METHODOLOGY

40 patients of ASA grade I and II aged between 18-50 years posted for elective non ophthalmic surgery under general anaesthesia were included in this study. The study was carried out at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

Study Design: Randomized clinical trial.

Sample size: 40 patients.

Sample size calculation:

The sample size was calculated to keep the power of the study more than 90% and alpha error less than 0.01. The sample size was calculated to be 40 that is 20 in each group (i.e.Group R=20, Group S=20).

Inclusion Criteria:

1. Patients of American Society of Anaesthesiologists (ASA) grade I & II
2. Age group of 18 to 50 years.
3. Patients undergoing elective non ophthalmologic surgeries.
4. Patients with Mallampati grade 1& 2.

Exclusion criteria

1. Patients with ophthalmologic diseases.
2. Patients of ASA grade III & IV.
3. Patients with Mallampati grade 3& 4.

4. Patients undergoing ophthalmologic surgeries.
5. Patients with contraindications to Succinylcholine like patients with electrolyte abnormalities, burns etc.
6. Patients with head injury.

Methods:

Approval from institutional ethical committee was obtained.

After explaining the anaesthetic procedure, written informed consent for participation in the study was obtained from the patients.

40 Patients were allocated by computer generated randomization table into group S (Succinylcholine, n= 20) and group R (Rocuronium, n = 20).

A thorough pre-anaesthetic evaluation was carried out in all patients.

On the day of surgery, IV line secured with 18G cannula in a peripheral vein. Baseline IOP was measured using Schioetz tonometer after application of 4% Lignocaine in the right eye.

Preoperatively monitors like Pulse oximeter, ECG, Noninvasive blood pressure were attached and baseline heart rate and blood pressure were measured.

Patients were preoxygenated with 100% oxygen for three minutes. Patients were premedicated with IV Glycopyrrolate 0.005mg/kg, IV Midazolam 0.05mg/kg and IV Fentanyl 2 micrograms/kg. Patients were induced using IV Thiopentone 5mg/kg & IV Succinylcholine 1. 5mg/kg in the group S or with IV Thiopentone 5mg/kg & IV Rocuronium 0.9mg/kg in the group R. Laryngoscopy was done 60 seconds after the

muscle relaxant and endotracheal intubation with appropriate size endotracheal tube performed. Patients were maintained with oxygen, nitrous oxide, intermittent positive pressure ventilation and intermediate acting muscle relaxant i.e. vecuronium.

Intraocular pressure (IOP) was measured at baseline; 60 seconds after relaxant; 1minute, 3 minute and 5 minutes after intubation. Measurements of heart rate (HR), diastolic blood pressure (DBP), systolic blood pressure (SBP) were obtained at baseline, at induction and thereafter every 1 minute after intubation for 5 minutes.

Statistical analysis: The results were tabulated**;** A paired t test and two-way analysis of variance for repeated measurements (ANOVA) were used to analyse the changes in IOP.

RESULTS

The present study consisted of 40 patients in the age group of 18-50 years posted for non ophthalmic surgeries under general anaesthesia. The patients were divided randomly into two groups of twenty each using computer generated randomization table.

Group R consisted of twenty patients who received Rocuronium 0.9mg/kg and Group S consisted of twenty patients who received Succinylcholine 1.5mg/kg to facilitate endotracheal intubation.

Data was collected in both groups and observations of the analysed data are presented as mean ± standard deviation in the tabular form.

The demographic data of both the groups was as follows.

Table 4: Demographic data

	Group R	**Group S**	**P value**
Age in years	40.35±14.61	39 ±8.67	0.8754 (NS)
Gender (M/F)	10/10	9/11	0.337(NS)
ASA I	13	14	0.110(NS)
II	7	6	0.110(NS)
Weight in kg	52.65±11.55	58.10±6.51	0.0738(NS)

NS - Not Significant(P>0.05)

The student's t test was used to compare the demographic data between the 2 groups. There was no significant difference in the demographic data between the two groups. (p value >0.05) (Table 4)

The hemodynamic changes during induction, intubation and in the subsequent time periods of observation in the two groups were tabulated.(Table 5)

Table 5: Hemodynamic parameters of Group R & Group S

	B	**I**	**M_1**	**M_2**	**M_3**	**M_4**	**M_5**
SBP(mmHg)							
Group R	123.45	114.70	121.35	112.70	106.70	101.90	98.20
Group S	133.80	114.20	119.80	114.90	107.05	106.95	107.05
DBP(mmHg)							
Group R	67.20	69.55	72.55	65.00	59.85	57.70	53.55
Group S	76.05	65.00	67.95	65.70	61.75	63.20	63.70
HR(mmHg)							
Group R	72.60	78.45	87.60	90.20	89.25	88.35	84.65
Group S	79.60	81.40	86.30	86.30	82.50	82.45	80.00

[Systolic blood pressure(SBP), diastolic blood pressure(DBP) and heart rate(HR) in the Rocuronium group(Gr R) and Succinylcholine group(Gr S). B=baseline, I= 60 sec after relaxant, M_1-M_5=1 minute intervals after intubation for 5 min]

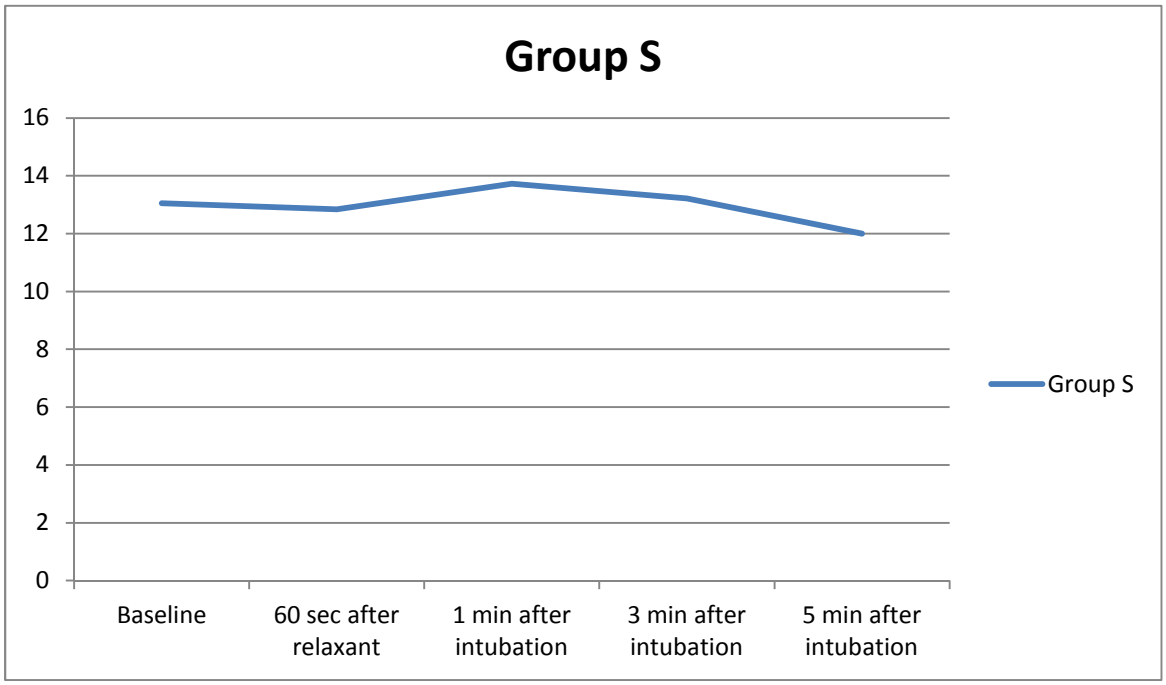
The IOP was recorded using Schioetz tonometer. The IOP readings were taken at baseline; 60 seconds after relaxant; 1min, 3min and 5 min after intubation in both Group R and Group S. The IOP readings have been tabulated as follows.

Table 6: Comparison of intraocular pressure in mm Hg between Group R and Group S at various periods (MeanïSD)

	Group R	Group S	P value
Baseline	13.22±1.10	13.05±1.62	0.6918
60 seconds after relaxant	10.43±1.33	12.84±2.63	0.0008
1 minute after intubation	11.92±1.44	13.73±2.42	0.0065
3 minutes after intubation	11.89±1.05	13.22±2.14	0.0168
5 minutes after intubation	12.83±0.94	12.91±1.44	0.8463

The baseline values of IOP in the two groups did not show any statistically significant difference ($P<0.05$). The IOP in Group R and Group S was compared using ANOVA and the difference in IOP between the groups 60 sec after relaxant, 1 min and 3 min after intubation was found to be significant ($P<0.05$); whereas 5 min after intubation it was not significant. (Table 6).

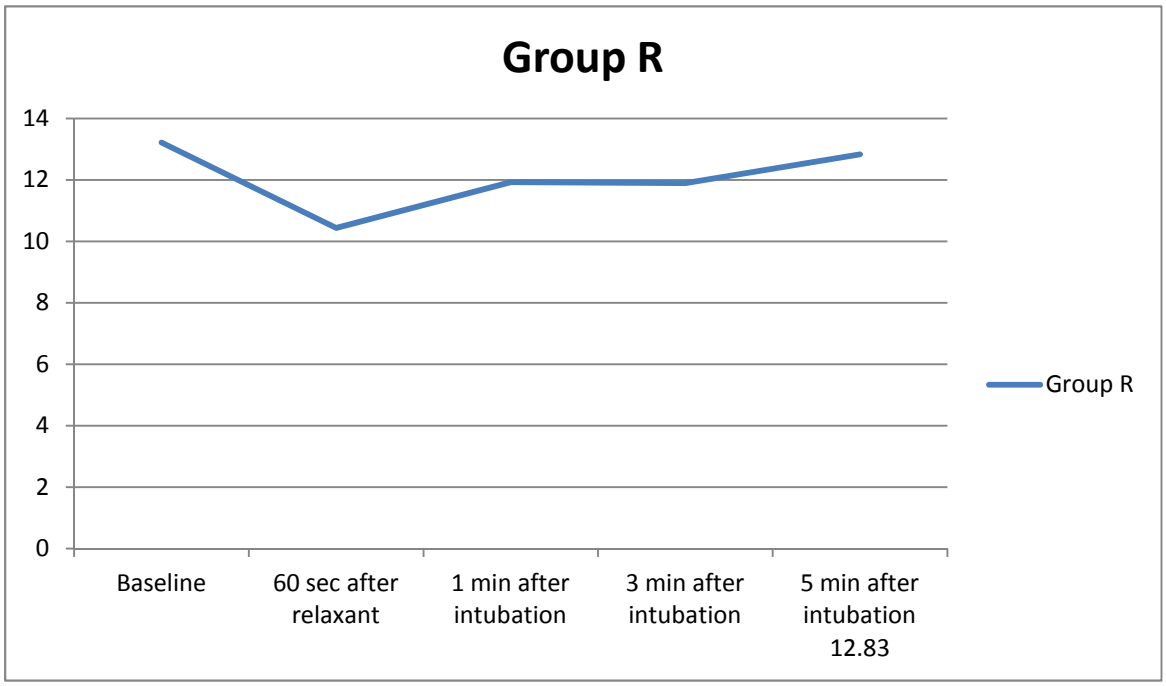
IOP readings (mean±SD) in group S at baseline, 60 sec after relaxant, 1 min, 2 min and 5 min after intubation were plotted (Graph 1).



Graph 1: Intraocular pressure Changes in Group S

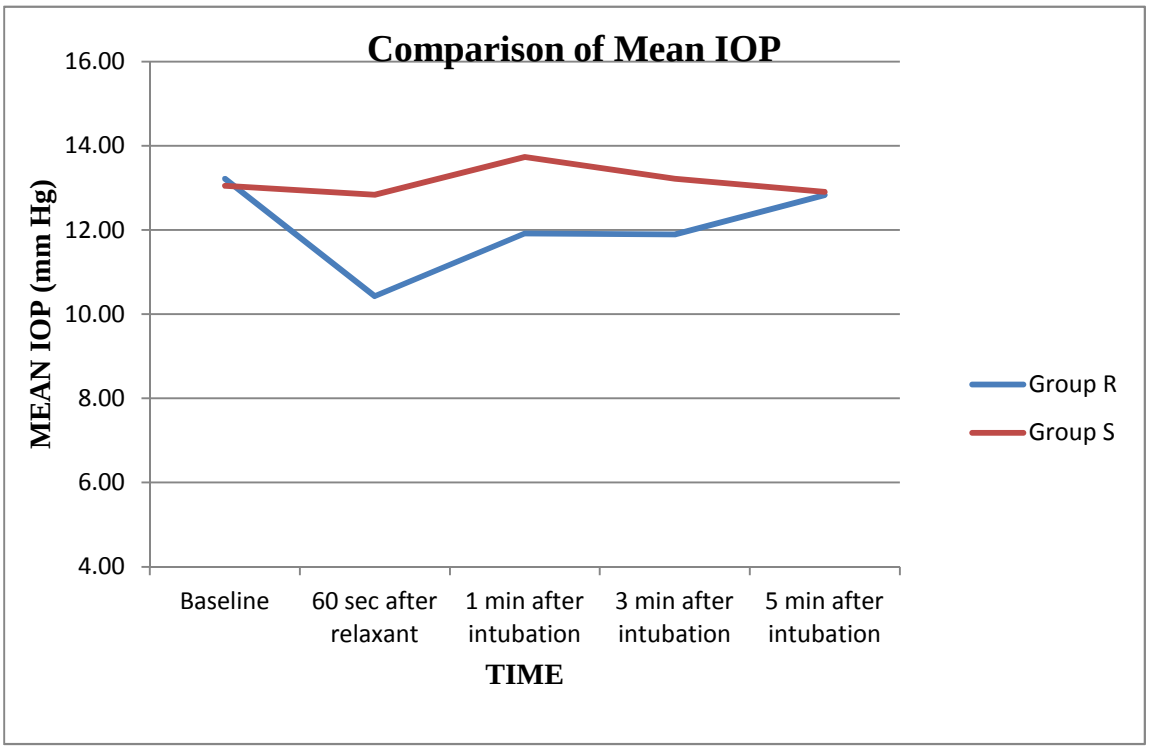
The baseline reading of IOP in Group S was (13.05±1.62) mmHg (mean±SD). At 60 sec after relaxant IOP remained near baseline with a value of (12.84±2.63). 1 min after intubation the rise in IOP was maximum with a value of (13.73±2.42). 3 min after intubation IOP showed a fall with a value of (13.22 ±2.14) but still remained higher than the baseline. 5 min after intubation the IOP showed a further fall coming close to the baseline with a value of (12.91±1.44) (Table 6 and Graph 1).

IOP readings (mean±SD) in group R at baseline, 60 sec after relaxant, 1 min, 3 min and 5 min after intubation were plotted (Graph 2).



Graph 2: Changes in IOP in Group R

The baseline reading of IOP in Group R was (13.22±1.10). The IOP showed a maximum fall with a value of (mean±SD) of (10.43±1.33) mmHg 60 seconds after relaxant. It increased to a value of (11.92±1.44) mmHg 1 minute after endotracheal intubation. It remained almost the same 3 minutes after intubation with a value of (11.89±1.05) mmHg, slowly rose towards baseline by 5 minutes after intubation with a value of (12.83±0.94) mmHg which was still below the baseline value (Table 6 and Graph 2).



Graph 3 : Comparison of Mean IOP between Group R and Group S

The mean IOP in the two groups was compared using unpaired t test.

There was a reduction in IOP one minute after administration of relaxant in Group R (10.43±1.33 mmHg) whereas it remained near baseline in Group S (12.84±2.63 mmHg). The difference was highly significant with a P value of 0.0008.

Endotracheal intubation resulted in a slight rise in IOP within 1 minute in both the groups. However, it did not reach baseline levels in Group R (11.92±1.44 mmHg) but was higher than baseline in Group S (13.73±2.42 mmHg) and the difference between the groups was highly significant with a P value of 0.0065.

At 3 min there was a significant fall in IOP as compared to 1 min after intubation and still remained below baseline in group R. In group S there was a fall in IOP at 3 min

as compared to 1 min after intubation but was still higher than group R. The difference in IOP when compared was found to be highly significant with a p value of 0.0168.

At 5 min the IOP gradually increased towards baseline levels with value of (12.83±0.94) in group R. The IOP gradually decreased towards baseline (12.91±1.44 mmHg) in Group S (P= 0.8463 respectively). The difference in IOP was compared and was not found to be significant (Table 5).

DISCUSSION

The successful outcome in ophthalmic surgical procedures lies in good control of IOP during induction and perioperative period.

Normal IOP is approximately 12 to 20 mm Hg, with a diurnal variation of 2 to 3 mm Hg. The most important influences on IOP are aqueous humor dynamics, changes in choroidal blood volume (CBV), central venous pressure and extraocular muscle tone. Events such as coughing, straining, Valsalva maneuver or vomiting can cause transient, but significant increases in IOP.[77]

In general, narcotics, tranquilizers and anaesthetics reduce IOP. They relax extraocular muscle tone, depress the CNS (diencephalon), improve the outflow of aqueous humor, reduce aqueous production and lower venous and arterial blood pressure. Only Succinylcholine and Ketamine may increase IOP.

The anaesthetic management of the patient with a penetrating eye injury and a full stomach creates a dilemma. Rapid sequence induction with tracheal intubation is advisable, but the use of Succinylcholine is theoretically contraindicated as it produces an increase in IOP which could expel the ocular contents. It may be possible to delay surgery for a few hours, but following trauma, gastric emptying is not assured in the usual time-scale. In choosing a muscle relaxant for tracheal intubation, the risks for further damage to the eye must be weighed against the life-threatening dangers of pulmonary aspiration.[78]

During ocular sugery, the control of IOP is very vital and hence every attempt must be made to maintain the IOP at or below normal levels. A sudden rise in IOP during anaesthesia can cause considerable damage to the eye especially in a patient with penetrating eye injury. The rise in IOP during anaesthesia can be due to varied factors such as pressure from the face mask during preoxygenation or induction, hypoxia, hypercarbia and reflex blepharospam. All these factors can be well prevented if proper precautions are taken. Certain factors such as administration of premedication, induction of anaesthesia, administration of muscle relaxants especially Succinylcholine, stimuli of intubation and extubation also cause significant fluctuations in IOP. The effects of these factors should be well known to the anaesthesiologists, especially where intraocular surgeries are indicated.

Succinylcholine remains the drug of choice to provide good conditions for rapid intubation but is known to cause an increase in IOP following its administration. Succinylcholine causes a transient (4 to 6 minutes), but significant increase in IOP of 10 to 20 mm Hg. [78] Mechanisms postulated are tonic contraction of extraocular muscles, choroidal vascular dilation, and relaxation of orbital smooth muscle as well as the cycloplegic action of Succinylcholine.[32] Anaesthesiologists the world over, have tried various pretreatment methods to attenuate this rise in IOP with varying degrees of success. The pretreatment methods include defasciculating dose of non-depolarising neuromuscular blocking agents, Lignocaine, Nifedipine, Nitroglycerine and Diazepam. None of these methods has provided optimal control over IOP following Succinylcholine and tracheal intubation. [59to62]

Nondepolarising neuromuscular blockers such as Pancuronium, Vecuronium and Atracurium have been used for facilitating tracheal intubation but the delayed onset of action makes these drugs potentially dangerous in full stomach patients. Also these drugs do not avoid rise in IOP in response to laryngoscopy and intubation.

The need of a nondepolarising muscle relaxant with a faster onset of action comparable to that of Succinylcholine, with minimal side effects was fulfilled with Rocuronium. Rocuronium bromide is a newer aminosteroid-based nondepolarising muscle relaxant with shorter onset of action (within 1 minute at a dose of 0.9mg/kg which is comparable to Succinylcholine) and intermediate duration of action.

In our study, IOP was measured using Schioetz indentation tonometer, which is a simple and most suitable method for use in patients under anaesthesia. IOP readings were taken at baseline; 60 seconds after relaxant ; 1 min, 3 min and 5 min after intubation.

In our study we studied the effect of Rocuronium on IOP in comparison with Succinylcholine in 40 patients. Glycopyrrolate 0.005mg/kg IV, Midazolam 0.05mg/kg IV, Fentanyl 2μg/kg IV were given as premedication. Patients were induced with Thiopentone 5mg/kg for induction followed by either Succinylcholine 1.5mg/kg or Rocuronium 0.9mg/kg to facilitate endotracheal intubation.

In Rocuronium group, there was initial fall in IOP immediately after the administration of Rocuronium . Gradually IOP rose towards baseline but it did not touch the baseline even after 5 minutes post intubation. This finding is similar to the findings observed by Mitra et al[75], Chiu et al[74] and Malik P et al[76].

In our study, in Succinylcholine group pressor response to intubation was statistically comparable between the two groups (p=0.0061) and was similar to that observed by Chiu et al[74], Mitra et al[75] and Malik et al[76]. In our study there was an intraocular pressor response to intubation with a mean increase in IOP from baseline IOP (0.69±2.44 mmHg) in Succinylcholine group and IOP started falling towards baseline at 5 minute interval after the intubation. This finding was in contrast to the other studies where they had a significant change in IOP after laryngoscopy and intubation and this change persisted more than five minutes.

The mean change in hemodynamics (systolic blood pressure, diastolic blood pressure and heart rate) did not reach clinical significance in either group.

The results of this study showed that Rocuronium does not cause a significant increase in IOP, in fact causes a decrease in IOP whereas Succinylcholine causes an increase in IOP. Rocuronium hence appears to be the muscle relaxant of choice in patients with penetrating eye injuries especially where rapid sequence induction with tracheal intubation is required.

CONCLUSION

The results of this study showed that Rocuronium does not cause a significant increase in IOP, in fact causes a decrease in IOP whereas Succinylcholine causes an increase in IOP. Rocuronium hence appears to be the muscle relaxant of choice in patients with penetrating eye injuries especially where rapid sequence induction with tracheal intubation is required.

SUMMARY

The present study 'Comparison of the effect of Rocuronium and Succinylcholine on Intraocular pressure during General Anaesthesia – A Randomized Clinical Trial' was carried out in the Department of Anaesthesiology , KLES Dr. Prabhakar Kore Hospital and MRC, Belgaum .

40 patients of either sex, in the age group of 18-50 years scheduled to undergo elective non-ophthalmologic surgeries under general anaesthesia after meeting inclusion and exclusion criteria were enrolled for the study. The patients were randomly allocated to two groups of 20 each. In group R patients received Rocuronium 0.9mg/kg and in group S patients received Succinylcholine 1.5mg/kg for tracheal intubation following standard induction protocol. IOP was then measured using Schioetz tonometer at baseline; 60 seconds after relaxant; 1minute, 3minute and 5 minutes after intubation. The results were tabulated**;** A paired t test and two-way analysis of variance for repeated measurements (ANOVA) were used to analyse the changes in IOP.

The results of this study showed that Rocuronium does not cause a significant increase in IOP, in fact causes a decrease in IOP whereas Succinylcholine causes an increase in IOP.. Rocuronium hence would appear to be the muscle relaxant of choice in patients with penetrating eye injuries especially when rapid sequence induction with tracheal intubation is required.

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INFORMED CONSENT FORM

You Mr/Mrs/Ms. _____ I.P. No._____are being asked to participate in the research study titled **" COMPARISON OF THE EFFECT OF ROCURONIUM AND SUCCINYLCHOLINE ON INTRAOCULAR PRESSURE DURING GENERAL ANAESTHESIA: A RANDOMISED CLINICAL TRIAL."** conducted by Dr Dewan Roshan Singh Postgraduate Student, Department of Anaesthesiology, JNMC, Belgaum. You are eligible after looking into inclusion criteria. You read this form and ask any questions you may have before agreeing to participate.

RESEARCH BEING DONE

TO COMPARE THE EFFECT OF ROCURONIUM AND SUCCINYLCHOLINE ON INTRAOCULAR PRESSURE DURING GENERAL ANAESTHESIA.

Purpose of research

- To assess the change in intraocular pressure when rocuronium and succinylcholine are used during general anaesthesia.

Procedures involved

You will be randomly allocated either into group S (Succinylcholine) or group R (Rocuronium). If you are in group S then induction of anaesthesia will be done with thiopentone and succinylcholine. If you are in the group R induction

will be done with thiopentone and rocuronium. Subsequently endotracheal intubation will be done in both the groups.

Heart rate, blood pressure and intraocular pressure are to be recorded at baseline i.e. before the start of the operation in the recovery, at induction, then at intervals of one minute after intubation for five minutes.

Potential risks and discomforts

- No serious side effects

Benefits

The study may not be directly beneficial to you but it may be beneficial to the community at large.

Decline from participation

You have the option to decline from participation in the study without any discrimination and you will be treated as per the existing protocol of your condition.

New information

All information collected during the study from participant will be told as and when required.

Privacy and confidentiality

Privacy of individual will be respected & any information about you or provided by you during the study will be kept strictly confidential.

Injury as a result of participation

There will neither be any compensation to or for the patient and his or her relatives nor there any monetary benefits for the damage incurred.

Costs of participation in this research

Participation is free of cost.

Reimbursement for any expenses for participation in research

No reimbursement for any of your expenditures.

Withdrawal or be removed

To start with as the participation is voluntary so is the decision to withdraw. Such a step will not alter the participant's management by any staff in hospital. Researcher can remove you from the study if circumstances arise.

Whom to contact

For any information about the study during the study or after that may be collected from

- Dr. V.D. Patil, Principal, JNMC, Belgaum.

- Dr. Vandana Gogate M.D. Associate Professor, Department of Anaesthesiology, JNMC, Belgaum. Ph.No. 9844083030
- Dr. Dewan Roshan Singh, Postgraduate student in Anaesthesiology, JNMC, Belgaum Ph.No. 9986694500

Signature of the participant or legally authorized person

Participants name

Signature:

Witness name

Signature:

Date:

Place:

PROFORMA

"COMPARISON OF THE EFFECT OF ROCURONIUM AND SUCCINYLCHOLINE ON INTROCULAR PRESSURE DURING GENERAL ANAESTHESIA: A RANDOMISED CLINICAL TRIAL"

Patients Name : I.P.No:

Age : Weight: Sex:

Occupation : Date of operation:

Address :

Anaesthesiologist:

PRE-ANAESTHETIC EVALUATION:

Chief Complaints:

Past History:

a) Hypertension, Diabetes, Asthma, Epilepsy, Drug allergy

b) Drug therapy

c) Previous exposure to anaesthesia.

Family History:

General Physical Examination

Pallor/Icterus/Clubbing/Lymphadenopathy/Odema

P.R: B.P.:

R.R:

Musculoskeletal System Examination:

Jaw movements: Teeth:

Airway assessment: Spine:

Systemic Examination:

a. R.S. b. CNS

c. C.V.S. d. GIT

Investigations:

Hb%

Urine routine

Serum electrolytes

Any others

Pre operative physical status: ASA grade I II

Inclusion criteria

2. Patients of American Society of Anaesthesiologists (ASA) grade 1 and 2 between the age group of 18 to 60 years.
3. Patients undergoing elective non ophthalmologic surgeries.
4. Patients with Mallampati grade 1 & 2.

Exclusion criteria:

1. Patients with ophthalmologic diseases.
2. Patients of ASA grade 3 & 4.
3. Patients with Mallampati grade 3 & 4.
4. Patients undergoing ophthalmologic surgeries.

5. Patients with contraindications to succinylcholine like patients with electrolyte abnormalities, burns.
6. Patients with head injury.

Diagnosis

Proposed surgery

Patients will be allocated by computer generated randomization into group S (Succinylcholine) and group R (Rocuronium).

On the day of surgery, IV line secured with 18G cannula in a peripheral vein.

Preoperative baseline

Heart rate

Blood pressure

Intraocular pressure

Monitors attached:

Pulse oximeter Non invasive blood pressure

ECG

Patients are to be preoxygenated with 100% oxygen for three minutes. Patients are to be premedicated with Glycopyrrolate 0.005mg/kg, Midazolam 0.05mg/kg and Fentanyl 2 micrograms/kg. Patients are to be induced using Thiopentone 5mg/kg & Succinylcholine 1. 5mg/kg in the group S or with Thiopentone 5mg/kg & Rocuronium 0.9mg/kg in the group R. Laryngoscopy to be done 60 seconds after the muscle relaxant and endotracheal intubation to be done with appropriate size endotracheal tube. Patients

are to maintained with Oxygen, Nitrous oxide, intermittent positive pressure ventilation and intermediate acting muscle relaxant i.e. Vecuronium.

Schioetz tonometer is to be used to measure intraocular pressure after topical application of 4% xylocaine and the reading obtained in the right eye at each measurement to be recorded. Measurements of heart rate (HR), diastolic blood pressure (DBP), systolic blood pressure (SBP), intraocular pressure (IOP) are to be obtained at baseline, at induction and thereafter every 1 minute after intubation for 5 minutes.

The recordings are to be tabulated as follows

IOP changes

	Group R	**Group S**
Baseline		
60 sec after relaxant		
After intubation 1 min		
3 min		
5 min		

Hemodynamic changes

	B	**I**	**M_1**	**M_2**	**M_3**	**M_4**	**M_5**
SBP(mmHg) Gr R Gr S							

DBP(mmHg) Gr R Gr S							
HR(mmHg) Gr R Gr S							

[Systolic blood pressure(SBP), diastolic blood pressure(DBP), heart rate(HR) and intraocular pressure(IOP) in the Rocuronium group(Gr R) and Succinylcholine group(Gr S). B=baseline, I=at induction, M_1-M_5=1 minute intervals after intubation for 5 min]

Signature of the Staff incharge:

MASTER CHART 1: Group R- Demographic data, intubation time, intubating conditions & changes in intraocular pressure										
S No.	Age	Sex	Weight	ASA	Intubating conditions	Changes in IOP				
			(Kg)		conditions	Baseline	1 min after relaxant	1 min after intubation	3 min after intubation	5 min after intubation
1	45	M	70	1	Excellent	14.2	10.2	12.2	12.2	14.6
2	22	M	57	1	Excellent	12.2	10.2	14.6	12.2	12.2
3	50	F	72	2	Excellent	13.4	8.5	10.2	11.2	13.4
4	25	F	60	1	Excellent	13.4	10.2	11.2	12.2	13.4
5	32	F	54	2	Excellent	12.2	12.2	13.4	12.2	12.2
6	60	F	31	1	Good	14.6	10.2	11.2	11.2	13.4
7	36	M	60	1	Excellent	13.4	11.2	12.2	13.4	13.4
8	42	M	62	2	Excellent	13.4	11.2	12.2	13.4	13.4
9	35	F	41	1	Excellent	13.4	11.2	12.2	12.2	13.4
10	60	F	40	2	Excellent	12.2	10.2	11.2	11.2	12.2
11	18	M	51	1	Excellent	13.4	12.2	12.2	12.2	13.4
12	28	F	50	1	Excellent	14.6	9.4	10.2	10.2	11.2
13	58	M	48	2	Excellent	13.4	8.5	10.2	10.2	11.2
14	52	M	56	1	Excellent	10.2	7.8	10.2	10.2	11.2
15	35	M	52	1	Excellent	14.6	13.4	14.6	13.4	13.4
16	22	M	57	1	Excellent	12.2	10.2	14.6	12.2	12.2
17	25	F	60	1	Excellent	13.4	10.2	11.2	12.2	13.4
18	60	F	30	1	Good	14.6	10.2	11.2	11.2	13.4
19	42	M	62	2	Excellent	13.4	11.2	12.2	13.4	13.4
20	60	F	40	2	Excellent	12.2	10.2	11.2	11.2	12.2

MASTER CHART 2: Group S-Demographic data, intubating conditions & changes in intraocular pressure

S No.	Age	Sex	Weight	ASA	Intubating	Changes in IOP					
			(kg)		conditions	Baseline	1 min after relaxant	1 min after intubation	3 min after intubation	5 min after intubation	
1	34	F	60	1	Excellent	10.2	12.2	13.4	11.2	11.2	
2	46	M	61	1	Excellent	12.2	14.6	15.9	14.6	12.2	
3	59	M	58	2	Excellent	13.4	15.9	14.6	14.6	13.4	
4	30	M	65	1	Excellent	11.2	13.4	13.4	12.2	11.2	
5	45	M	71	1	Excellent	12.2	10.2	11.2	11.2	11.2	
6	42	F	60	1	Excellent	14.6	12.2	13.4	13.4	14.6	
7	42	F	62	1	Excellent	14.6	17.3	18.9	15.9	14.6	
8	32	F	55	1	Excellent	13.4	8.5	10.2	10.2	12.2	
9	34	F	45	1	Excellent	14.6	11.2	11.2	11.2	12.2	
10	42	F	54	1	Excellent	12.2	10.2	11.2	11.2	12.2	
11	53	F	52	2	Excellent	14.6	14.6	15.9	15.9	14.6	
12	31	M	65	2	Excellent	10.2	12.2	13.4	13.4	12.2	
13	24	F	45	1	Excellent	14.6	17.3	15.9	15.9	14.6	
14	42	M	54	2	Excellent	13.4	12.2	14.6	14.6	13.4	
15	47	M	60	2	Excellent	15.9	15.9	17.3	17.3	15.9	
16	46	M	61	1	Excellent	12.2	14.6	15.9	14.6	12.2	
17	30	M	65	1	Excellent	11.2	13.4	13.4	12.2	11.2	
18	42	F	60	1	Excellent	14.6	12.2	13.4	13.4	14.6	
19	32	F	55	1	Excellent	13.4	8.5	10.2	10.2	12.2	
20	42	F	54	2	Excellent	12.2	10.2	11.2	11.2	12.2	

MASTER CHART 3: Group R-Changes in Systolic & Diastolic blood pressure															
		Systolic blood pressure							Diastolic blood pressure						
S. No.	Baseline	1 min after relaxant	Minutes after intubation					Baseline	1 min after relaxant	Minutes after intubation					
			1	2	3	4	5			1	2	3	4	5	
1	134	114	129	110	89	88	90	76	68	76	66	37	37	37	
2	123	129	139	115	105	101	97	56	67	66	52	47	45	43	
3	147	113	126	109	116	112	101	82	67	77	55	73	69	52	
4	116	128	140	130	123	111	103	72	99	85	76	64	60	52	
5	110	105	117	100	96	101	95	66	60	67	56	53	52	48	
6	103	98	108	110	95	86	86	41	56	60	54	48	41	41	
7	109	106	94	88	82	82	81	74	63	55	51	54	51	51	
8	118	109	127	107	105	109	105	84	78	87	70	69	78	74	
9	140	144	107	107	100	96	92	79	79	81	78	54	51	47	
10	141	106	113	110	97	92	90	66	67	70	65	~~63~~	~~56~~	~~52~~	
11	127	130	150	160	149	130	113	37	41	72	67	57	~~46~~	37	
12	112	99	93	90	88	85	87	62	67	60	56	55	54	58	
13	114	125	127	126	127	123	119	69	84	79	84	79	77	76	
14	142	100	105	104	124	111	111	91	66	80	80	98	88	87	
15	132	118	125	116	113	112	113	70	62	68	73	55	69	54	
16	123	129	139	115	105	101	97	56	67	66	52	47	45	43	
17	116	128	140	130	123	111	103	72	99	85	76	64	60	52	
18	103	98	108	110	95	86	86	41	56	60	54	48	41	41	
19	118	109	127	107	105	109	105	84	78	87	70	69	78	74	
20	141	106	113	110	97	92	90	66	67	70	65	63	56	52	

MASTER CHART 4: Group S-Changes in Systolic & Diastolic blood pressure															
		Systolic blood pressure							Diastolic blood pressure						
S. No.	Baseline	1 min after relaxant	Minutes after intubation					Baseline	1 min after relaxant	Minutes after intubation					
			1	2	3	4	5			1	2	3	4	5	
1	130	118	127	109	107	105	109	86	84	87	78	70	69	78	
2	107	104	119	112	100	100	119	58	59	59	54	52	52	77	
3	183	133	129	128	96	96	83	91	69	88	75	65	59	54	
4	126	122	114	115	109	109	106	66	68	49	58	58	56	56	
5	123	118	121	106	95	95	97	74	90	89	78	73	72	72	
6	136	98	124	116	98	98	94	72	55	54	60	58	56	58	
7	179	113	134	159	137	137	125	87	69	78	82	66	65	58	
8	115	118	114	107	115	115	115	75	78	90	72	64	87	80	
9	121	98	92	99	88	88	90	75	38	34	31	34	31	31	
10	148	127	136	130	113	113	106	87	60	78	78	78	63	55	
11	134	132	138	101	104	104	109	69	72	67	66	61	81	70	
12	139	135	127	126	128	128	128	83	71	85	82	57	75	80	
13	144	98	110	104	106	106	112	87	54	57	54	62	66	62	
14	125	100	98	90	96	96	102	74	57	54	60	65	60	60	
15	134	101	106	116	114	114	106	79	56	60	64	62	58	57	
16	107	104	119	112	100	100	119	58	59	59	54	52	52	77	
17	126	122	114	115	109	109	106	66	68	49	58	58	56	56	
18	136	98	124	116	98	98	94	72	55	54	60	58	56	58	
19	115	118	114	107	115	115	115	75	78	90	72	64	87	80	
20	148	127	136	130	113	113	106	87	60	78	78	78	63	55	
MEAN	133.80	114.20	119.80	114.90	107.05	106.95	107.05	76.05	65.00	67.95	65.70	61.75	63.20	63.70	
S.D.	20.06	13.07	12.47	14.76	11.73	11.74	11.58	9.75	12.09	17.13	12.85	9.77	13.10	12.68	
IT'S PAIRED t TEST :		0.0002 S	0.0010 S	4.48E-06 S	3.14E-06 S	2.96E-06 S	6.54E-05 S		0.0017 S	0.0124 S	0.0002 S	9.13E-07 S	0.0004 S	2.72E-03 S	
TEST TO COMPARE TWO GROUPS :		0.032641 S	0.969571 NS	0.686713 NS	0.589633 NS	0.875833 NS	0.183092 NS	0.028021 S	0.0242 S	0.206461 NS	0.251102 NS	0.858565 NS	0.604352 NS	0.199524 NS	0.044322 S

MASTER CHART 5: Group R-Changes in Mean blood pressure & Heart rate															
	Mean blood pressure							Heart rate							
S.No.	Baseline	1 min	Minutes after intubation					Baseline	1 min	Minutes after intubation					
		after							after						
		relaxant	1	2	3	4	5		relaxant	1	2	3	4	5	
1	106	95	105	92	64	64	64	90	102	112	118	108	107	100	
2	82	91	106	76	73	69	66	79	98	110	110	96	92	88	
3	104	92	102	87	96	91	71	62	70	70	80	90	94	94	
4	82	112	106	99	97	82	75	82	76	96	102	104	102	94	
5	89	82	92	78	78	79	78	69	90	104	90	106	100	91	
6	84	79	83	77	78	68	68	62	67	90	96	91	91	112	
7	84	72	67	67	61	65	65	59	78	81	80	80	82	85	
8	97	90	101	82	82	90	85	80	91	93	83	98	98	82	
9	103	102	68	61	72	70	63	77	82	72	74	64	64	64	
10	96	106	87	84	76	68	64	57	58	68	68	64	64	60	
11	71	79	110	116	100	88	75	64	66	64	112	110	104	78	
12	87	67	60	56	55	54	58	60	64	74	70	72	74	74	
13	84	98	95	98	95	93	86	65	76	75	72	72	64	63	
14	110	75	68	70	84	79	77	105	92	95	100	95	100	94	
15	96	93	93	96	89	91	83	81	69	91	90	82	84	78	
16	82	91	106	76	73	69	66	79	98	110	110	96	92	88	
17	82	112	106	99	97	82	75	82	76	96	102	104	102	94	
18	84	79	83	77	78	68	68	62	67	90	96	91	91	112	
19	97	90	101	82	82	90	85	80	91	93	83	98	98	82	
20	96	106	87	84	76	68	64	57	58	68	68	64	64	60	

MASTER CHART 6: Group S-Changes in Mean blood pressure & Heart rate															
	Mean blood pressure							Heart rate							
S.No.	Baseline	1 min	Minutes after intubation					Baseline	1 min	Minutes after intubation					
		after							after						
		relaxant	1	2	3	4	5		relaxant	1	2	3	4	5	
1	103	97	101	90	82	82	86	73	83	93	91	83	77	82	
2	116	77	77	78	73	73	93	68	72	74	74	66	70	84	
3	115	91	105	91	81	69	65	83	78	82	90	86	88	76	
4	113	96	77	90	89	90	88	74	57	78	75	74	78	63	
5	93	72	73	61	57	55	58	68	96	100	100	97	94	96	
6	94	65	82	82	74	74	72	89	104	94	92	84	86	82	
7	118	88	82	114	98	97	88	104	104	120	106	98	92	88	
8	89	91	98	85	79	98	94	68	74	85	88	85	90	88	
9	102	58	56	56	60	56	54	81	88	78	76	82	70	68	
10	118	99	82	108	93	93	95	88	86	90	92	95	92	88	
11	99	96	97	78	72	90	80	75	62	77	70	65	75	67	
12	110	93	103	97	91	99	95	104	102	88	104	114	101	99	
13	102	69	72	65	72	71	71	88	84	82	82	62	65	63	
14	102	81	73	70	72	70	77	70	65	80	85	80	85	80	
15	113	83	85	92	91	87	86	72	80	84	80	75	70	71	
16	116	77	77	78	73	73	93	68	72	74	74	66	70	84	
17	113	96	77	90	89	90	88	74	57	78	75	74	78	63	
18	94	65	82	82	74	74	72	89	104	94	92	84	86	82	
19	89	91	98	85	79	98	94	68	74	85	88	85	90	88	
20	118	99	82	108	93	93	95	88	86	90	92	95	92	88	

"COMPARISON OF THE EFFECT OF ROCURONIUM AND SUCCINYLCHOLINE ON INTRAOCULAR PRESSURE DURING GENERAL ANAESTHESIA: A RANDOMISED CLINICAL TRIAL"

DISSERTATION

BY

Dr. DEWAN ROSHAN SINGH

SUBMITTED TO
KLE UNIVERSITY, BELGAUM
KARNATAKA
IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR THE

MASTER DEGREE
IN
ANAESTHESIOLOGY

UNDER THE GUIDANCE OF

Dr. VANDANA GOGATE M.D.

ASSOCIATE PROFESSOR

DEPARTMENT OF ANAESTHESIOLOGY,
JAWAHARLAL NEHRU MEDICAL COLLEGE,
BELGAUM – 10, KARNATAKA

MAY 2010

KLE UNIVERSITY, BELGAUM, KARNATAKA

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"COMPARISON OF THE EFFECT OF ROCURONIUM AND SUCCINYLCHOLINE ON INTRAOCULAR PRESSURE DURING GENERAL ANAESTHESIA: A RANDOMISED CLINICAL TRIAL"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. VANDANA GOGATE** **M.D.** Associate Professor, Department of Anaesthesiology, Jawaharlal Nehru Medical College, Nehru Nagar, Belgaum-590010.

Date :

Place : Belgaum **Dr. DEWAN ROSHAN SINGH**

KLE UNIVERSITY, BELGAUM, KARNATAKA

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **"COMPARISON OF THE EFFECT OF ROCURONIUM AND SUCCINYLCHOLINE ON INTRAOCULAR PRESSURE DURING GENERAL ANAESTHESIA: A RANDOMISED CLINICAL TRIAL"** *is a bonafide research work done by* **Dr. DEWAN ROSHAN SINGH** *under my guidance in partial fulfillment of the requirement for the award of the degree of* **M.D. (Anaesthesiology)**.

Dr. Vandana Gogate M.D.
Associate Professor,
Department of Anaesthesiology,
J. N. Medical College, Belgaum

Date :
Place : Belgaum

KLE UNIVERSITY, BELGAUM, KARNATAKA

ENDORSEMENT BY THE HOD, PRINCIPAL/HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled **"COMPARISON OF THE EFFECT OF ROCURONIUM AND SUCCINYLCHOLINE ON INTRAOCULAR PRESSURE DURING GENERAL ANAESTHESIA: A RANDOMISED CLINICAL TRIAL"** *is a bonafide research work done by* **Dr. DEWAN ROSHAN SINGH**, *under the guidance of* **Dr. VANDANA GOGATE** **M.D.** *Associate Professor, Department of Anaesthesiology, Jawaharlal Nehru Medical College, Nehru Nagar, Belgaum-590010.*

Dr. C. S. SANIKOP **M.D.**
Professor & Head,
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Date :
Place : Belgaum

Dr. V. D. PATIL **M.D. D.C.H**
Principal,
J. N. Medical College,
Nehru Nagar, Belgaum-590010.

Date :
Place : Belgaum

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Declaration by the Candidate

I hereby declare that the KLE University, Belgaum, Karnataka shall have the rights to preserve, use and disseminate this dissertation in print or electronic format for academic / research purpose.

Date :
Place : Belgaum

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Department of Anaesthesiology,
J. N. Medical College,
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Date:

Place: Belgaum

Dr. Dewan Roshan Singh

LIST OF ABBREVIATIONS

ASA	American Society of Anaesthesiologists
ED	Emergency Department
Group R	Rocuronium group
Group S	Succinylcholine group
SCh	Succinylcholine
HR	Heart rate
IOP	Intraocular Pressure
IV	Intravenous
kg	Kilogram
mg	Milligram
sec	seconds
min	Minutes
µg	Microgram
NMBA	Neuromuscular blocking agents
NS	Non significant
S	Significant
SD	Standard Deviation
RSI	Rapid Sequence Intubation

ABSTRACT

Background: Succinylcholine remains unsurpassed in providing ideal intubating conditions in the shortest time among all available neuromuscular blocking agents and hence is advocated as the drug of choice for rapid sequence endotracheal intubation. However, an increase in intraocular pressure (IOP) is one of its undesirable effects, especially in patients with open eye injury. Rocuronium is a nondepolarising neuromuscular blocking drug which provides rapid onset of action in a dosage of 0.9 to 1.2mg/kg. Absence of tonic contraction of extraocular muscles precludes any increase in IOP following administration of Rocuronium. However very few studies have studied the effect of Rocuronium on IOP. Hence this study was done to compare effect of Succinylcholine and Rocuronium on IOP during general anaesthesia.

Objective: To compare the effect of Rocuronium and Succinylcholine on intraocular pressure during general anaesthesia.

Study design: Randomized clinical trial.

Methods: 40 patients of either sex, in the age group of 18-50 years scheduled to undergo non-ophthalmologic surgeries under general anaesthesia after meeting inclusion and exclusion criteria were enrolled for the study. The patients were randomly allocated to two groups (Group R=20 patients) and (Group S=20 patients). In group S, patients received Succinylcholine 1.5mg/kg and in group R, Rocuronium 0.9mg/kg for tracheal intubation following standard induction protocol. IOP was measured using Schioetz tonometer at baseline, 60 sec after relaxant, 1min, 3min and 5min after intubation.

Results: While there was an increase in IOP with the administration of Succinylcholine, with Rocuronium there was a significant decrease in IOP.

Conclusion: Rocuronium does not cause a significant increase in IOP, in fact causes a decrease in IOP whereas Succinylcholine causes an increase in IOP. Rocuronium hence appears to be the muscle relaxant of choice in patients with penetrating eye injuries requiring rapid sequence induction with tracheal intubation.

Key words: Intraocular pressure; Rocuronium; Succinylcholine.

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INTRODUCTION

Ocular trauma, once described as the 'neglected disorder'[1], has recently been highlighted as a major cause of visual morbidity. World-wide, there are approximately 1.6 million people blind from eye injuries, 2.3 million bilateral visual impairement and 19 million with unilateral visual loss; this being the commonest cause of unilateral blindness today. The age distribution for the occurrence of serious ocular trauma is bi-modal, with the maximum incidence in young adults and a second peak in the elderly.[2,3] Both hospital and population based studies indicate a large preponderance of injuries affecting males.[4,5,6] So in addition to the impact on affected individuals there are profound social implications regarding the lost productivity by young men and requirement of caring facilities and rehabilitation for the elderly.

The spectrum of injuries ranges from very mild, non-sight threatening to extremely serious with potentially blinding consequences. The majority of injuries are minor, affecting the periorbital structures or the ocular surface such as corneal abrasions or superficial corneal foreign bodies. Only 2-3% of all eye injuries require hospital admission[5,7] and it is this small minority of cases that are of interest with regard to management and outcome. Over 10% of these people loose useful vision in the injured eye.

Serious eye injuries involving the orbit or intraocular structures are usually classified into those caused by blunt objects, sharp objects, small flying particles or burns. Penetrating injuries, whether due to large or small objects, are known to carry a poorer prognosis than contusional injuries. However, considerable disruption of the globe

may occur with severe blunt trauma which causes tearing of intraocular structures and diffuse changes secondary to energy absorption by the tissues.

In the immediate period after the injury, the rapidity with which treatment is instituted has an important effect on the final result. Speed is vital in penetrating injuries where measures to prevent secondary loss of intraocular tissues from the eye are required. Control of raised intraocular pressure after blunt trauma reduces the patient's pain and prevents secondary corneal and optic nerve damage.

An open eye should be repaired as soon as feasible and closure of a rupture or penetrating wound should always be attempted, even in an apparently disrupted eye, as it is impossible to give an accurate prognosis at the time of injury.

The repair of penetrating eye injuries is an emergency and requires general anaesthesia. The management of emergency anaesthesia requires balancing the need to prevent aspiration of gastric contents against prevention of sudden significant rises in intraocular pressure that may cause further eye damage and loss of vision. In addition, patients may also present with a potential difficult airway posing a further challenge to the anaesthesiologist.

Local anaesthesia is not recommended for repair of ruptured or lacerated globes for the following reasons:

1. Squeezing associated with peribulbar anaesthesia could result in the expulsion of intraocular contents.
2. The corneoscleral contour is often irregular preoperatively, making scleral perforation with the needle used for local anaesthesia more likely.

3. Repair of complicated scleral lacerations may require manipulation of extraocular muscles, which may cause significant discomfort in the locally anaesthetised eye.
4. Local anaesthesia may result in an increased orbital volume because of the volume of anaesthesia, which may cause deleterious pressure on the globe.
5. Retrobulbar hemorrhage is an unpredictable complication of retrobulbar anaesthesia and can be massive and occur rapidly. This may quickly result in the expulsion of intraocular contents if the eye is open at the time of hemorrhage.

Anaesthetic management of a full stomach patient with penetrating eye injury requiring emergency surgery is an anaesthetic dilemma. The above study which compares the effect of Succinylcholine and Rocuronium on IOP makes an attempt to manage the above scenario. Succinylcholine because of its rapid onset of action and good intubating conditions is the muscle relaxant of choice to facilitate endotracheal intubation in full stomach patients by rapid sequence induction. However Succinylcholine causes an increase in IOP which is particularly undesirable in patients with penetrating eye injury.

Rocuronium, a non-depolarising muscle relaxant while providing excellent intubating conditions has a quick onset of action which is comparable to Succinylcholine. It is hence particularly useful in full stomach patients. The above study seeks to determine the effect of Rocuronium on IOP. Very few studies are available which study the effect of Rocuronium on IOP. An absence of increase in IOP would be extremely useful in the management of patients with penetrating eye injuries.

AIMS AND OBJECTIVES

Aim of the study is to compare the effect of Rocuronium and Succinylcholine on intraocular pressure during general anaesthesia.

REVIEW OF LITERATURE

Anaesthesia for the patient with a penetrating eye injury has always been a challenge. During ocular surgery the control of IOP is very vital and every attempt must be made to maintain it within normal limits. A sudden increase in IOP during anaesthesia can cause considerable damage to the eye especially in a patient with a penetrating injury of the eye.

Succinylcholine remains unsurpassed in providing ideal intubating conditions.[68] However, an increase in intraocular pressure is one of its undesirable effects, [69] which may prove disastrous in patients with penetrating eye injury.

Various methods have been tried to attenuate the rise in IOP due to the administration of Succinylcholine such as use of defasciculating dose of non-depolarizing muscle relaxants before Succinylcholine, self taming, Diazepam, Lidocaine, Nifedipine and Alfentanyl but the results were found to be inconsistent. [46,47,48,51,52,56,58]

The search for a nondepolarising muscle relaxant with a quicker onset resulted in the development of Rocuronium. Rocuronium is the first nondepolarising muscle relaxant having an onset time as short as that of Succinylcholine without the adverse effects associated with succinylcholine. Various studies have been conducted to compare the intubating conditions provided by Rocuronium and Succinylcholine.

Perry J, Lee J, Wells G in the year 2002 in a Cochrane Database Review attempted to determine if Rocuronium creates comparable intubating conditions to Succinylcholine during rapid sequence intubation. They concluded that Succinylcholine

created superior intubating conditions when compared with Rocuronium. Using the less stringent outcome, clinically acceptable intubation conditions, the two agents were not statistically different. Intubation conditions were found satisfactory with both the agents.[70]

Huizinga AC et al in the year 1992 investigated the intubating conditions and neuromuscular blocking profile following 600μg/kg Rocuronium as compared to 1.5 mg/kg Succinylcholine. Rocuronium produced good to excellent intubating conditions at 60 as well as 90 seconds after administration. Intubating conditions following Succinylcholine were comparable with those following Rocuronium. The results indicated that Rocuronium may replace Succinylcholine in procedures in which rapid sequence induction is required.[71]

Some studies have been done to assess the intubating conditions using different doses of Rocuronium as compared to Succinylcholine.

Magorian T, Flannery KB, Miller RD et al in the year 1993 compared Rocuronium with Succinylcholine and Vecuronium for rapid-sequence induction of anaesthesia. Fifty patients, ASA Grade I-III, were randomly designated to receive one of three intravenous doses of Rocuronium (0.6, 0.9 and 1.2mg/kg), Vecuronium (0.1mg/kg) or Succinylcholine (1.0mg/kg). Sixty seconds after receiving a muscle relaxant, intubation of the trachea was attempted. Neuromuscular monitoring was established before administration of the muscle relaxant. Onset times for patients receiving 0.9mg/kg and 1.2mg/kg Rocuronium and Succinylcholine were similar. Onset times for the groups given 0.6mg/kg Rocuronium and Vecuronium were significantly longer. Clinical

duration of action was longest with 1.2mg/kg Rocuronium, similar with 0.6 and 0.9 mg/kg Rocuronium, and Vecuronium, and least with Succinylcholine. They concluded that there is a dose-dependent decrease in onset time with Rocuronium. The onset times for the two larger doses of Rocuronium were similar to that for Succinylcholine, but clinical duration of action with Rocuronium was significantly longer. The brief onset time achieved with Rocuronium indicates that administration of 0.9-1.2 mg/kg is an acceptable alternative to Succinylcholine for rapid-sequence induction of anaesthesia.[72]

Subsequently, Heier T and Caldwell JE in the year 2000 determined the dose of Rocuronium that gives a high probablility of achieving perfect conditions for rapid (within 60 seconds) tracheal intubation by administering a range of doses of Rocuronium, some larger than used previously. Sixty adults, anaesthetized with thiopental 4 mg/kg IV and Alfentanyl 10μg/kg IV, received Rocuronium 0.4 to 2.0 mg/kg IV. They estimated the doses giving 90% and 95% probability of achieving perfect intubation. Rocuronium 1.85 mg/kg and 2.33 mg/kg gave respectively 90% and 95% probability of perfect intubating conditions. They concluded that, it is possible to achieve perfect intubating conditions with large doses of Rocuronium, but the long duration of action and expense may limit the usefulness of the technique. [73]

The management of anaesthesia in emergency situations such as penetrating eye injuries requires balancing the need to prevent aspiration of gastric contents against prevention of sudden significant rises in intraocular pressure that may cause further eye damage and loss of vision. This brought about the interest of investigators to study the effect of Succinylcholine and Rocuronium on intraocular pressure.

Chiu et al in the year 1999 compared the effect of Rocuronium and Succinylcholine on intraocular pressure (IOP) during rapid sequence induction of anaesthesia using Propofol and Fentanyl, in a randomized, double-blind study. They studied 30 adult patients, allocated to one of two groups. Anaesthesia was induced with Fentanyl 2μg/kg and Propofol until loss of verbal response. This was followed by Succinylcholine 1.5mg/kg (group S; n=15) or Rocuronium 0.9mg/kg (group R; n=15). Laryngoscopy was performed 60 seconds later. IOP, mean arterial pressure (MAP) and heart rate (HR) were measured before induction, immediately before intubation and every minute after intubation for 5 minutes. A Keeler Pulsair air impulse tonometer was used to measure IOP and the mean of two readings obtained in the right eye at each measurement time was recorded. IOP in the Succinylcholine group was significantly greater that that in the Rocuronium group ($P<0.001$). Intubating conditions were equally good in both groups. They concluded that rapid sequence induction of anaesthesia using Propofol Fentanyl and Rocuronium did not cause as great an increase in IOP as Succinylcholine and may be an alternative in open eye injury cases.[74]

In a similar study Mitra S, Gombar KK and Gombar S in the year 2002 compared the effects of Rocuronium (0.6 mg/kg) on intraocular pressure with that of Succinylcholine (1.5mg/kg) (n=20 each) following premedication with tab diazepam and induction with Propofol (2mg/kg). [75]Upon induction, the fall in IOP in both the groups was significant ($p<0.05$), but it increased significantly after laryngoscopy and intubation in the Succinylcholine group only, reaching a peak of 16 mmHg at 2 minutes, a mean rise of IOP by 4 mmHg. In contrast, IOP values never exceeded baseline values in the Rocuronium group. IOP values remained significantly below baseline at 1,4 and 5

minutes after induction. Thus they concluded, in comparison to Succinylcholine, Rocuronium 0.6mg/kg did not produce any rise in intraocular pressure.

Subsequently, Malik P et al in the year 2004 compared Succinylcholine and Rocuronium in 40 patients.[76] Patients in Group 1 received Succinylcholine 1.5mg/kg and in Group 2, Rocuronium 0.9mg/kg for tracheal intubation after induction with Thiopentone 5mg/kg. There was a significant increase in intraocular pressure with administration of Succinylcholine which further increased after tracheal intubation and remained elevated up to five minutes after tracheal intubation ($p<0.001$). With Rocuronium, there was a significant decrease in intraocular pressure and it remained lower than the baseline in the post intubation period ($p<0.001$). They concluded that Rocuronium in a dose of 0.9mg/kg provides good to excellent intubating conditions comparable to that of Succinylcholine and is a suitable agent for tracheal intubation in patients undergoing elective and emergency ophthalmic surgery where rise in intraocular pressure is undesirable.

Hence this study was undertaken to compare the effect of Succinylcholine and Rocuronium on IOP.

PHYSIOLOGY OF INTRAOCULAR PRESSURE (IOP)

The normal value of IOP is in the range of 12 to 20 mmHg. [77] The maintainance of IOP in this range is essential for preservation of corneal curvature and proper refractive index. The main physiologic determinant of IOP is the dynamic balance between the production of aqueous humour, a watery, clear fluid in the ciliary body of the posterior chamber and its drainage into the episcleral venous system via the spaces of Fontana and the canal of Schlemm at the iridocorneal angle. Several minor diurnal variations in IOP of the order of 2-3mmHg are common, with higher readings being noted early in the morning.

Three major categories of factors which affect IOP during anaesthesia include:

a) Aqueous humour fluid dynamics
b) Choroidal blood volume
c) Extraocular muscle tone and vitreous volume

a) Aqueous humour fluid dynamics

A rise in IOP may be due to increased production of aqueous humour, impaired drainage or both. Aqueous humour is a clear fluid with a pH of 7.1 to 7.2, a specific gravity of 1.003 and a viscosity of 1.025-1.040 relative to water. It has a low protein, urea and glucose content. The total volume of aqueous humour in each eye is approximately 300µl, five-sixth of this amount being present in the anterior chamber and the rest in the posterior chamber.

Two third of the aqueous humour is formed in the posterior chamber by the epithelial cells of the ciliary body by an active secretory process involving carbonic

anhydrase and cytochrome oxidase. The remaining one-third is formed in the anterior chamber by simple filtration through the anterior surface of the iris.

From the posterior chamber, aqueous humour circulates through the pupil, enters the anterior chamber, bathes the lens and cornea and exits via the trabecular meshwork in the angle of the anterior chamber between the peripheral cornea and iris. After its passage through the trabecular spaces of Fontana and the canal of Schlemm, aqueous humour enters the aqueous veins in the episcleral tissues, which drain into the orbital venous system and eventually into the cavernous sinus and the superior venacava. The outflow of aqueous humour through the canal of Schlemm is governed by the Hagen-Poiseuille relationship.

$$Q=\pi Pr^4 / 8l\eta$$

Where,

Q = flow of aqueous humour in unit time

π = A mathematical constant (π=3.142)

P = IOP – venous pressure

r = Radius of canal of Schlemm

l = Length of canal of Schlemm

η = The coefficient of viscosity of aqueous humour

It is apparent from the above formula that while the radius of the canal of Schlemm is the single most important determinant of outflow of aqueous humour, any rise in venous pressure has to be compensated by an equivalent (secondary) increase in IOP if constant outflow of aqueous is to be maintained, other factors remaining constant.

i) Effect of change of aqueous humour formation on IOP

Aqueous humour is formed both by ultrafiltration from plasma through the ciliary epithelium and by active secretion from these cells. It is difficult to measure its rate of formation and hence, the relative importance is poorly understood and central controlling areas have not been isolated. Decreases in systemic arterial pressure have been shown to depress aqueous formation only when reduced to levels incompatible with adequate perfusion.[8] Acetazolamide has a significant effect on aqueous formation.[9] The most important action of acetazolamide is inhibition of the enzyme carbonic anhydrase that is present on the nonpigmented cells of the ciliary process, where it plays an important role in formation of aqueous humour. It has been suggested that beta-adrenergic blockers decrease IOP by depressing aqueous formation, but evidence for this mechanism of action is still inconclusive.

ii) Effect of change of aqueous humour drainage on IOP

Drainage of aqueous humour occurs by two routes. The main route is entrance of aqueous humour into the anterior chamber via the pupil and hence laterally to the iridocorneal angle. From there most of the aqueous enters the canal of Schlemm by passing through three layers of mesh work that separate the anterior chamber from the canal. A smaller proportion of aqueous moves through the interstitial spaces of the ciliary muscle and leaves the eye through the substance of the sclera. Any obstruction along the drainage path can lead to increase in IOP. Resistance to outflow drainage is also influenced by adrenergic stimulation.[10] Alpha stimulation induces mydriasis, a decrease in IOP and increased tonographic outflow facility. Beta stimulation decreases IOP without affecting pupillary size or outflow facility. It was postulated that alteration of

blood flow through the ciliary processes was the main mechanism by which these various responses were affected.

b) Choroidal blood volume

Intraocular blood volume depends on a balance between the rate of blood inflow to and outflow from the eye. Factors known to affect IOP include arterial blood pressure oscillations (1 to 2 mmHg), central venous pressure, deep inspiration (up to 5 mmHg), changes in body posture and plasma oncotic pressure. Apart from this, the baseline intraocular blood volume depends on the degree of constriction of the intraocular blood vessels.

i) Effects of change of systemic arterial pressure on intraocular pressure

The choroid is a highly vascular structure. Its vasculature has a well-developed autoregulatory control resulting in the choroidal blood flow remaining constant over a wide range of perfusion pressures. A sudden increase in arterial blood pressure is followed by a transient, acute increase in IOP, until the outflow of aqueous humour accommodates the rise. Administration of vasopressors increases IOP but the extent of rise does not correlate with the concomitant rise in arterial pressure.

In primates, IOP approaches a value of zero when systolic arterial pressure falls to levels below 50-60 mmHg. When the globe is intact, any increase in the volume of choroid or aqueous humour within the relatively inelastic sclera envelope causes a sharp increase in IOP. If the globe is open, the volume changes may result in prolapse of the vitreous.

Moderate decreases in arterial pressure have a little effect on IOP. Below a mean pressure level of 90 mmHg, marked reductions in IOP occur. Decrease in aortic pressures to 60% of control values were not accompanied by changes in IOP.[11] Choroidal blood flow is directly related to perfusion pressure with IOP up to 30 mmHg.[12] Some evidence of active choroidal blood flow autoregulation is found above this IOP. In a clinical study on the effects of hypotensive anaesthesia, a correlation was found between IOP and systemic arterial pressure.[13] Two groups of patients were identified. In those with an initially low IOP, a significant correlation was found between IOP and systemic arterial and venous pressures. It can be concluded that arterial pressure plays some role in IOP control, but over physiological range of arterial pressure, this effect is relatively minor.

ii) Effect of change in venous pressure on IOP

The venous drainage from the iris, ciliary body and the choroid enters the four vortex veins, which pass through the sclera behind the equator and join the orbital venous plexus, which in turn drains into the cavernous sinus. With an elevation in central venous pressure, blood efflux from the eye is inhibited resulting in an increase in IOP. In both intact and enucleated eyes, increasing venous pressure causes parallel changes of similar magnitude in chamber pressure.[14] Changes of the venous pressure produce or result in corresponding changes in the diameter of intraocular blood vessels.

Increases in central venous pressure associated with events such as coughing, vomiting, valsalva manoeuvre and straining on the tracheal tube results in an acute rise in choroidal blood volume besides reducing the outflow of aqueous humour. The increase in the volume of the choroid and aqueous humour leads to a sharp increase in IOP. A cough may cause IOP to rise by as much as 34-40 mmHg. Of particular relevance is the effect of

posture on venous pressure and thus IOP. Instantaneous parallel changes in CVP and IOP occur with a change from Trendelenberg to head-up position.[15]

iii) Effect of changes of basal intraocular blood volume on intraocular pressure

In an equilibrium state, the other factor affecting intraocular blood volume is the tone of the intraocular vessels because alteration in vascular tone alters the capacitance of these vessels. Intraocular tone is predominantly affected by arterial carbon dioxide tension ($PaCO_2$) and by central controlling areas in the diencephalon. The effect of changes in $PaCO_2$ and IOP is well documented. Hypercarbia increases choroidal blood volume and IOP while hypocarbia has the opposite effect. [16]It was postulated that a decrease in IOP could result from vasoconstriction of the choroidal blood vessels as also from a decrease in aqueous formation, the latter of which is controlled by enzyme carbonic anhydrase. The central control of IOP is complex because it involves control of vascular and extraocular muscle tone apart from a possible direct effect on IOP.

Other factors such as metabolic disturbances of acid-base balance, hyperoxia and hypothermia are known to affect the choroidal blood volume and IOP.

c) Extraocular muscle tone and volume of vitreous humour

The central nervous system, directly through the control on the tone of extraocular muscles and indirectly through hormonal and haemodynamic effects, exerts a central controlling influence on IOP so that the eyes can respond to the needs of a given point in time. General anaesthesia lowers IOP partly by depressing the central nervous system. Marked increases in IOP follow contraction or contracture of the orbicularis oculi muscle.

The vitreous is an unstable gel consisting mainly of water with fine fibrillar supporting structure. Dehydration of the vitreous by administration of appropriate quantities of osmotic diuretics such as Mannitol 20% by intravenous route or Glycerol orally produces dramatic reduction in IOP in acute angle glaucoma.

d) Effect of external compression on IOP

Sudden external compression of the eye elevates IOP. Compensatory effects are also induced that offset this increase in pressure. Elevated pressure within the eye might be expected to have an effect on aqueous outflow facility and thus on aqueous and vitreous volumes as well as on intraocular blood volume and pressure. Digital pressure for 5 minutes before commencement of surgery significantly reduces IOP. [17]The eye may be compressed before surgery through incorrect application of an anaesthetic mask prior to tracheal intubation.

MEASUREMENT OF INTRAOCULAR PRESSURE

Intraocular pressure may be measured directly (manometrically) or indirectly (tonometrically). The manometric method involves cannulation of the anterior chamber and its use is therefore confined to experimental studies on laboratory animals. Indirect or tonometric methods of measurement of IOP are used in clinical practice.

Applanation tonometry is based on the Imbert-Fink principle. The pressure in a fluid-filled sphere such as the eyeball is equal to the force required to just flatten a specific area of the boundary membrane (i.e. cornea). The tonometer is in contact with the tear film and the area of the applanation is visualized by addition of the dye fluorescein to the tear film. Applanation tonometry produces minimal fluid displacement

and minimal changes in ocular volume and is independent of sclera rigidity. The Gold and Schmidt applanation tonometer uses a variable force to applanate a constant area. Applanation tonometry is usually done in the sitting position. Perkins described a simple, portable, hand-held applanation tonometer incorporating the Goldman head. This instrument uses a constant force and measures the area of applanation. The split prism end-point of the instrument is easily visible. Its correct use requires considerable expertise although it is probably the best instrument for measurement for IOP.

The Schioetz indentation tonometer is a simple indirect method of measuring IOP. Indentation tonometry uses a calibrated plunger with a sterilized concave surface and a known weight (5.5 to 10grams) to indent the cornea. The extent of indentation for a given weight is inversely proportional to the IOP. A Fridenwald nomogram is used to convert pointer count on scale to mmHg. Normal corneal elasticity is required for accurate readings. The tonometer is calibrated to zero before each measurement. Frequent, repeated indentations within a short period of time (60seconds) can displace significant aqueous humour from the eye to lower IOP. Errors in measurement can be due to contraction of orbicularis oculi muscle (in awake patients), accommodation, ocular rigidity that varies with IOP and changing volume of the globe. Despite these disadvantages, the Schioetz indentation tonometer is quite useful for comparative measurement between the two eyes or in between successive measurements on the same eye. The normal range of IOP as measured by this instrument is approximately 15-20mmHg.

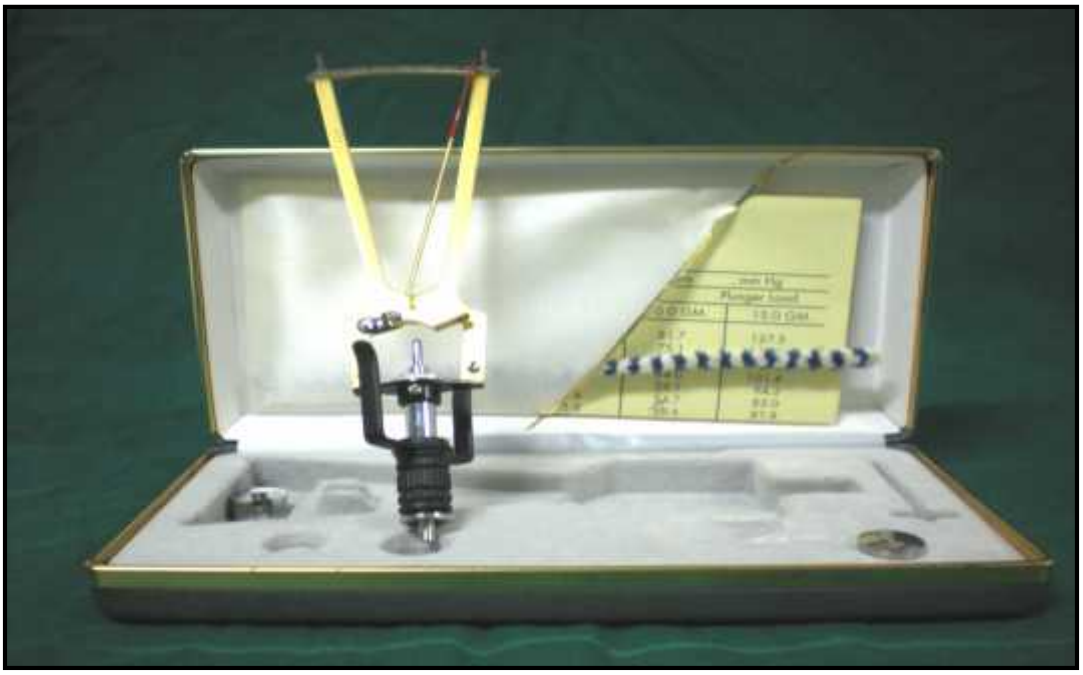

Photo 1: Schioetz Tonometer

Intraocular pressure can be measured by pneumatic tonometry where in a jet of air by constant pressure from a fixed distance indents the cornea and a photo cell measures the reflection of a light beam from the cornea. The prohibitive cost precludes the use of the instrument.

PHARMACOLOGICAL MODIFICATION OF IOP BY ANAESTHETIC AGENTS

IOP may be affected in a variety of ways by drugs given in the perioperative period. These effects are produced by alteration of the physiological determinants of IOP. Anaesthetic agents may act directly on the eye to induce changes in aqueous or intraocular blood volume. They may act locally by altering the tone of extraocular muscles and thus alter external compression of the sclera or they may act indirectly by

altering the vascular tone. Centrally acting drugs act on the central diencephalic control centres.

Premedicants

Diazepam has been used as an oral premedicant in ophthalmologic surgery. The rationale behind the use of diazepam in ophthalmologic surgery is based on the belief that diazepam has centrally mediated muscle relaxing properties.[18] Peripheral muscle relaxant properties have also been suggested. Diazepam has been found to be ineffective when used as pretreatment to attenuate the effects of Succinylcholine-induced rise in IOP.[19]

Opiates

Morphine decreases IOP when given intramuscularly. [20]Other opiates have similar effects.

Anticholinergic agents

Atropine, Scopolamine and Glycopyrrolate when administered intramuscularly as antisialogogues do not affect IOP.[21]

Intravenous induction agents

Thiopentone significantly decreases the IOP by acting on central controlling areas as well as by facilitating aqueous outflow.[22] Midazolam causes reduction in IOP comparable to Thiopentone. [23]Etomidate also has been found to decrease IOP both during induction and during maintainance of anaesthesia. [24]Propofol causes profound reduction in IOP. [25]Ketamine has been shown by different workers to significantly increase the IOP.[26]

Inhalational agents

Most inhalational agents decrease IOP. This is due to multipronged effect of these agents on central controlling areas in midbrain, aqueous outflow facility and tone of intra and extra ocular muscles. Diethylether and Cyclopropane produce a decrease in IOP corresponding to the concentrations of the agents used. [27]Choloroform and Halothane have similar effects. [28]Halothane causes a decrease in IOP by 18% to 33% in spontaneously breathing patients.[29]Isoflurane reduces IOP to the same extent as Halothane.[30] Enflurane reduces IOP by 21% to 41% in spontaneously breathing patients.[31]

Neuromuscular blocking agents

a) Depolarising neuromuscular blocking agents: The Succinylcholine-induced rise in IOP is probably due to several mechanisms including tonic contraction of extraocular muscles, choroidal vascular dilation and relaxation of orbital smooth muscle as well as the cycloplegic action of Succinylcholine. [32]The rise in IOP is further aggravated by tracheal intubation and may be secondary to a sudden increase in arterial pressure, straining or reflex venospasm.

RAPID SEQUENCE INDUCTION OF ANAESTHESIA

In the emergency department (ED), Rapid Sequence Intubation (RSI) is often chosen over other intubation techniques because the simultaneous onset of deep sedation and paralysis, followed rapidly by tracheal intubation, minimizes the risk of pulmonary aspiration of gastric contents. Rapid-sequence intubation has therefore become the technique of choice for intubation of patients at risk of having a full stomach. Indeed, several recent studies have shown RSI as the most common method to achieve airway

control in the ED. [33,34]Since most patients with perforating eye injuries are operated on an emergency basis, they are considered to have a 'full stomach'.

The success of RSI relies on the availability of medications that can rapidly and reliably establish profound sedation and complete neuromuscular blockade. The standard induction agent for rapid sequence induction is Thiopentone sodium. Until recently, however, only one neuromuscular-blocking agent (NMBA), Succinylcholine, has been shown to consistently provide rapid and adequate paralysis in less than 1 minute.[35,36,37] Fifty years of clinical experience with succinylcholine has demonstrated its safety in most patients. However succinylcholine does possess some side-effects that can limit its use in small subset of patients presenting to Emergency Department.

PHARMACOLOGY OF SUCCINYLCHOLINE

Photo 2: Succinylcholine

Succinylcholine (SCh) has been known to science since the early twentieth century. It was first prepared in 1906 by Hunt and Taveau who were investigating the actions of

drugs that bear a structural similarity to ACh, in an attempt to elucidate the muscarinic actions of Ach. These workers did not however appear to have made any remark on the neuromuscular blocking property of SCh. This property of SCh appears to have been investigated only four decades later.

Chemistry

The molecule of SCh consists of two molecules of acetylcholine (ACh) linked back to back through the acetate methyl groups. The drug is supplied in two forms, viz., the chloride and the bromide salts. The chloride is a white crystalline solid with a melting point of 160^0C. It is freely soluble in water and the solution is sufficiently stable to permit the supply of drugs as a 5% solution for clinical use. It is necessary to refrigerate the drug as significant degree of spontaneous hydrolysis occurs in warm surroundings. SCh is rapidly hydrolysed in the body by pseudocholinesterase .

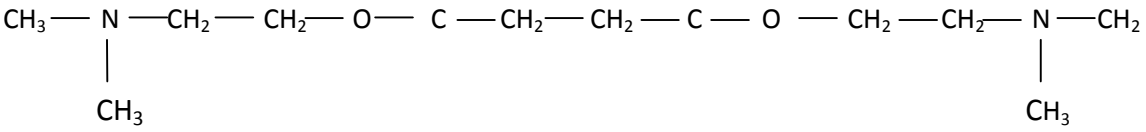

Figure 1:Structure of Succinylcholine

The hydrolysis of SCh is a two-stage process: SCh is initially hydrolysed to succinyl monocholine and choline and this succinyl monocholine is then further broken down into succinic acid and choline. The action of SCh is prolonged in patients who have either an acquired deficiency of serum cholinesterase (e.g. malnutrition, hepatic cirrhosis, etc.) or a congenital defect characterized by the presence of an atypical form of pseudocholinesterase (which hydrolyses SCh extremely slowly).

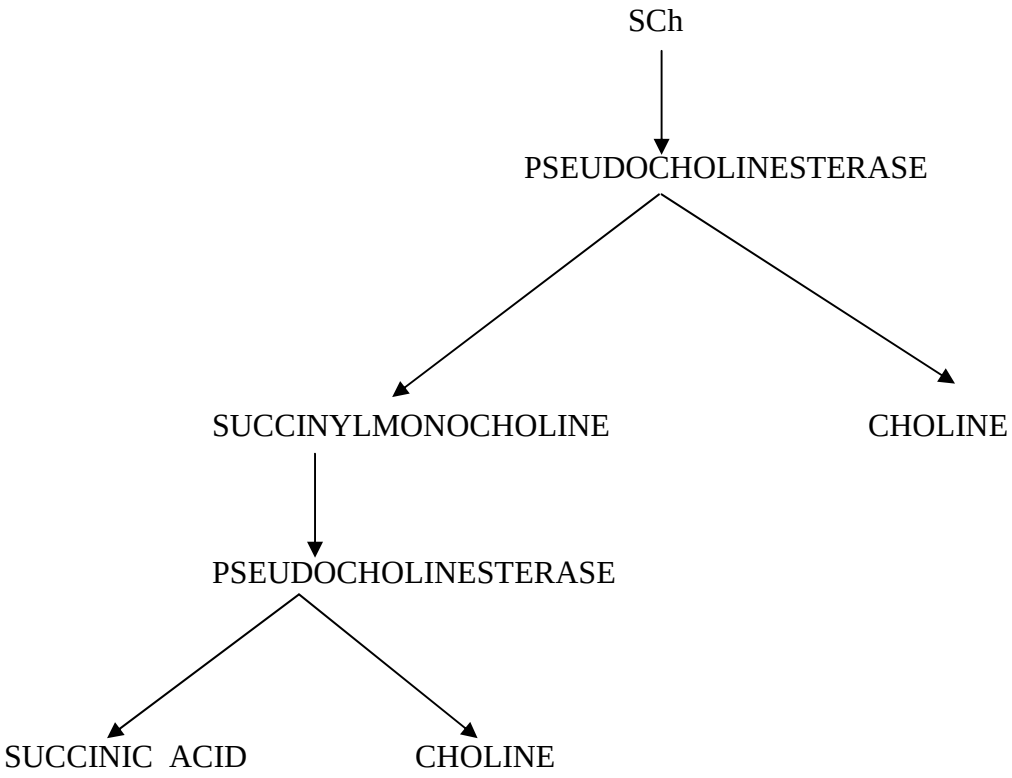

Figure 2: Hydrolysis of succinylcholine

Only a small fraction of the original IV dose of SCh reaches the neuromuscular junction because of the enormous capacity of pseudocholinesterase to hydrolyse SCh. Since there is little or no pseudocholinesterase at neuromuscular junction, SCh returns back into the circulation. So pseudocholinesterase levels influence the onset and the duration of SCh.

Pharmacodynamics

Succinylcholine and the neuromuscular system: SCh is the only depolarizing neuromuscular blocking drug in clinical use. SCh in a dose of 1 to 2mg/kg IV, has a rapid onset (30-60 seconds) and short duration of action (3-5 minutes). These characteristics make SCh the ideal drug for rapid intubation of trachea.

The drug produces a flaccid paralysis of skeletal muscles by causing a persistent depolarization of the motor endplate. SCh attaches to each of the alpha sub-units of the nicotinic cholinergic receptors and mimics the action of acetylcholine. Compared to ACh the hydrolysis of SCh is slow, resulting in sustained depolarization of receptors. Depolarizing neuromuscular blockade is also know as phase 1 blockade.

The onset of paralysis is immediately preceeded in most patients by coarse, evanescent fasciculations of the skeletal muscle that can be seen by the naked eye through the intact skin. These fasciculations first appear in the head and neck and pass caudad. In humans, these fasciculations are probably related to spindle activity and antidromic nerve discharges. The neuromuscular blockade produced by SCh has all the characteristics of depolarizing blockade (presence of fasciculations, absence of fade and absence of post-tetanic potentiation). Tachyphylaxis often follows the administration of intermittent bolus doses of SCh but is rarely seen when the drug is administered as a continuous intravenous infusion.

Rarely, the neuromuscular blockade caused by SCh is abnormally prolonged. Besides congenital or acquired, quantitative abnormalities of serum cholinesterase, the transformation of the depolarizing block into a non-depolarising block can also prolong

recovery from SCh. If SCh is administered in a large dose (greater than 2mg/kg), repeated doses, or as continuous infusion, it may result in a type of blockade where the postjunctional membranes do not respond normally to ACh even when the postjunctional membranes have become repolarised. The mechanism of this type of blockade is not known but is known as 'Phase II block or dual block'.

Cardiovascular effects

The administration of SCh may cause bradycardia; this effect appears to be mediated through the stimulation of muscarinic cholinoceptors in the sinus node.

Evaluation of the effect of SCh on heart rate is often complicated by the fact that the administration of the drug is very often immediately followed by the insertion of the laryngoscope and tracheal intubation, manoeuvres which often cause strong vagal stimulation in the lightly anaesthetized patient. A good rule of thumb is as follows: if the bradycardia resolves immediately following tracheal intubation, withdrawal of the laryngoscope and administration of a few breaths of oxygen through the tube, it is probably the result of physical stimulation caused by the laryngoscopy. If it persists, it is probably due to Succinylcholine. The slowing of the sinus rate is occasionally severe enough to permit the emergence of the atrioventricular node as the pacemaker; this results in an escape junctional rhythm.

The administration of a second dose of Succinylcholine is very often followed by bradycardia. This suggests that the products of the hydrolysis of SCh (succinylmonocholine and choline) probably sensitise the sinus node to the slowing effect of the second (or subsequent) dose of SCh.

Under stable anaesthetic conditions, SCh lowers the threshold of the ventricle to catecholamine-induced dysrhythmias. This effect may be potentiated by several factors including but not limited to autonomic stimuli (such as tracheal intubation, hypoxemia and hypercapnia) and drugs which are known to lower the threshold of the ventricle for ectopic activity (such as Digitalis, monoamine oxidase inhibitors, tricyclic antidepressants and inhalational anaesthetics).

Succinylcholine and hyperkalaemia

The initial depolarization caused by SCh causes the efflux of potassium ions, myoglobin, creatine phosphokinase and other substances from the skeletal muscle cell. This efflux of potassium ions causes the plasma [K^+] to rise by an average of 0.5 mmol/L over the next ten minutes. The potassium then returns to the intracellular fluid. A few healthy individuals exhibit a greater degree of hyperkalaemia than this (increases as high as 1.0-1.5 mmol/L being occasionally seen); even this degree of hyperkalaemia is without consequence.

In the late-1960s, attention was drawn to the high incidence of severe bradycardia and circulatory arrest in extensively burnt or traumatized patients who received SCh as a part of their anaesthetic induction sequence. Investigation of this problem led to the interesting discovery that administration of SCh to a patient with a significant mass of denervated skeletal muscle during the “vulnerable period” (1 day-6 months) almost always caused severe hyperkalaemia, with the plasma [K^+] acutely rising by several mmol/L. However, in patients with progressive neuromuscular disease (e.g. muscular dystrophies), the tendency to hyperkalaemia persists beyond the distal limit referred to above.

Patients with chronic renal failure often have an elevated baseline plasma [K+]. These patients however do not appear to be at any increased risk of developing acute, life-threatening hyperkalaemia following the administration of SCh. Though the possibility of such a patient developing hyperkalaemia as a consequence of denervation of a significant mass of skeletal muscle (caused in turn by uraemic neuropathy) should always be borne in mind, there appears to be little evidence that such an event actually occur. Studies have shown that in patients with certain diseases and conditions, an exaggerated release of potassium occurs in response to SCh.[38,39] Such conditions include burns, nerve damage or neuromuscular disease, closed head injury, intra-abdominal infection and renal failure.

SCh induced rhabdomyolysis and hyperkalaemia may occur when SCh is administered to children with undiagnosed myopathy. For these reasons some anaesthesiologists avoid the use of SCh in paediatric patients and prefer nondepolarising neuromuscular blocking drugs. Proliferation of extrajunctional cholinergic receptors providing more sites for potassium to leak outward from cells during depolarization is the presumed explanation for hyperkalaemia that follows the administration of SCh to patients with denervation injury.

Succinylcholine and intragastric pressure

SCh produces inconsistent increase in intragastric pressure. When intragastric pressure increases, it seems to be related to the intensity of skeletal muscle fasciculations induced by SCh. The muscle fasciculations that follow the administration of SCh cause the intragastric pressure to rise. However, the concomitant increase in the tone of the lower oesophageal sphincter probably prevents any passive regurgitation in an overwhelming majority of patients.

In infants and children, SCh does not appear to cause any apparent increase in intragastric pressure; this difference from adults has been attributed to the fact that muscle fasciculations (following the administration of SCh) are either absent or minimal in this subset of patients. Pretreatment with either a nondepolarising muscle relaxant or Lignocaine decreases both the fasciculations and the increased intragastric pressure effectively.

Succinylcholine and intracranial pressure

Increase in intracranial pressure after administration of SCh to patients with intracranial tumours or head trauma has not been a consistent observation. Patients in whom such an increase in intracranial pressure is not acceptable, a nondepolarising muscle relaxant should be substituted for SCh, if possible.[40]

Succinylcholine and myalgia

Postoperative skeletal muscle myalgia can occur after administration of SCh. The myalgia that often accompanies recovery from SCh-induced muscle paralysis is more commonly seen in females than in males and in patients who are ambulated early following relatively minor procedures. It has been postulated that the muscle pain is secondary to damage produced in the skeletal muscle by unsynchronized contraction of adjacent muscle fibres just before paralysis occurs. Pretreatment with a subparalysing dose of a nondepolarising muscle relaxant prevents SCh-induced muscle fasciculation and reduces the incidence and severity of muscle pain. Defasciculation necessitates an increase (by upto 50%) in the dose of SCh, but this appears to present no problems.

Succinylcholine and Duchenne muscle dystrophy

There have been several reports in the literature indicating an association between muscular dystrophy and MHS(Malignant Hyperthermia Syndrome). However, in most of these, neither the diagnosis nor the association has been established by diagnostic techniques that would be regarded as valid today. In one case report, the diagnosis had been made by the calcium uptake test. The major reason for avoiding SCh in patients with muscular dystrophies is the likelihood of life-threatening hyperkalaemia, not MHS.

SUCCINYLCHOLINE AND IOP

The controversy surrounding the use of Succinylcholine in ocular surgery is longstanding. Succinylcholine has been said to be safe for surgery upon intact eye but its use in open eye injuries is contraindicated.

The intravenous administration of SCh is typically followed by an increase in the intraocular pressure (IOP) that manifests within one minute, peaks between two and four minutes followed by a return to baseline in about seven minutes. Dillon and colleagues reported a case of extrusion of ocular contents following SCh.[41,42] Therefore, the patient undergoing ophthalmic procedures are likely to be at risk of increased IOP.

In 1955 Lincoff reported a transient but significant rise in IOP when Succinylcholine was given intravenously to facilitate intubation and vitreous loss followed the administration of Succinylcholine in the presence of an open eye. Conflicting reports on the effect of Succinylcholine on the intraocular pressure in anaesthetized humans followed, with some claiming minimum effects while others reported an increase. [43,44,45]Mechanisms postulated are tonic contraction of extraocular

muscles, choroidal vascular dilation, and relaxation of orbital smooth muscle as well as the cycloplegic action of Succinylcholine. [32]It is not known whether all these mechanisms are functional in the injured eye.

Methods used to attenuate the increase in IOP due to succinylcholine

Various attempts have been made to abolish or minimize the Succinylcholine induced rise in IOP, keeping in mind the unique position it occupies as the muscle relaxant of choice in emergency situations.[46,47,48,49]

a) Deep planes of anaesthesia: Under deep planes of anaesthesia, there is no electrical activity in extraocular muscles. Therefore, deepening the planes of anaesthesia was suggested as one method of preventing rise in intraocular pressure following Succinylcholine.

b) Time and dose of Succinylcholine: Clinical studies have demonstrated the time course of changes in IOP produced by Succinylcholine following induction with Thiopentone. Following induction of anaesthesia with Thiopentone and Succinylcholine, IOP increased within the first minute, with a peak rise of 6-8 mmHg between 2-4 minutes, and by six minutes IOP had returned to control values. [44]Tracheal intubation following Succinylcholine exaggerated the rise in IOP was found by Joshi and Bruce to be dependent on the timing of the administration of Succinylcholine and Thiopentone.[50] A 1mg/kg dose of Succinylcholine given immediately following 3mg/kg Thiopentone was associated with reduced IOP while a 1mg/kg dose given 2 minutes after 3mg/kg Thiopentone maintained a constant IOP.

c) Diazepam: Diazepam, given intravenously, decreases intraocular pressure but does not prevent the rise in IOP following Succinylcholine. The rationale behind the use of Diazepam is that a presynaptic action of diazepam would probably decrease the release and synthesis of acetylcholine and thus the intensity of fasciculations. Cunnigham AJ et al found that pre-treatment with Diazepam (0.1 mg/kg) given intravenously 5 minutes before induction reduces the increase in IOP seen following Succinylcholine.[48] The mechanism of action of Diazepam in reducing IOP is uncertain but it is postulated that it may inhibit the tonic contraction of the extraocular muscles following Succinylcholine.

d) Lignocaine failed to prevent increase in IOP when given as pre-treatment before Succinylcholine.[51]

e) Pre-treatment with Acetazolamide (500mg intravenously) was also suggested but the drug was found to cause intense choroidal vasodilatation, a mechanism probably responsible for masking the effects of Succinylcholine on IOP.

f) Pretreatment with small doses of nondepolarising agents has been recommended. Conflicting results have been reported regarding the efficacy of this method.[52]Miller et al found pre-treatment with Gallamine 20mg or d-Tubocurarine 3mg, given 3 minutes prior to administration of Succinylcholine prevented any increase in IOP with Succinylcholine.[46] D-Tubocurarine has been found to decrease the IOP in most of the studies. Mechanisms postulated are decrease in extraocular muscle tone, decrease in arterial blood pressure, autonomic ganglion blocking action and effect on intraocular muscles. Pancuronium was found not to affect IOP significantly in some studies[53], but in

others a decrease in IOP was demonstrated. Atracurium does not alter intraocular pressure[55]. Vecuronium has been found to be satisfactory as it does not allow increase in IOP following intubation.

g) Self-taming: Meyers EF et al found that pre-treatment with a small sub-paralysing dose of Succinylcholine before administration of full paralyzing dose increases the intraocular pressure. They concluded that it cannot be used safely in patients in whom the integrity of the eye is lost or threatened.[56] The efficacy of this method is again controversial. Some workers found self-taming effective, while others found it ineffective in the attenuation of rise in IOP following an intubating dose of Succinylcholine.

h) Nifedepine: Indu et al found a decrease in IOP from control values when subjects were given 10 mg of Nifedipine sublingually 10 minutes prior to induction. These patients did not exhibit a rise in intraocular pressure above baseline. The use of nifedipine as pre-treatment can cause prolonged and unwanted hypotension.[57]

i) Nitroglycerine: Mahajan RP et al tried intranasal nitroglycerine for attenuating the rise in IOP seen following tracheal intubation. [58]Nitroglycerine has many advantages over other drugs when used as pre-treatment. Nitroglycerine gives predictable reduction in IOP. The drug is prepared prior to induction and instilled intranasally. The hypotension caused is short-lived and the blood pressure returns to normal values within 15 minutes. It is helpful in patients who are at risk such as patients with hypertension, myocardial ischaemia and angina.

None of the above methods are reliable hence alternatives to Succinylcholine for rapid sequence intubation had to be developed.

ALTERNATIVES TO SUCCINYLCHOLINE FOR RAPID SEQUENCE INTUBATION

Concerns regarding the occasional but unpredictable risks associated with the use of Succinylcholine have prompted some clinicians to use nondepolarising NMBAs (Neuromuscular Blocking Agents) in selected patients. Vecuronium is the usual alternative NMBA for RSI when Succinylcholine is contraindicated. Its nondepolarising mechanism of action avoids the side-effects associated with Succinylcholine. However, Vecuronium is not ideal for use in the ED setting. Its onset is much slower than Succinylcholine, in the order of 2 minutes or longer[59]. This slow onset generally results in the need to provide bag-valve-mask (BVM) ventilations in order to prevent oxygen desaturation of hemoglobin. Even with high-dose Vecuronium (0.3mg/kg), the onset time can only be reduced to 90 seconds and BVM ventilations are still frequently needed. The use of BVM ventilation during RSI is undesirable because gastric insufflation can occur, which can increase the risk of vomiting and pulmonary aspiration.

The search for a nondepolarising NMBA with a quicker onset resulted in the development of Rocuronium, a structural analogue of Vecuronium. It has been extensively evaluated in the operating room and in multiple studies it has been shown to have an onset of action of less than 1 minute. Due to its nondepolarising mechanism of action at the neuromuscular junction[59-62], it does not cause changes in serum potassium level, nor does it possess any of other side effects of Succinylcholine. Only recently has it become available in EDs, but there are few data evaluating its safety and efficacy in this setting.

PHARMACOLOGY OF ROCURONIUM

Photo 3: Rocuronium bromide

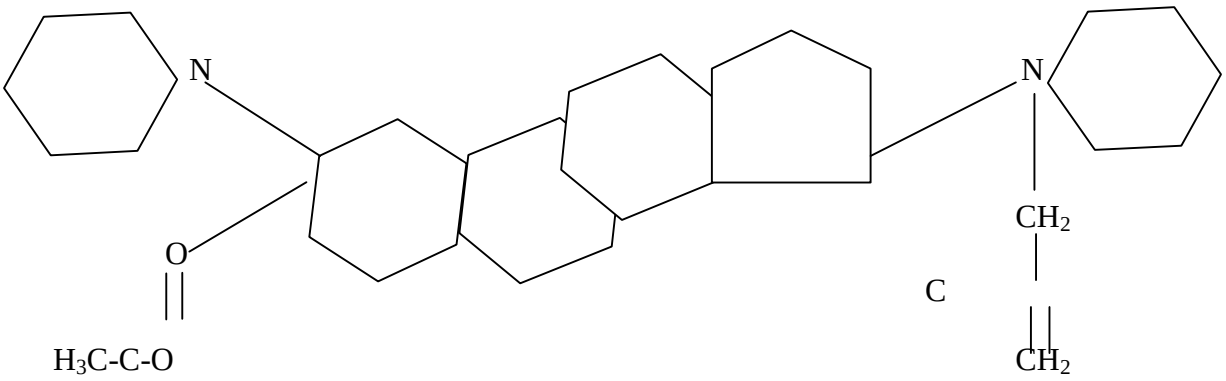

Figure 3: Structure of Rocuronium

STRUCTURE OF ROCURONIUM

Rocuronium is a newer aminosteroid-based neuromuscular blocking agent with shorter onset of action and intermediate duration of action. Rocuronium is the 2-morpholino, 3-desacetyl, 16-N-allyl pyrrolidino derivative of Vecuronium. It differs from Vecuronium at 3 positions on the steroid nucleus and the absence of acetylcholine like fragment that is found in the steroid nucleus of Vecuronium in the A-ring. The

replacement of the methyl group attached to the quaternary nitrogen of Vecuronium by an allyl group and the absence of acetylcholine like fragment in the A-ring may be partly responsible for the decrease in potency seen with Rocuronium. It possesses tertiary nitrogen at the A-ring end of the molecule. Replacement of acetate group attached to the A-ring by a hydroxyl group makes it possible to present Rocuronium as a stable solution.

PHARMACOKINETICS

Rocuronium is taken up into the liver by a carrier mediated active transport system. Rocuronium is largely excreted unchanged in the bile (upto 50% in 2 hours). Deacetylation of Rocuronium does not occur and the metabolite 17-desacetyl rocuronium has not been detected in significant quantity. In patients with liver disease there is increase in the volume of distribution and may result in prolonged duration of action. Renal excretion of Rocuronium may be more than 30% in 24 hours and in patients with renal failure, Rocuronium may produce longer duration of action.

PHARMACODYNAMICS

Mechanism of action: Rocuronium being amino steroid based neuromuscular blocking agent has a post junctional effect and high degree of selectivity for receptors at the neuromuscular junctions. Muscle paralysis is produced by competitive antagonism of nicotinic cholinergic receptors of skeletal muscle. Its potency is about 10-15% of vecuronium. Rocuronium antagonises acetylcholine receptors. Therefore, it is likely that it competes with acetylchline at its binding site. The tetanic fade phenomenon is observed with Rocuronium indicating activity not only at postsynaptic but also at presynaptic nicotinic receptors. Activity is terminated by gradual dissociation from the receptor shifting the agonist/antagonist equilibrium in favour of acetylcholine.

Dosage, onset and duration of action: Rocuronium has a rapid onset of neuromuscular block, presumably due to its relatively low potency. This ensures the presence of more relaxant molecules in the blood stream and results in large concentration gradient towards biophase. It has been assumed that this is the main rate-limiting step overriding individual differences in affinity constant for the receptors. Intubating dose of Rocuronium is 0.6mg/kg.

Table 1: Doses of Rocuronium for intubation and maintainance of neuromuscular blockade[63]

	Dosage mg/kg	**Clinical duration (min)**
ED95	0.3-0.4	
Intubation at 60-90 seconds	0.6-1.0	35-75
Maintanance	0.1-0.15	15-25
Infusion	8-12μg/kg/min	

Onset of action of Rocuronium is shorter when compared with other nondepolarising muscle relaxants. When the dose of Rocuronium is increased, onset of action decreases further.

Table 2: Onset and clinical duration of action of different doses of Rocuronium[59]

	Dose of Rocuronium		
	0.6 mg. Kg^{-1}	0.9 mg. Kg^{-1}	1.2 mg. Kg^{-1}
Onset (s)			
Mean	89	75	55
SD	33	28	14
Range	48-156	48-144	36-84
Duration (min)			
Mean	37	53	73
SD	15	21	32
Range	23-75	25-88	38-150

Variables: Onset= the time interval between the completion of injection of NMB and time to maximal depression of T1.

Duration= The time interval between the completion of injection of NMB and time to recovery of 25% of control.

Rocuronium and continuous infusion

Rocuronium can be used for continuous infusion. The infusion rate depends on the anaesthetic technique and age of the patient. It can be used at a rate of 8-12μg/kg/min.[64]

Recovery

For an intubating dose of Rocuronium 0.6mg/kg, the time required for the recovery of twitch height from 25% to 75% is approximately 14 minutes.[59]

Table 3: Recovery profile of different doses of Rocuronium

	Rocuronium 0.6 mg/kg	Rocuronium 0.9 mg/kg	Rocuronium 1.2 mg/kg
Mean(minutes)	14	22	24
SD	8	14	11
Range	6-27	8-29	11-43

Recovery index= The time from T25 to T75% of recovery.

Rocuronium and cardiovascular effects

Rocuronium is typically devoid of cardiovascular effects. Circulatory effects or release of histamine do not occur after rapid IV administration of even large doses of Rocuronium. The structural feature for this difference is the absence of ACh-like character of A-ring substitution, which decreases the action on cardiac muscarinic receptors.

Rocuronium, however, may produce a slight vagolytic action. This feature of Rocuronium may be useful in patients undergoing surgical procedures that may be associated with vagal stimulation.

Rocuronium and age

In neonates and infants, the volume of distribution of Rocuronium is increased and the plasma clearance is diminished. This results in longer elimination half-life. In children, the volume of distribution is unchanged but clearance is increased, resulting in shorter half- life of Rocuronium. In the elderly, the volume of distribution of rocuronium is unaltered or slightly reduced and clearance is diminished. This results in a similar or slightly longer half-life compared to adults.[65]

ROCURONIUM AND ANAPHYLAXIS

Since release of Rocuronium on to the worldwide market, concern has been expressed about its propensity to cause anaphylaxis. Rose M, Fisher M identified 24 patients who met clinical and laboratory (intramedal, mast cell tryptase and morphine radioimmunoassay) criteria for anaphylaxis to Rocuronium. Data from intradermal testing suggested that Rocuronium is intermediate in its propensity to cause allergy in known relaxant reactors compared with low-risk agents (e.g. Pancuronium, Vecuronium) and higher-risk agents (e.g. Alcuronium, Succinylcholine).[66]

Baillard C et al reported two cases of documented anaphylaxis.[67]