ORIGINAL RESEARCH

Assessment of effect of pre administration of a small dose of ephedrine on onset time of cisatracurium

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ABSTRACT
Background: Muscle relaxants with a short duration of action are particularly useful at the time when there is difficult mask ventilation. Hence; the present study was undertaken for assessing the effect of pre administration of a small dose of ephedrine on onset time of cisatracurium. **Materials & methods:** A total of 40 patients scheduled for elective and emergency surgical procedures under general anaesthesia were enrolled. All patients were assessed preoperatively with history, physical examination and relevant investigations. All were kept nil per oral 6 hours prior to surgery. These patients were divided into two groups of 20 each- GROUP 1: Receiving ephedrine (70 micrograms/kg), and GROUP 2: Receiving saline. Effects of intravenous ephedrine on the onset time of cisatracurium after a bolus dose of cisatracurium (0.15 mg/kg) were studied. Patients anesthetized with fentanyl (1.5micrograms/kg) and propofol (1-2mg/kg) were randomly divided into 2 groups to receive either ephedrine (70micrograms/kg) or saline 5 seconds before propofol. Cisatracurium was administered after loss of consciousness. Neuromuscular block was assessed at adductor pollicis using accelography with train of four stimulation. Intubation with appropriate size endotracheal tube following muscle relaxation. **Results:** Mean age of the patients of Group 1 and group 2 was 35.3 years and 34.7 years respectively. Both the study groups were comparable in terms of age-wise distribution of patients. 60 percent of the patients of group 1 and 65 percent of the patients of group 2 were males while the remaining were females. Both the study groups were comparable in terms of gender-wise distribution of patients.None of the patient of both the study groups showed the presence of allergy.Non-significant results were obtained while comparing the distribution of patients according to Viby Mogenson Score.Mean time of onset among the patients of Group 1 and Group 2 was 141.8 seconds and 169.2 seconds respectively. Significant results were obtained while comparing the mean time of onset among the patients of two study groups. **Conclusion:** Pretreatment with ephedrine 70 µg/kg improved intubating conditions after cisatracurium administration and facilitated the early onset of cisatracurium without adverse hemodynamic effects.

Key words: Ephedrine, Cisatracurium.

INTRODUCTION

The neuromuscular blocking potency of cisatracurium (NIMBEX) is approximately three-fold that of atracurium besylate, the time to maximum block is up to 2 min longer for equipotent doses of NIMBEX compared to atracurium besylate. The clinically effective duration of action and rate of spontaneous recovery from equipotent doses of NIMBEX and atracurium besylate are similar.[1-4]

Muscle relaxants with a short duration of action are particularly useful at the time when there is difficult mask ventilation. Mask ventilation with 100% oxygen should begin as soon as possible after induction of anaesthesia. Neuromuscular block abolishes laryngeal reflexes, increases chest compliance, and facilitates face-mask ventilation. Complete neuromuscular block should be ensured if any difficulty is encountered with airway management.[5]

Ephedrine, a stereoisomer to better-known pseudoephedrine, is a sympathomimetic amine that has unique effects due to its indirect mechanism compared to other sympathomimetic agents like pseudoephedrine and phenylephrine. Ephedrine acts as both a direct and indirect sympathomimetic. It binds directly to both alpha and beta receptors; however, its primary mode of action is achieved indirectly, by inhibiting neuronal norepinephrine reuptake and by displacing more norepinephrine from

storage vesicles. This action allows norepinephrine to be present in the synapse longer to bind postsynaptic alpha and beta receptors. Ephedrine's indirect mechanism results in a sustained or even increased heart rate due to norepinephrine's ability to bind both alpha and beta receptors, whereas more direct sympathomimetics like phenylephrine result in reflex bradycardia. While the indirect effect is most profound on the arterial blood pressure, the direct vasoconstricting action functions more on the venous system. It is, therefore, effective in elevating central venous pressure when the patient is fluid challenged.[6, 7]Hence; under the light of above-mentioned data, the present study was undertaken for assessing the effect of pre administration of a small dose of ephedrine on onset time of cisatracurium.

MATERIALS & METHODS

The present study was undertaken for assessing the effect of pre administration of a small dose of ephedrine on onset time of cisatracurium. A total of 40 patients scheduled for elective and emergency surgical procedures under general anaesthesia were enrolled. All patients were assessed preoperatively with history, physical examination and relevant investigations. All were kept nil per oral 6 hours prior to surgery.These patients were divided into two groups of 20 each- GROUP 1: Receiving ephedrine (70 micrograms/kg), and GROUP 2: Receiving saline.Effects of intravenous ephedrine on the onset time of cisatracurium after a bolus dose of cisatracurium (0.15 mg/kg) were studied. Patients anesthetized with fentanyl (1.5micrograms/kg) and propofol (1-2mg/kg) were randomly divided into 2 groups to receive either ephedrine (70micrograms/kg) or saline 5 seconds before propofol. Cisatracurium was administered after loss of consciousness. Neuromuscular block was assessed at adductor pollicis using accelography with train of four stimulation. Intubation with appropriate size endotracheal tube following muscle relaxation. The data were entered into Microsoft excel sheet. Data was summarized using frequency distribution and descriptive analysis.

RESULTS

Mean age of the patients of Group 1 and group 2 was 35.3 years and 34.7 years respectively. Both the study groups were comparable in terms of age-wise distribution of patients. 60 percent of the patients of group 1 and 65 percent of the patients of group 2 were males while the remaining were females. Both the study groups were comparable in terms of gender-wise distribution of patients.None of the patient of both the study groups showed the presence of allergy.Non-significant results were obtained while comparing the distribution of patients according to Viby Mogenson Score.Mean time of onset among the patients of Group 1 and Group 2 was 141.8 seconds and 169.2 seconds respectively. Significant results were obtained while comparing the mean time of onset among the patients of two study groups.

Table 1: Gender-wise distribution of patients

Gender	Group 1		Group 2	
	Number of patients	Percentage	Number of patients	Percentage
Males	12	60	13	65
Females	8	40	7	35
Total	20	100	20	100

Table 2: Allergy

Allergy	Group 1		Group 2	
	Number of patients	Percentage	Number of patients	Percentage
Absent	20	100	20	100
Present	0	0	0	0
Total	20	100	20	100

Table 3: Time of onset

Time of onset (seconds)	Group 1	Group 2	p- value
Mean	141.8	169.2	0.001*
SD	19.4	23.5	

*: Significant

DISCUSSION

Cisatracurium, a benzyl isoquinoline compound of the intermediate-acting neuromuscular blockade (NMB) class, has high potency, causes a minor release of histamine, less laudanosine production, undergoes organ-independent Hofmann elimination, and has a slower onset time.[8- 10]Hence; under the light of above-mentioned data, the present study was undertaken for assessing the effect of pre administration of a small dose of ephedrine on onset time of cisatracurium.

Mean age of the patients of Group 1 and group 2 was 35.3 years and 34.7 years respectively. Both the study groups were comparable in terms of age-wise distribution of patients. 60 percent of the patients of

group 1 and 65 percent of the patients of group 2 were males while the remaining were females. Both the study groups were comparable in terms of gender-wise distribution of patients.None of the patient of both the study groups showed the presence of allergy.Non-significant results were obtained while comparing the distribution of patients according to Viby Mogenson Score.Mean time of onset among the patients of Group 1 and Group 2 was 141.8 seconds and 169.2 seconds respectively. Significant results were obtained while comparing the mean time of onset among the patients of two study groups.Anandan K et al compared the effects of priming and ephedrine pretreatment on the onset time of intubating dose of vecuronium. Hemodynamic parameters were comparable between groups at all time frames ($P > 0.05$). Pretreatment with ephedrine 70 µg/kg shortens the onset time of vecuronium for intubation and is superior to the priming technique.[11]
Chumak P et al examined the effects of Nicardipine on the onset time and intubating conditions of Cisatracurium. Ninety-nine patients were randomized into one of three groups; NS (C group), Nicardipine 10 mcg/kg (N10 group), and Nicardipine 20 mcg/kg (N20 group). After which, these patients received the study drugs, according to the group they were assigned to, intravenously before the induction of anesthesia. Train of Four (TOF) ratio or count, blood pressure, pulse rate, laryngoscopic view, grade of intubation, intubating conditions, minimal mean arterial pressure, total propofol, and vasopressors doses were recorded. The onset times of Cisatracurium were 420, 420, and 360 seconds in the C, N10, and N20 groups respectively, with a p-value of 0.636, while, intubating conditions were acceptable in 93.8, 96.8 and 100% respectively with a p-value of 0.771. Heart rates were higher in the N10 and N20 groups than that of those in the C group. Additionally, mean arterial pressures were lower in N20 group than both N10 and C groups, which showed similar MAPs. Total propofol, ephedrine and atropine doses were similar within all groups. The use of Nicardipine neither reduces the onset time, nor improves intubating conditions of Cisatracurium.[12]Sharma M et al in 2019 compared the influence of Ephedrine 30, 70 and 110 mcg/kg on intubating conditions and hemodynamics using Propofol and low dose Rocuronium. 90 patients of either sex, ranging from 18-50 years belonging to ASA grade 1 and 2 undergoing elective surgeries under general anesthesia were taken up for study. Patients were randomly allocated to one of the three groups of 30 patients each. Group 1: Rocuronium 0.6 mg/kg and Ephedrine 30 mcg/kg Group 2: Rocuronium 0.6 mg/kg and Ephedrine 70 mcg/kg Group 3: Rocuronium 0.6 mg/kg and Ephedrine 110 mcg/kg. So, the combination of Propofol 2.5 mg/kg, Rocuronium 0.6 mg/kg and ephedrine 70 mcg/kg may be of value when use of Succinylcholine is contraindicated for RSI.[13]

CONCLUSION

Pretreatment with ephedrine 70 µg/kg improved intubating conditions after cisatracurium administration and facilitated the early onset of cisatracurium without adverse hemodynamic effects.

REFERENCES

1. El-Kasaby AM, Atef HM, Helmy AM, El-Nasr MA. Cisatracurium in different doses versus atracurium during general anesthesia for abdominal surgery. Saudi J Anaesth. 2010;4(3):152-157.
2. Kisor DF, Schmith VD. Clinical pharmacokinetics of cisatracurium besilate. Clin Pharmacokinet 1999;36:27-40.
3. Lighthall GK, Jamieson MA, Katolik J, Brock-Utne JG. A comparison of the onset and clinical duration of high doses of cisatracurium and rocuronium. J Clin Anesth 1999; 11: 220-5.
4. Jimsheleishvili S, Marwaha K, Sherman Al. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jul 10, 2020. Physiology, Neuromuscular Transmission.
5. Omar A, Marwaha K, Bollu PC. Physiology, Neuromuscular Junction. [Updated 2020 May 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470413/
6. Slater CR. The Structure of Human Neuromuscular Junctions: Some Unanswered Molecular Questions. Int J Mol Sci. 2017 Oct 19;18(10)
7. Jones RA, Harrison C, Eaton SL, Llavero Hurtado M, Graham LC, Alkhammash L, Oladiran OA, Gale A, Lamont DJ, Simpson H, Simmen MW, Soeller C, Wishart TM, Gillingwater TH. Cellular and Molecular Anatomy of the Human Neuromuscular Junction. Cell Rep. 2017 Nov 28;21(9):2348-2356.
8. Fagerlund MJ, Eriksson LI. Current concepts in neuromuscular transmission. Br J Anaesth. 2009 Jul;103(1):108-14.
9. Hunter JM. New neuromuscular blocking drugs. N. Engl. J. Med. 1995 Jun 22;332(25):1691-9.
10. Forel JM, Roch A, Marin V, Michelet P, Demory D, Blache JL, Perrin G, Gainnier M, Bongrand P, Papazian L. Neuromuscular blocking agents decrease inflammatory response in patients presenting with acute respiratory distress syndrome. Crit. Care Med. 2006 Nov;34(11):2749-57.
11. Anandan K, Suseela I, Purayil HV. Comparison of Effect of Ephedrine and Priming on the Onset Time of Vecuronium. Anesth Essays Res. Apr-Jun 2017;11(2):421-425.
12. Chumak P, Thertchanakun S, Wasinwong W, Plansangkate P, Mahatthanathporn S, Chantarokorn A. The Effects of Nicardipine on the Onset Time and Intubating Conditions of Cisatracurium. J Clin Res Med. 2019; 2(3): 1–6
13. Sharma M, Jamwal A, Mehta A, Jyoti R. A Comparative Study of Different Doses of Ephedrine on Intubating Conditions and Hemodynamics Using Propofol and Low Dose Rocuronium. J Anesth Clin Res 2019, 10:11