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ORIGINAL ARTICLE

INTUBATING CONDITIONS WITH TWO DIFFERENT DOSES OF ROCURONIUM BROMIDE FOR CAESAREAN SECTION: A COMPARATIVE CLINICAL STUDY

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ABSTRACT: A study was conducted in fifty full term pregnant patients divided into two groups - A and B (twenty five each) posted for caesarean section under general anesthesia. **AIM OF THE STUDY**: To compare the intubating conditions with two different doses of rocuronium bromide for rapid sequence intubation for caesarean section. Secondary aim: To assess neonatal APGAR score. **METHODS**: The groups A and B received intravenously 0.6mg/kg and 0.9mg/kg of rocuronium respectively after thiopentone sodium 5mg/kg. Intubation was attempted at 60 seconds and intubating conditions were rated (Copenhagen consensus rating scale). **RESULT**S: All patients in both groups had clinically acceptable conditions for intubation and could be intubated in the first attempt within 75 seconds after rocuronium. However, 0.9mg/kg of rocuronium offered better intubating conditions than 0.6mg/kg (44% and 56% excellent and good respectively in group A vs 88% and 12% excellent and good respectively in group B. Excellent condition was significantly more with Group B, P=0.001). There were no serious adverse events. All except two patients had healthy babies with an Apgar score of at least 8 at one minute. While one patient with antenatal diagnosis of intra uterine death of the fetus delivered a dead baby, another patient with difficult extraction had a baby with an Apgar score of 6 at one minute which responded to simple measures resulting in a score of 8 at 5 minutes. All babies were seen to do well in the post-operative period. **CONCLUSION**: Rocuronium is a good muscle relaxant for caesarean section in select group of patients because it provides clinically acceptable conditions for rapid sequence intubation in the doses of 0.6 and 0.9mg/kg. However the conditions after 0.9mg/kg are better than those offered by 0.6mg/kg of the drug.

KEYWORDS: pregnancy, caesarean section, rocuronium doses, intubating conditions, rapid sequence intubation.

INTRODUCTION: High rate of caesarean section characterizes modern obstetrics.[1] Hence it is a surgery frequently encountered by the anesthetist. Despite the popularity of central neuraxial blockade, general anesthesia may have to be offered to these patients at times because of their choice or condition. Succinylcholine is the commonly used muscle relaxant for rapid sequence intubation due to its fast onset, excellent intubating conditions and short time course of action on the diaphragm and adductor muscles of the larynx involved in respiration and airway protection.[2] However it may have adverse effects which can limit or even contraindicate its use at times. An alternative drug suggested and used in recent times for rapid sequence induction is rocuronium in the dose of 0.6 to 1.2mg/kg.[3-6] Hence a study was conducted to evaluate the intubating conditions after two different doses (0.6 and 0.9 mg/kg) of rocuronium in pregnant patients undergoing caesarean section.

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METHODS: Post ethical committee clearance and written informed consent of patients; this randomized study was conducted in two groups of healthy full term pregnant patients (ASA Class 1) of 25 each posted for emergency caesarean section opting for general anesthesia. The exclusion criteria included any co-morbid condition, obesity allergy history, neuromuscular disease, use of anticonvulsants or other drugs and airway grading other than of Mallampatti-1.

All patients had live healthy singleton fetuses except for one patient diagnosed with antenatal intrauterine death of the fetus. After adequate preparation, the patient was shifted to the operation theatre, connected to pulse oximeter, ECG, $ETCO_2$ and non-invasive blood pressure apparatus. An intravenous line of ringers lactate was started on the non-dominant hand. Left uterine displacement was achieved with a sand bag under the right hip.

After adequate pre-oxygenation and recording of heart rate, blood pressure and ECG, rapid sequence induction was achieved with thiopentone sodium-5mg/kg injected intravenously over 20 seconds followed by rocuronium-0.6mg/kg in group-A and thiopentone 5mg/kg followed by rocuronium 0.9mg/kg in group-B. Sellicks maneuver was employed. After 60 seconds, intubation was attempted by an experienced anesthetist with an appropriate McIntosh laryngoscope blade who recorded the intubating conditions as per Copenhagen Consensus Conference rating scale [Table 1].[7, 8]

This was followed by controlled ventilation with nitrous oxide and oxygen until the delivery of the baby when midazolam and an inhalational agent were introduced. Intubating conditions and Apgar score of the baby were noted. Induction-delivery intervals, uterine incision-extraction intervals and the minimum duration of action of the relaxant in the two groups as judged clinically by the need for repeat dose of the relaxant necessitated by the appearance of respiratory attempts were also observed.

Statistical methods Applied: Results were expressed in percentage proportion. Chi-square and Fischer extract tests were applied to know the statistical significance.

RESULTS: The groups were comparable with respect to age, weight and physical status [Table 2].

Intubating Conditions:

Group A: Laryngoscopy was considered easy in 20(80%) patients and fair in 5(20%) patients [Graph-1]. Vocal cords were abducted without any movement in 18 (72%) patients and intermediate with some movement in 7(28%) patients [Graph 2]. While 11 (44%) patients had no peripheral movements, 14 (56%) patients showed the same [Graph 3]. Cough and mild diaphragmatic movement were absent in18 (72%) patients while in 7(28%) patients, the latter was observed. [Graph 4].

Group B: Laryngoscopy was easy in all 25(100%) patients [Graph 1]. Vocal cords were abducted without movement in 24(96%) patients while it was intermediate with mild movement in one (4%) patient [Graph 2]. While 22(88%) patients were still, 3 (12%) patients had mild peripheral movements [Graph 3]. 24 (96%) patients did not cough or have diaphragmatic movements, but one (4%) patient exhibited the latter. [Graph 4].

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The difference between the various parameters of the two groups showed consistently better conditions for group B than for group A, statistical significance with P-value being 0.018, 0.021, 0.001and 0.021 for laryngoscope insertion ease, vocal cord position and movement, peripheral (limb) movements and cough respectively.

Overall in both groups, all patients came under the clinically acceptable category, endotracheal tube being placed within 75 seconds post rocuronium. However in group A, 11 patients (44%) were considered to have excellent intubating conditions and 14 (56%) patients were considered to have good conditions. In contrast 22 patients (88%) were considered to have excellent intubating conditions while 3 (12%) patients came under good category in group B (P=0.001 for excellent condition between the two groups) [Table 3] [Graph 5]. No patient came under poor/clinically unacceptable condition.

The minimum duration action of intubating dose of rocuronium as judged by appearance of respiratory attempts in the whole study population was 25 minutes and occurred in one patient from Group A. The duration of action exceeded 25mins in the rest of the patients in both groups. While 20 patients (80%) required repeat dose of the relaxant in Group A for completion of surgery, only 4 patients (16%) required the repeat dose in Group B indicating an increased duration of action of the higher dose.

Neonatal Considerations: Induction- delivery intervals ranged from 5 to 15 minutes in all patients and uterine incision to extraction intervals were within 90 seconds in all except in one patient from Group A (201sec). All the newborns in our study had an Apgar score of 8 or more at 1 minute except in one patient with difficult extraction due to obstetric factor where it was 6 at 1 minute but improved to 8 at 5 minutes with simple measures. One patient with intrauterine death had the expected dead baby. All babies were followed up for 7days and were seen to do well.

There were no adverse events and haemodynamic stability was well maintained in all patients in both groups.

DISCUSSION: Caesarean section is a high priority surgery with special problems. It involves two lives and requires skilled anaesthesia. Rapid sequence intubation becomes part of general anesthesia whether the surgery is done on an elective or emergency basis. Succinylcholine has been the relaxant of choice for this purpose because the condition warrants rapid securing of the airway in order to prevent hypoxia and pulmonary complications. However, its adverse effects such as muscle fasciculations, post-operative myalgia, rise of intragastric & intra ocular pressures as well as the contraindication in malignant hyperpyrexia in susceptible patients and in hyperkalaemia have paved way for research with alternative agents like pancuronium, vecuronium, ropacuranium etc.[9-11]

Among the nondepolarisers, the mono quaternary amino steroid rocuronium has been used for rapid sequence intubation and is reported to provide conditions similar to that offered by succinylcholine.[12,13] Rocuronium is a drug with quick onset because of its low potency (ED_{95}-0.3mg/kg^{-1}).[4,5,14,15] Onset time of a neuromuscular blocker is considered important because it serves as a predictive parameter for the rate of development of ideal intubating conditions and stimulation of adductor pollicis has been used earlier to assess the onset of block.

However it is seen that this onset at the adductor pollicis may vary from that in laryngeal muscles and masseters,[16-18] predicts intubating conditions poorly and hence its meticulous recording for that purpose is probably obsolete.[8,19] We did not use any neuromuscular monitoring

to assess vocal cord paralysis but selected the cut off time of 60 seconds to start intubation post rocuronium injection in our study. We used the Copenhagen Consensus Conference rating scale whose basis is the assumption that "excellent" and "good" intubating conditions can be considered as clinically acceptable and "poor" condition as clinically unacceptable.

Studies have shown that the choice of the induction agent and the dose in which it is used with the relaxant influences the onset of appropriate intubating conditions.[6,20-22] Increasing the dose of thiopentone from 4 to 6mg/kg body weight with rocuronium improves intubating conditions. [6] Other studies have found that the higher dose of rocuronium - 1mg/kg after 5mg/kg of thiopentone equals succinylcholine action.[23, 24] High doses of induction agents may carry concerns of potential risk of neonatal depression and increasing the dose of neuromuscular blocker raises questions about increased duration of the block and so it is desirable to employ the minimum effective dose of a drug especially in a parturient. Keeping these things in view we have used thiopentone 5mg/kg along with rocuronium in the dosage of 0.6mg/kg and 0.9 mg/kg in the two groups in our study.

Rocuronium in the dose of 0.6mg/kg was found to produce good to excellent intubating conditions for caesarean section after 6mg/kg of thiopentone by Abouleish and also by Larsen et al who got intubating conditions equaling those of succinylcholine for rapid sequence intubation after propofol and alfentanyl.[5,13] As per Sparr et al, rocuronium in the above dose after thiopentone 5mg/kg produced intubating conditions similar to succinylcholine only when alfentanyl was part of the regime. But even without alfentanyl the above regime could result in rapid sequence intubation within 75 seconds though it could not be considered to be as good as with succinylcholine.[12]

Cheng et al in a comparative study with different doses of rocuronium (0.6 and 0.9 mg/kg) after thiopentone and alfentanyl for rapid sequence intubation, obtained intubating conditions similar to succinylcholine after 0.9 mg/kg of rocuronium but found 0.6mg/kg dose inadequate.[25]

In our study we completed intubation in all our patients in both groups in the first attempt within 75 seconds post rocuronium. No patient came under the poor or clinically unacceptable category, but 0.9mg/kg of rocuronium offered better intubating conditions than 0.6mg/kg dose (rate of excellent conditions - 88% vs. 44%. P=0.001). That rocuronium has dose related effects on the upper airway muscle has been commented upon earlier. [23] Our experience with 0.6 mg/kg dose concurred with the earlier studies of Abouleish, Sparr and Larsen. Similar to the study of Cheng, 0.9mg/kg dose provided satisfactory conditions in our study. However, we are not aware any study comparing the above two doses of rocuronium during Caesarean section in particular.

One main difference in the two groups pertained to mild peripheral movements – event that occurred post intubation and hence patient's safety was not compromised. Opioids reduce the incidence of diaphragmatic response after rocuronium and constitute an integral part of an induction regime containing 0.6mg//kg of rocuronium in order to achieve intubating conditions similar to those after succinylcholine.[12] But opioids were not employed in our study for obvious neonatal reasons.

The minimum duration of action of the intubating dose of rocuronium in our study as judged by the appearance of respiratory attempts was 25 minutes in a patient from Group A. It exceeded 25 minutes in all other patients in both groups. While 20 patients (80%) required repeat dose of the relaxant with 0.6 mg/kg of rocuronium for completion of surgery, only 4 patients (16%) required the repeat dose with 0.9mg/kg dose indicating an increased duration of action of the higher dose. All the above findings could be issues of serious concern in the event of a failure to intubate. Availability of sugammadex could perhaps be helpful here in future.

All patients had good cardiovascular stability and showed no adverse effects.

Neonatal Considerations: Induction- delivery intervals ranged from 5 to 15 minutes and uterine incision - extraction intervals were within 90 seconds in all patients in both groups except in one patient from Group A (201 seconds). Rocuronium and its metabolite 17 desacetylcuronium are seen not to cross the placental barrier significantly in studies involving the estimation of umbilical venous/maternal venous ratio of rocuronium during caesarean section.[5]

Consistent with the above, all the newborns in our study had an Apgar score of 8 or more at 1 minute except in one patient with difficult extraction (uterine incision delivery interval-201seconds) due to breech presentation where it was 6 at 1 minute but improved to 8 at 5 minutes with simple measures. Uterine incision to delivery intervals exceeding 3 minutes is said to adversely affect the apgar scoring of the newborn.[26,27] One patient with intrauterine death had the predicted dead baby.

All babies were followed up for 7 days and were seen to do well.

A limitation of our study was the absence of blinding. Rapid sequence intubation being a high risk procedure especially in caesarean section, due to considerations of optimal patient safety in our setup, a conscious decision was made not blind the study. Also, neuromuscular monitoring of corrugator supercilii muscle in the study could perhaps have shed additional light on timing the optimum conditions for tracheal intubation in the two study groups as current best evidence suggests that the corrugator supercilii reflects laryngeal relaxation better than monitoring of adductor pollicis.[28]

CONCLUSION: Rocuronium in the dose of 0.6 and 0.9 mg/kg provides clinically acceptable conditions for rapid sequence intubation during caesarean section. The conditions provided by 0.9mg/kg of rocuronium are significantly better than those produced by 0.6mg/kg of the same. However the duration of action of the drug in the event of an inability to secure the airway can be a serious concern but may perhaps be answered in future by the availability of sugammadex. The drug has no other notable unwanted effects.

There is clinically insignificant effect on the fetus with the birth of healthy babies with both doses. Rocuronium can thus be thought of for use in select group of parturients posted for caesarean section when succinylcholine is contraindicated provided there is no expectation of difficult intubation. Meanwhile the search for the ideal neuromuscular blocking drug with a rapid onset but short duration of action has to continue.

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Intubating condition Variables		Clinically acceptable		Clinically unacceptable
		Excellent	good	Poor
Laryngoscopy		easy	fair	Difficult
Vocal cord	position	abducted	intermediate	closed
	movement	none	moving	closing
Reaction to intubation	Limb movements	none	slight	vigorous
	Cough	none	diaphragm	sustained(>30 sec)

Table 1[7,8]: CCC (Copenhagen Consensus Conference) rating scale

Intubating conditions: Excellent- All variables listed under excellent**. Good-**only variables listed under excellent and good. **Poor-** presence of any variable listed under poor.

Characteristics		Group-A	Group-B
Number		25	25
Mean age in yrs.		25.08 (range 20-35)	24.28 (range 19 – 34)
Mean weight in kg.		57.96 (range 48-70)	56.96 (range 47-71)
Gravida	Primi	3	6
	Multi	22	19
Previous caesarean section		19	17
Foetal presentation	Cephalic	24	25
	Breech	1	0

Table 2: Demographic characteristics

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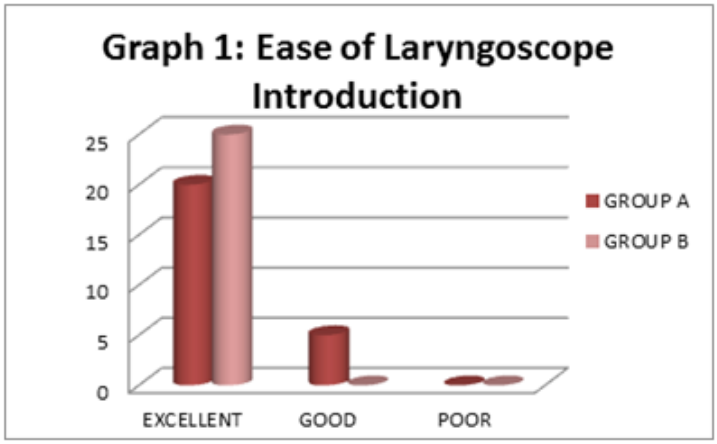
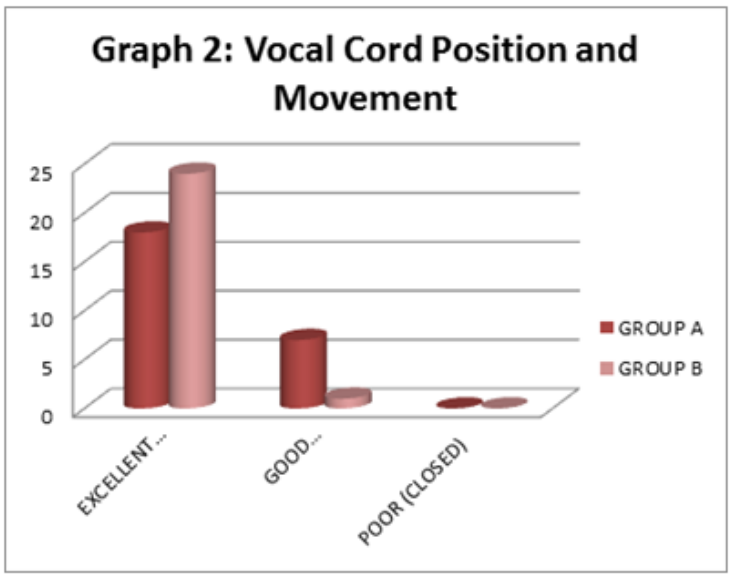
Intubation Condition	Group A (n=25)		Group B (n=25)	
	No	%	No	%
Excellent	11	44.0	22	88.0
Good	14	56.0	3	12.0

Table 3: Correlation of overall Intubation conditions in the two groups studied

Excellent intubating condition was significantly associated with Group B with $\chi 2=10.80$, P=0.001**
No patient came under poor category in both groups.

INTUBATING CONDITION PARAMETERS:





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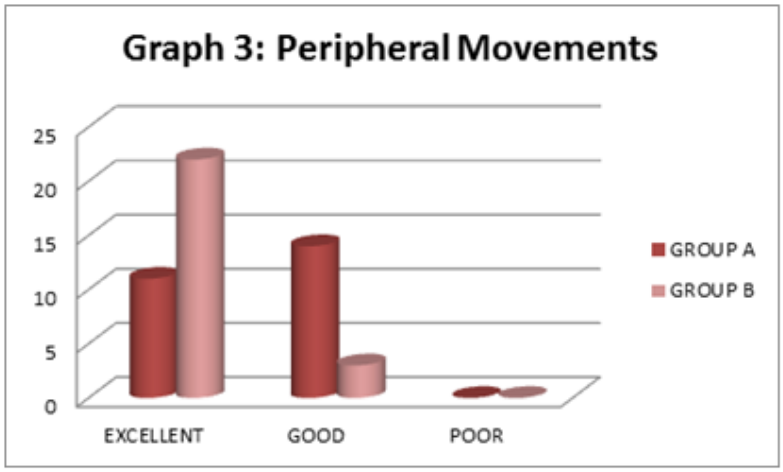

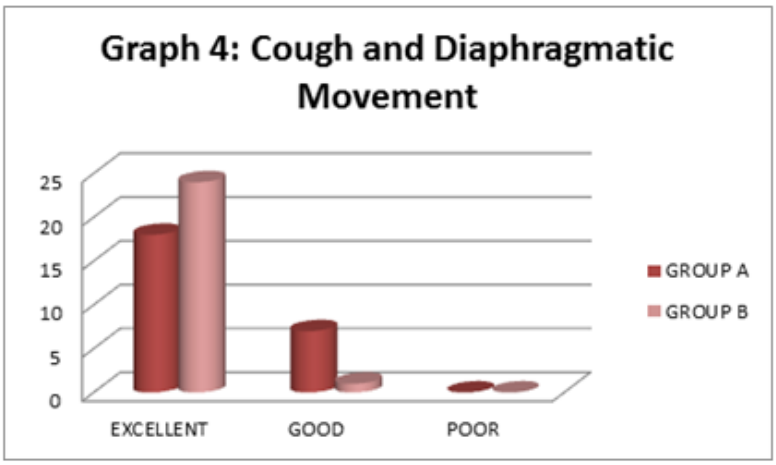

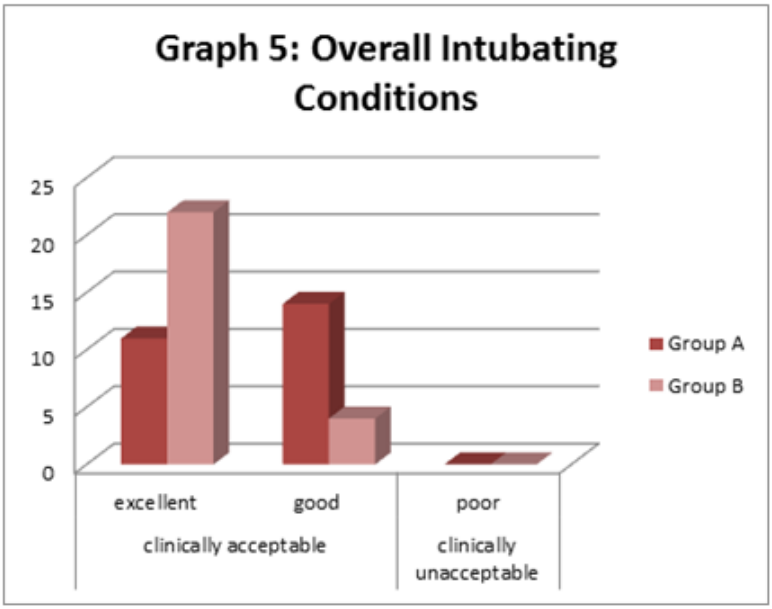

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