these values were 120.83±6.81 sec and 86.16±5.2 respectively.

Table 1:

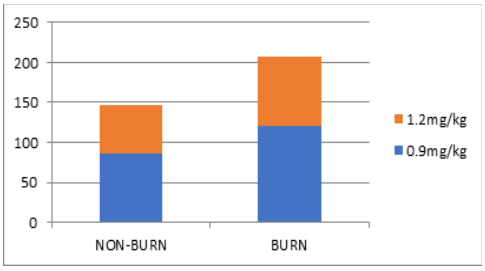
Percentage of burn	Number of patients in group	
	B1	B2
30-40	17(56.66%)	13(43.33%)
41-50	12(40.00%)	15(50.00%)
51-60	1(3.33%)	2(6.66%)
MEAN±SD	34.26±5.95	41.61±6.38



MEAN TIME OF ONSET OF BLOCK(seconds): The time of onset to 95% neuromuscular block was significantly delayed in the burn patients compared with non-burn patients (120 versus 85 s for 0.9 mg/kg and 86 versus 60 s for 1.2 mg/kg doses, respectively; $P < 0.05$). The onset times within the two non-burn groups were not significantly different. On the contrary, in the burn group, an intubating dose of 1.2 mg/kg had a faster onset than the 0.9 mg/kg dose

Table 2:

CATEGORY	DOSE	
	0.9 mg/kg	1.2 mg/kg
NON-BURN	85.35±4.80	60.55±7.04
BURN	120.83±6.81	86.16±5.20



INTUBATING CONDITIONS:
Intubating conditions were excellent in most non-burn patients, even with rocuronium 0.9 mg/kg. Increasing the dose to 1.2 mg/kg improved the excellent intubating conditions only marginally (93% versus 100%; $P > 0.05$). In contrast, in the burn group receiving rocuronium 0.9 mg/kg, more than 50% of patients had some diaphragmatic movement, nonsustained coughing, or slight movements in the upper extremities at the time of tracheal intubation, despite reportedly easy laryngoscopy. These conditions were improved when the burned patients were given the larger dose; the 1.2 mg/kg dose gave excellent conditions significantly more often than the 0.9 mg/kg dose in the burn groups .

Table 3:

INTUBATING CONDITION	NUMBER OF PATIENTS IN GROUP			
	N1	N2	B1	B2
EXCELLENT	28(93.33%)	30(100%)	21(70.0%)	28(93.33%)
GOOD	2(6.66%)	…..	6(20%)	2(6.66%)
POOR	……	…..	3(10.0%)	…..

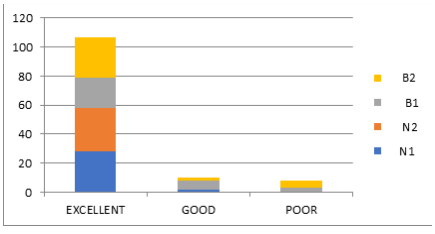


Table 4:

Approximate percentage of receptors blocked	Clinical significance
<75	May be able to move although may experience weakness amenable to reversal of blockade with antagonists.
75	May need to administer additional drug to prolong relaxation short to intermediate acting agent may be reversible.
80	Suitable for short term relaxation as well as long term mechanical ventilation.
90	Usually gives conditions suitable for short term procedures including intubation and long term mechanical ventilation
100	Condition for intubation

DISCUSSION:
Rocurorium has a similer structure to that of vecuronium,is less potent with an ED95 of 0.3mg/kg ,having an onset of action in 1-2 minutes and duration of NMB lasting for 20-35 min. The onset time of maximum single twitch depression after administration of 3-4 x ED95 of Rocuronium resemble the onset of action of suxamethonium 1mg/kg iv thus Rocuronium is the only non depolarising NMB drug that may serve as an alternative to suxamethonium when the rapid onset of NMB is needed for tracheal intubation specially in burn patient who has an altered NMJ and Na,K level.In doses upto 1.2mg/kg Rocuronium has minimal cardiovascular effects both in healthy and with cardiovascular disease.

In the present study mean time of onset in group N1 was 85.35±4.8 sec and in group N2 was 60.55±7.04 sec ($P<0.0001$). Mean time of onset in group B1 was 120.85 sec and in group B2 was 86.16+5.2($p<0.0001$).Thus increasing the intubating dose shortens the onset of action (TOF >90%)in both the burn and non-burn patients. Comparing group N1 with B1 and N2 and B2 the onset time was significant delay in burn patient. Our findings are
in accordance with that of Tanet al7 who studied neuromuscular pharmacodynamics of Rocuronium in patient with major burns and reported the onset time to 95% neuromuscular block was prolonged in burned patients as compared with non-burn patients(115±5.8vs 68±16 sec for 0.9mg/kg)

Intubating conditions were excellent in 93.33% non burn patients with ED95x3 intubating dose of rocuronium &100% non-burn patients with ED95x4 these values were 70% and 93.33% in burn patient respectively. Our findings are comparable to that of Tan et. al who reported excellent intubating conditions with rocuronium in dose of ED95 X 3 increasing the dose to ED95 X 4 improves the condition marginally in non burn while in burn patient receiving rocuronium 0.9mg/kg,more then50% had diaphragmatic movement,non-sustained coughing or slight movement of upper extremity,despite easy laryngoscopy .These conditions were improved when burn patient were given larger dose of 1.2mg/kg.

Martyn, Goldholl et. al. studied the clinical pharmacology of muscle relaxants in patients with burn1,the pathophysiological changes that can be potentially affect kinetics in hypermetabolic phase of burn injury include increase hepatic blood flow, increased glomerular filtration rate and increase protein binding. The aberrant pharmacological responses to neuro-muscular relaxants in burn patients include the potential for lethal hyperkalaemia with the administration of depolarizing muscle relaxants and 2.5-5.0 fold increase in the dose or plasma concentration requirement for non-depolarising muscle relaxants.The altered pharmacokinetic responses are probably related to an increase in nicotinic acetylcholine receptor numbers.

CONCLUSION :
There is delay in onset time with increased dose requirement (4xED95) of Rocuronium in burn patients as compared to non-burn patients to achieve the similar intubating condition.

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