EFFECT OF PRETREATMENT WITH INTRAVENOUS THIOPENTONE VERSUS LIGNOCAINE ON PAIN DUE TO ROCURONIUM BROMIDE: A COMPARATIVE STUDY

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ABSTRACT

BACKGROUND

Rocuronium bromide is a non-depolarising neuromuscular blocking drug commonly used in modern anaesthetic practice to facilitate endotracheal intubation and provide skeletal muscle relaxation. Pain on intravenous administration is an undesirable side effect of this drug. This study compares the effect of pretreatment with intravenous Thiopentone sodium 50 mg versus Lignocaine hydrochloride 40 mg in reducing this pain.

STUDY DESIGN

Double blind randomised control study conducted at the department of Anaesthesiology of a tertiary care teaching hospital.

MATERIALS AND METHODS

110 patients of age 16-60 years of American Society of Anaesthesiologists (ASA) physical status grade I and II of either sex for elective surgery under general anaesthesia were randomly divided into two groups using random number table. Group L received 40 mg of 2% lignocaine hydrochloride and Group T 50 mg of 2.5% thiopentone sodium intravenously before the administration of one tenth of the intubating dose of rocuronium bromide. Patients were asked to report the severity of pain on a Numerical Pain Rating Scale.

RESULTS

Mean age group in the study was 40.2 in Group L and 40.17 in Group T with female dominance of 78.5% and 87% in either group respectively. Mean body weight was 61.86 Kg in Group L and 60.19 Kg in Group T. 54.5% in the study population belonged to ASA physical status I and 45.5% were of ASA physical status II with no significant difference between the groups. There was statistically significant difference in the pain score between the two groups with 15.4% reduction in pain score with Group L compared to Group T.

CONCLUSION

From this study it is concluded that pretreatment with intravenous 40 mg of 2% lignocaine hydrochloride is more effective than 50 mg of 2.5% thiopentone sodium in reducing the pain due to intravenous administration of rocuronium bromide.

KEYWORDS

Pretreatment, Rocuronium Bromide, Lignocaine Hydrochloride, Thiopentone Sodium.

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INTRODUCTION: Neuromuscular blocking agents are an integral part of everyday anaesthetic practice for tracheal intubation and skeletal muscle relaxation during general anaesthesia. Conventionally succinylcholine, a depolarising neuromuscular blocking drug is being widely used for tracheal intubation especially for rapid sequence induction-intubation (RSI), due to its rapid onset of action, profound muscle relaxation and short duration of action. However, undesirable side effects like cardiac dysrhythmias including sinus arrest, potential for hyperkalaemia and malignant hyperthermia, rise in intracranial, intraocular and intragastric pressures and postoperative muscle pain probably due to muscle fasciculations make this drug undesirable in many emergency situations. Fatalities have been reported in otherwise healthy children and adolescents following administration of succinylcholine due to life threatening dysrhythmias and cardiac arrest, who were later found to have undiagnosed Duchenne muscular dystrophy[(1)].

Rocuronium bromide is a relatively newer aminosteroid non-depolarising neuromuscular blocking agent used in modern anaesthetic practice, which has emerged as useful alternative to succinylcholine especially for RSI. This is due to its rapid onset and intermediate duration of action and lack of the undesirable side effects of the depolarising neuromuscular drug, succinylcholine. It has also the advantage of lack of muscle fasciculations and postoperative myalgia. Studies have found that time of onset of action and clinically acceptable intubating conditions are comparable with these two drugs, which is especially useful in emergency situations for RSI.

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Rocuronium bromide at a dose of 1 mg/kg intravenously has its onset of action in about 60 seconds which is comparable to that of succinylcholine and the effect lasts for about 45 minutes, which is 6-10 minutes longer than that of the latter. Hence, it is often used as a better alternative to succinylcholine for tracheal intubation due to its rapid onset of action and lack of the potential side effects of depolarising neuromuscular blocking drugs.

Rocuronium is a good choice for tracheal intubation in children because of its definite advantages over succinylcholine. However, pain on injection and withdrawal movement characterised by sudden flexion of the wrist and arm lasting for 10-20 seconds which could cause injury or dislodgement of central venous catheter has been reported in 50-80% of patients following its administration.[2] The incidence and severity is more in children than in adults.[3] This can limit its use in clinical practice of an otherwise safer and useful neuromuscular blocking drug devoid of the side effects of succinyl choline.

The mechanism of pain on intravenous injection of rocuronium is not clear. Peripheral veins are innervated with polymodal nociceptors that mediate the response to the injection of anaesthetic agents like propofol and rocuronium. Significant rise in histamine and tryptase release from mast cells after the administration of rocuronium causing the activation of perivascular nociceptive nerve endings and polymodal nociceptors in the peripheral vein wall may be the reason for this pain.[4]

Pain during induction of anaesthesia caused by intravenous administration of anaesthetic drugs is distressing, which can increase the stress and anxiety of the patients. It can also precipitate myocardial infarction, bronchospasm [5,6] and pulmonary aspiration.

Neuromuscular blocking drugs are at times administered during general anaesthesia before loss of consciousness as a priming dose to decrease the fasciculations produced by depolarising drug succinylcholine or to time the onset of skeletal muscle paralysis of the non-depolarising drug with that of loss of consciousness. Rocuronium bromide at times produces severe burning pain in the vein or arm when administered before loss of consciousness after induction of anaesthesia.[6,7] It has been shown that even after induction of general anaesthesia, there is still 84% incidence of withdrawal of arm after injection of rocuronium.[3] This can limit its use, which is an otherwise safer alternative to the more commonly used depolarising drug, succinylcholine. Techniques to reduce the incidence and intensity of this pain include diluting the drug, administering it as an infusion rather than as bolus injection and combining with drugs such as lignocaine, ondansetron, tramadol, fentanyl, alfentanil, remifentanil, ketamine, thiopentone sodium, dexmedetomidine esmolol and gabapentin.

There are several studies proving the effectiveness of lignocaine in decreasing the pain on injection of rocuronium injection.[8,9] Park et al[10] found that pretreatment with intravenous thiopentone sodium is effective in reducing this pain.

AIM OF THE STUDY: To compare the effect of pretreatment with intravenous 50 mg thiopentone sodium against 40 mg lignocaine hydrochloride in reducing the pain associated with the intravenous administration of rocuronium bromide.

MATERIALS AND METHODS: This study was conducted over a period of four months from March 2012 at the Department of Anaesthesiology, Government Medical College, Thrissur, Kerala, India which is a tertiary care teaching hospital. Approval from the institutional technical committee and human ethical committee was obtained and written informed consent from the patients was taken prior to the study.

110 patients of age 16-60 years of ASA I and II of either sex posted for elective surgery under general anaesthesia were enrolled for this study. They were randomly divided into two groups using random number table. Group L (56 patients) received 40 mg of 2% lignocaine hydrochloride and Group T (54 patients) received 50 mg of 2.5% thiopentone sodium intravenously which was followed by administration of one tenth the intubating dose (0.1 mg/kg) of rocuronium bromide.

Inclusion Criteria:

1) Patients for elective surgery.
2) American Society of Anaesthesiologist (ASA) class I – II.
3) Age 16 -60 years.
4) Body Weight 51 – 80 kg.

Exclusion Criteria:

1) Patient refusal.
2) Contraindication to barbiturates or aminosteroids.
3) Respiratory diseases like bronchial asthma and chronic obstructive pulmonary disease.
4) Pregnancy.
5) Patients on any other analgesics.
6) Patients with chronic pain.
7) Anticipated difficult airway.

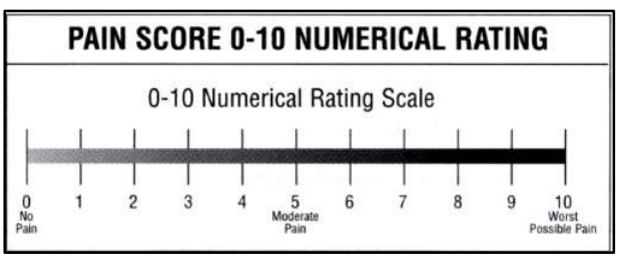
Procedure: All patients were evaluated on the day before surgery, procedure explained and written informed consent obtained. Tab. Alprazolam 0.5 mg was given orally as premedication on the night before surgery and a preoperative fasting of 8 hours to solid food was advised.

On the morning of surgery, patients were shifted to the operation theatre without further premedication. Non-invasive blood pressure, electrocardiogram and pulse oximeter were connected as pre-induction monitors. An 18 gauge intravenous cannula was inserted on the dorsum of the non-dominant hand under local anaesthesia, infusion of Ringer lactate was started and free flow was confirmed.

An independent anaesthesiologist prepared both the pretreatment test drugs and loaded in 2 mL syringes. The intravenous infusion line was occluded by applying rubber tourniquet at the middle of the arm, and the investigator administered the test drug who was unaware which drug was given. The tourniquet was released 30 seconds after

administration of the test drug and the infusion was run for removal of the residual drug. This was followed by intravenous administration of one tenth of the intubating dose (0.1 mg/kg) of rocuronium bromide. Patients were asked to report the severity of pain experienced if any on injection of rocuronium bromide on a 0-10 Numerical Pain Rating Scale.

Numerical Pain Rating Scale: This is a simple and commonly used self-reporting scale to assess the severity of pain used in adults and children above 10 years. [11] The patient is asked to indicate the intensity of the pain perceived on a scale from 0-10, in which 0 indicates no pain at all and 10 the worst imaginable pain.



OBSERVATION AND RESULTS: The data obtained were entered in a master chart and analysed using computer software Epi Info version 3.5.3. The data were expressed in its frequency, percentage, mean and standard deviation. To elucidate the associations and comparisons between different parameters, Chi-square (X^2) test was used as nonparametric test. Student's t test was used to compare mean values between the two groups for parametric data whereas Mann-Whitney U test was used to compare nonparametric data between the groups. For all statistical evaluations, a two-tailed probability of value <0.05 was considered significant.

Age (years)	Group L		Group T	
	Number	%	Number	%
16 - 20	02	3.6	0	0
21 - 30	07	12.5	12	22.2
31 - 40	18	32.1	14	25.9
41 - 50	21	37.5	22	40.8
51 - 60	08	14.3	06	11.1
Total	**56**	**100**	**54**	**100**

Table 1: Comparison of age between Groups

$X^2 = 4.09$, $p = 0.3939$.

Mean age of group L was 40.2 (SD = 9.5) and of group T was 40.17 (SD = 9.3), difference in mean age was not statistically significant, t test - t = 0.26, p = 0.979.

Gender	Group L		Group T	
	Number	%	Number	%
Male	12	21.4	07	12.9
Female	44	78.6	47	87.1
Total	**56**	**100**	**54**	**100**

Table 2: Distribution according to Gender

$X^2 = 1.3$, $p = 0.24$.

Gender distribution in the study group showed female dominance in both the groups with 78.6% in group L and 87.1% in group T. There was no statistical difference in gender in both groups.

Weight (kg)	Group L		Group T	
	Number	%	Number	%
51 - 60	28	50	31	57.4
61 - 70	17	30.4	17	31.5
71 - 80	11	19.6	06	11.1
Total	**56**	**100**	**54**	**100**

Table 3: Comparison of Weight between two Groups

$X^2 = 1.59$, $p = 0.45$.

Mean weight of group L was 61.86 and group T was 60.19 and the difference was not statistically significant, t test - t = 1.056, p = 0.293.

ASA	Group L		Group T	
	Number	%	Number	%
Grade I	33	58.9	27	50
Grade II	23	41.1	27	50
Total	**56**	**100**	**54**	**100**

Table 4: Distribution of Patients according to ASA PS

$X^2 = 0.88$, $p = 0.347$.

ASA PS distribution in the study showed 54.5% of patients belonged to grade I and 45.5% belonging to grade II. The groups were ASA PS matched as there was no statistically significant difference.

Pain score	Group L		Group T	
	Number	%	Number	%
0 - 1	48	85.7	38	70.4
2 - 3	08	14.3	11	20.4
4 - 5	0	0	05	9.2
> 6	0	0	0	0

Table 5: Distribution of Patients according to Pain

$X^2 = 6.6$, $p = 0.0368$.

Pain scores between the two groups were analysed using Mann Whitney test and difference was statistically significant, p = < 0.001. The two groups did not differ significantly on baseline characteristics.

In this study, 70.4% patients in the thiopentone group had pain score 0–1, but it was 85.7% in the lignocaine group. Pain score was 2-3 in 14.3% in group L but it was 20.4% in group T. None of the patient had pain score above 3 in the lignocaine group compared to 9.2% with pain score 4-5 in the thiopentone group.

There was statistically significant reduction in the incidence of pain score (p=0.0368) in patients pretreated with lignocaine hydrochloride compared to thiopentone sodium.

DISCUSSION: The excellent clinical intubating conditions with succinylcholine have made it the drug of choice conventionally for tracheal intubation, especially for RSI. However, the undesirable side effects and even fatalities associated with depolarising neuromuscular blocking drugs limits it use.[1] A non-depolarising agent with comparable intubating conditions to that of succinylcholine could replace it due to the lack of adverse effects of the depolarising agents. Such an ideal agent should have a rapid onset and shorter duration of action, with a wide therapeutic margin.

Rapacuronium is a non-depolarising neuromuscular blocking drug introduced in 1990 with the above properties and was thought to be an ideal agent for this purpose. Unfortunately, it had to be withdrawn from clinical use in 2001 due to its potential for histamine release, which resulted in bronchospasm causing fatalities.[12]

Rocuronium bromide has later emerged as the leading competitive non-depolarising neuromuscular drug for tracheal intubation and RSI when succinylcholine has to be avoided or contraindicated. At a dose of 1 mg/kg, it produces intubating conditions almost comparable to that of succinylcholine and its action lasts for about 45 minutes, which is 6-10 minutes longer than succinylcholine. Due to the lack of potential for malignant hyperthermia and the other side effects of depolarising agents, rocuronium bromide has emerged as a safer alternative to succinylcholine. However, the prolonged duration of action of rocuronium limits its use, especially in situations of anticipated difficult airway, when the patient has to be ventilated till recovery from the effect of neuromuscular blockade. However, sugammadex, a specific binding agent for rocuronium can be used to reverse the neuromuscular blockade within 1-2 minutes, shortening its duration of action even less than that of succinylcholine.[13]

Pain on intravenous administration is an undesirable side effect of rocuronium bromide which can limit the use of this useful non-depolarising neuromuscular blocking drug. Attenuation of this pain could make the drug more acceptable which is a safer alternative to the depolarising drug succinylcholine commonly used for tracheal intubation.

Peripheral veins are innervated with polymodal nociceptors [14] which mediate the response to injection of drugs causing pain. Steegers and Robertson [7] described that 47% of patients who received rocuronium while awake had pain on injection and 12% described their pain severe. No relationship was found between the site of injection or gender of the patient and pain on injection. Lui et al reported[15] a case of pulmonary aspiration of gastric contents in a child caused by spontaneous movement caused by pain due to injection of rocuronium bromide.

The most popular method used to reduce pain due to rocuronium bromide is the use of lignocaine. Memis et al [16] in their study concluded that 30 mg lignocaine was effective in reducing this pain. Ahmad et al [9] found 70% reduction in limb withdrawal in patients receiving 40 mg 2% lignocaine prior to the drug. Prasanna M et al [17] in their study reported that 40 mg lignocaine was effective in reducing pain due to rocuronium injection. Sharma et al [18] reported that inhalation of 50% nitrous oxide in oxygen reduces the incidence and severity of pain and withdrawal reactions associated with rocuronium administration. Borgeat and Kiatowski et al[19] had found that intravenous injection of rocuronium is associated with severe burning pain of short duration causing spontaneous movements of the limb. Chiarella et al[20] compared the addition of various drugs with rocuronium bromide to reduce the pain and found that fentanyl reduced the pain by 1.9 times, 2% lignocaine by 3.6 times and sodium bicarbonate by 8.4 times.

CONCLUSION: From this study it is concluded that pretreatment with intravenous 40 mg of 2% lignocaine hydrochloride is more effective than 50 mg of 2.5% thiopentone sodium in reducing pain due to intravenous administration of rocuronium bromide.

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