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Dexmedetomidine: A Novel Premedicant in RSI - A Clinical Study Conducted in a Tertiary Care Institution in South India

Authors
Beula G[1], Rajani Gandha Venkitachalam[2], Raman Naresh Kumar[3]
[1]Assistant Professor, Department of Anaesthesia, Sree Mookambika Institute of Medical Sciences, Kulasekharam, Tamilnadu, India
Email: *beulakiron@gmail.com*
[2]Assistant Professor, Department of Anaesthesia, Department of Anaesthesia, Govt. Medical College Thiruvananthapuram, Kerala, India
Email: *gauri20cn@gmail.com*
[3]Postgraduate Resident, Dept of Anaesthesia, Govt. Medical College, Thiruvananthapuram, Kerala, India
Corresponding Author
Raman Naresh Kumar
Add: 2/221 Thottakaran Street, Siruvapuri, Ponneri Taluk, Tiruvallur District, Chennai Tamilnadu 601206
Email: *nareshanesthetist@gmail.com, Mobile No.8939392787*

ABSTRACT

Background: *Patients often require a rapid sequence induction (RSI) endotracheal intubation technique during emergency ophthalmic surgeries which is often a nightmare to the anaesthesiologists as patients with penetrating eye injury often present with full stomach. Traditionally succinylcholine has been the most commonly used muscle relaxant for this purpose because of its fast onset and short duration; unfortunately, it can have serious side effects like increased intraocular pressure. Various drugs like sufentanil and clonidine has been studied in an attempt to use as a premedicant for blunting the rise in intraocular pressure with varying results. Dexmedetomidine is a selective alpha-2 adrenergic agonist that has IOP-lowering properties along with sedative and analgesic effects. Studies have shown dexmedetomidine reduces intraocular pressure, intubation responses and anaesthetic requirements in patients undergoing ophthalmic surgery.*

Aim: *To determine the effect of dexmedetomidine in the prevention of rise of IOP by succinylcholine during RSI intubation*

Methods: *70 patients who are undergoing elective non ophthalmic surgery have been enrolled in this study. Adult patients in the age group 20-65 years weighing 60-80 kg of either sex falling under ASA I / II of American Society Of Anaesthesiologists (ASA) physical status classification. We collected the data using structured proforma and interpreted using Ramsay sedation scale, Schiotz tonometry for measuring IOP.*

Results: *Dexmedetomidine as a premedicant in patients undergoing surgeries under GA was found to reduce the IOP by 34% after a single i.v. dose of dexmedetomidine (0.6 mg/kg). Additionally, the pressor response to laryngoscopy and endotracheal intubation was also significantly attenuated*

Conclusions: *Premedication with intravenous Dexmedetomidine under the dose given in the present study design attenuates the rise in intraocular pressure following succinylcholine and intubation. The attenuation of haemodynamic stress response to laryngoscopy and intubation is an additional advantage. Hence dexmedetomidine could be used as a premedicant in situations where an increase in intraocular pressure following succinylcholine and intubation is prejudicial for patients.*

Keywords-*Anaesthesia; ophthalmic, RSI, Dexmedetomidine, increased intra-ocular pressure.*

Introduction

Patients often require a rapid sequence induction (RSI) endotracheal intubation technique during emergency ophthalmic surgeries which is often a nightmare to the anaesthesiologists as patients with penetrating eye injury often present with full stomach, Traditionally succinylcholine has been the most commonly used muscle relaxant for this purpose because of its fast onset and short duration;[1] unfortunately, it can have serious side effects like increased intraocular pressure, blood pressure and heart rate.[2] Pretreatment with lignocaine in a dose of 2ml/kg has kept IOP significantly below basal values throughout the study but it also suppressed mean arterial pressure to such low level which is detrimental for patients.[3] Various drugs like diazepam, tubocurarine, sufentanil and clonidine has also been studied in an attempt to use as a premedicant for blunting the rise in intraocular pressure with failing results.[4],[5] Dexmedetomidine is a selective alpha-2 adrenergic agonist that has IOP-lowering properties along with sedative and analgesic effects.[6] Studies have shown that the hemodynamic responses(increased blood pressure and heart rate) produced by succinylcholine during the time of induction can be attenuated by dexmedetomidine is an added advantage along with reducing intraocular pressure.[7] Few studies[8] have also proved that dexmedetomidine brilliantly reduces the stress hormones postoperatively for prolonged duration as context-sensitive half-time ranging from 4 min after a 10-min infusion to 250 min after an 8-h infusion.[9] All these properties makes dexmedetomidine stands tall in the race of premedicant needed to be used during rapid sequence induction by succinyl choline and endotracheal intubation.

Materials and Methods

Subject

This study was conducted on 70 adult patients in the age group 20-65 years weighing 60-80 kg of either sex ASA I / II of American Society Of Anaesthesiologists (ASA) physical status classification who were scheduled for elective non ophthalmic surgeries under general anaesthesia at Government Trivandrum Medical college, Trivandrum, Kerala. 70 patients were divided into two groups with 35 in study group and 35 in control group respectively. All the patients included in the study were subjected to a detailed pre-anaesthetic check up and are fasted for 8 hours. Standard monitors like ECG, pulse oximeter, noninvasive blood pressure (NIBP) were attached and baseline vital parameters have been recorded. Topical Paracaine 0.5%, 2 drops in each eye was applied to the cornea and IOP was measured with a Schiöetz tonometer (made in Germany). Informed consent was obtained from all study subjects after explanation of the nature and possible consequences of the study. All study subjects were randomly allocated into two groups of 35 patients each to receive 0.6μg/kg dexmedetomidine (group 1) or normal saline (group 2) i.v. as premedication. Randomisation done using a computer generated random number. After 15minutes, sedation was assessed using Ramsay Sedation Scale, pre-oxygenation is done for 3 min, patients were induced with a sleep dose of thiopentonesodium. Succinylcholine was administered at a dose of 1.5 mg/kg to achieve muscle relaxation for intubation. After cessation of fasciculation, the trachea was intubated under direct vision laryngoscopy. The patient was excluded from the study if the trachea could not be intubated at the first attempt. After securing the airway, anaesthesia was maintained in all two groups with oxygen (33%), nitrous oxide (66%), isoflurane (1%), fentanyl citrate (1 μg/kg) and incremental doses of vecuronium bromide. Decrease in systolic blood pressure (more than 30% below baseline) was recorded as hypotension and treated with crystalloids and phenylephrine. Bradycardia [heart rate (HR) <50 beats/min] was treated by i.v. atropine.

Outcome measure

Mean arterial pressure (MAP), HR and IOP was recorded at the following time points:

T1: Before premedication

T2: Fifteen minutes after premedication

T3: Thirty seconds after thiopentone sodium
T4: Thirty seconds after suxamethonium
T5: One minute after intubation
T6: Two minutes after intubation
T7: Four minutes after intubation
T8: Six minutes after intubation

Statistical Analysis

Data were analysed using Standard SPSS 10.0 for Windows. Results are reported as mean + standard deviation. Demographic data and type of procedure were compared using unpaired t-test. Gender was compared using the chi square test. The changes occurring in IOP, heart rate, MAP in the two groups at each point of time were compared with each other using independent sample test. Sedation between the two groups was compared using Mann Whitney U test. A p-value of less than 0.05 was considered statistically significant.

Sedation score was recorded 15 minutes after dexmedetomidine administration using RAMSAY SEDATION SCALE

SCORE	DEFINITION
1	Patient anxious &agitated or restless or both
2	Patient cooperative ,oriented & tranquil
3	Patient responds to commands only
4	Patient has a brisk response to light glabellar tap or loud auditory stimulus
5	Patient asleep,sluggish response to light glabellar tap or loud auditory stimulus
6	Patient doesn't respond to painful stimulus

Result

As evidenced by statistical analysis there were no significant differences between the two groups with regard to age, sex, weight, procedure ($p < 0.05$). Table(1), Table(2), Table(3), Table(4).

There were also no significant differences at baseline heart rate, MAP and IOP.

There was no significant difference in the baseline IOP between the study and control population. (p 0.0706) 15 minutes after premedication. Even though the mean IOP of the study population 11.8 is lower than that of the control population (12.3) it is not statistically significant. But from T2 i.e., 30 seconds after thiopentone sodium onwards till T6 (2 minutes after intubation), the differences in IOP between study and control groups is statistically significant. Table (5), Figure (1). This shows that even though the IOP rises following succinyl choline and intubation in both groups the rise in the study group is significantly lower than that in the control group.The peak value of IOP is reached at T5 (one minute after intubation). This is 15.5 (mean) + 2.11 SD for study group and 18.93 (mean) +1.49SD for control group. The difference between the two from baseline 4.02 to study group is statistically significant. Table(9),Table (10),Table (11).In the present study heart rate increased significantly after intubation in the control group (mean of 77 beats / minute with SD 8 at baseline to mean of 97 beats / minute with SD 7.2 at 1 minute after intubation). On the contrary in patients who received dexmedetomidine premedication, this response was attenuated (mean of 80 beats / minute with SD 9.2 at baseline to mean of 84 beats per minute with SD 8.7 at T5). Statistically significant decrease in heart rate of the study group from control group continues after intubation at 2,4,6 minutes. The increase in heart rate at T3 (30 seconds after thiopentonesodium) is consistent with the tachycardia producing the effect of thiopentone sodium.[10] Table(6), Figure(2). In the placebo group 15 minutes after premedication the MAP shows a rise of ~ 2 mm Hg where as in the study group, MAP falls ~ 6 mm Hg. But after succinyl choline and intubation both study and control group show increase in MAP from previous value. However this stress induced increase in MAP is much attenuated in case of study group. (mean 86mm Hg with SD 8.6 at T5 for study group and mean of 99mm Hg with 4.8 SD for control group). The attenuation of MAP rise also continuous at 2,4, 6 minutes after intubation. Table(7), Figure(3). On comparing the sedation of score of patients 15 minutes after premedication, using Ramsay sedation scale. The dexmedetomidine group shows a significantly higher grade of sedation. Table(8), Figure(4). None of the patients in study group or control group developed bradycardia requiring atropine. None of the patients in study group or control group developed hypotension requiring phenylephrine.

Table 1: Comparison of sample based on age

Age	Case		Control	
	Count	Percent	Count	Percent
<=40	15	42.9	12	34.3
41 - 50	12	34.3	13	37.1
>50	8	22.9	10	28.6
Mean ± SD	42.5 ± 9.8		45.2 ± 9.3	

t = 1.16, p = 0.248

Table 2 : Comparison of sample based on sex

Sex	Case		Control		χ^2	p
	Count	Percent	Count	Percent		
Female	22	62.9	20	57.1	0.24	0.626
Male	13	37.1	15	42.9		

Table 3 : Comparison of sample based on weight

Weight	Case		Control	
	Count	Percent	Count	Percent
<60	11	31.4	12	34.3
60 - 69	13	37.1	15	42.9
>=70	11	31.4	8	22.9
Mean ± SD	65.1 ± 9.4		63.8 ± 9	

t = 0.6, p = 0.552

Table 4 : Comparison of sample based on procedure

Procedure	Case		Control	
	Count	Percent	Count	Percent
Cholecystectomy	4	11.4	3	8.6
Excision	5	14.3	5	14.3
Gastrectomy	0	0.0	2	5.7
Hemithyroidectomy	2	5.7	0	0.0
Mastectomy	5	14.3	4	11.4
Parotidectomy	2	5.7	5	14.3
Sistrunks operation	2	5.7	1	2.9
Thyroidectomy	14	40.0	15	42.9
Total thyroidectomy	1	2.9	0	0.0

Table 5: Comparison of IOP based on group at different time points

Time Points	Case			Control			t	p
	Mean	SD	N	Mean	SD	N		
Before premedication	13.5	2.0	35	13.3	2.1	35	0.38	0.706
Fifteen minutes after premedication	11.8	1.9	35	12.3	1.9	35	1.12	0.266
Thirty seconds after thiopentone sodium	11.0	1.6	35	11.9	1.8	35	2.21*	0.030
Thirty seconds after suxamethonium	14.1	2.1	35	16.8	2.2	35	5.3**	0.000
One minute after intubation	15.6	2.1	35	18.9	1.5	35	7.72**	0.000
Two minute after intubation	12.1	2.1	35	14.2	1.7	35	4.55**	0.000
Four minute after intubation	12.2	2.1	35	11.8	1.8	35	0.98	0.329
Six minute after intubation	11.6	2.0	35	11.7	1.9	35	0.35	0.727

**: - Significant at 0.01 level *: - Significant at 0.05 level

Fig1 : Comparison of IOP based on group at different time points

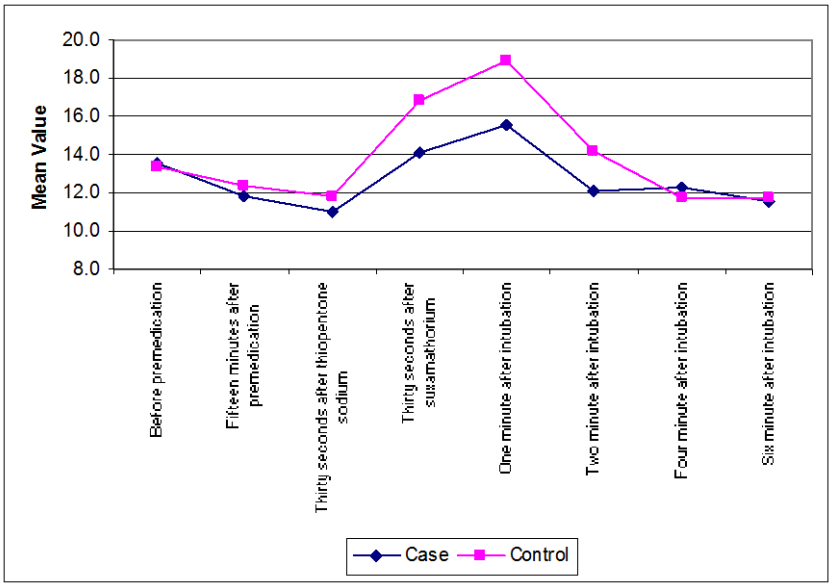

Table 6 : Comparison of HR based on group at different time points

Time Points	Case			Control			t	p
	Mean	SD	N	Mean	SD	N		
Before premedication	80.1	9.2	35	77.7	8.0	35	1.18	0.242
Fifteen minutes after premedication	72.0	7.6	35	82.7	7.4	35	6.02**	0.000
Thirty seconds after thiopentone sodium	79.4	9.8	35	88.3	6.4	35	4.5**	0.000
Thirty seconds after suxamethonium	80.3	8.7	35	92.9	6.0	35	7.07**	0.000
One minute after intubation	84.4	8.7	35	97.0	7.2	35	6.55**	0.000
Two minute after intubation	81.0	9.7	35	87.0	6.6	35	3.02**	0.004
Four minute after intubation	78.5	9.0	35	83.0	6.6	35	2.38*	0.020
Six minute after intubation	75.6	8.8	35	81.1	7.7	35	2.82**	0.006

**: - Significant at 0.01 level *: - Significant at 0.05 level

Fig. 2 : Comparison of HR based on group at different time points

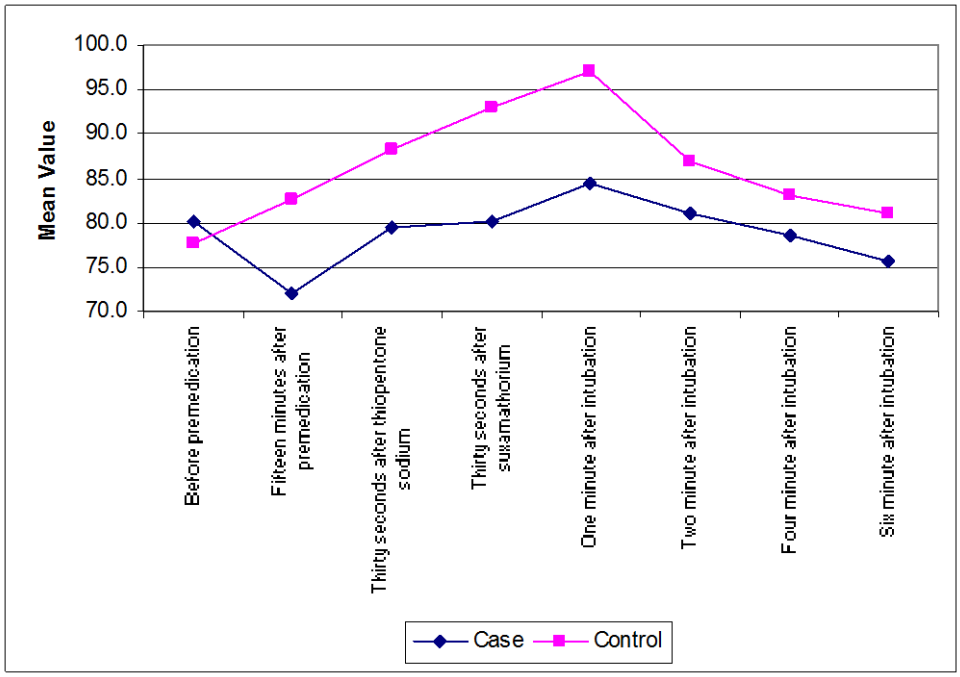

Table 7: Comparison of MAP based on group at different time points

Time Points	Case			Control			t	p
	Mean	SD	N	Mean	SD	N		
Before premedication	89.2	4.7	35	87.7	3.0	35	1.63	0.108
Fifteen minutes after premedication	83.9	7.4	35	89.6	3.4	35	4.17**	0.000
Thirty seconds after thiopentone sodium	82.1	6.9	35	89.2	2.3	35	5.8**	0.000
Thirty seconds after suxamathorium	83.4	8.4	35	92.2	4.0	35	5.63**	0.000
One minute after intubation	86.9	8.6	35	99.0	4.8	35	7.27**	0.000
Two minute after intubation	82.1	7.9	35	90.2	4.5	35	5.25**	0.000
Four minute after intubation	80.1	8.4	35	88.0	4.2	35	5.01**	0.000
Six minute after intubation	79.4	7.8	35	86.3	4.2	35	4.64**	0.000

**: - Significant at 0.01 level

Fig 3. Comparison of MAP based on group at different time points

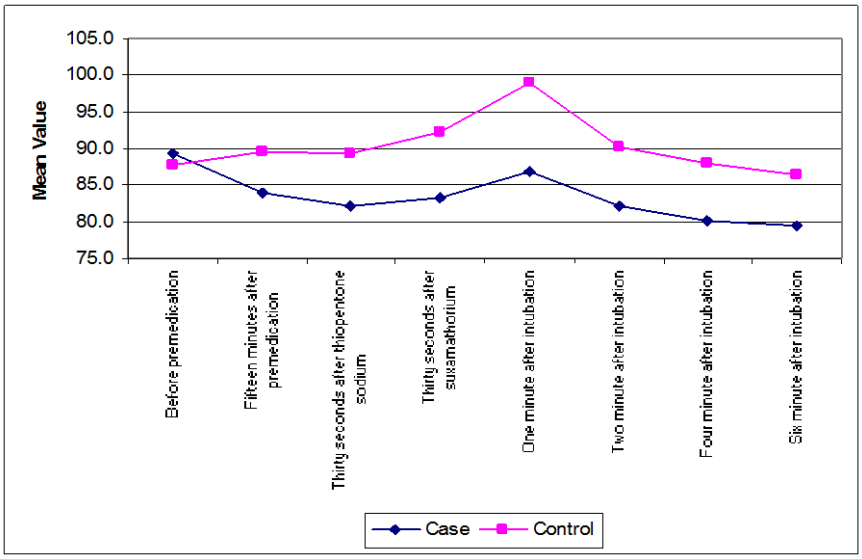

Table 8 : Comparison of sample based on sedation

Sedation	Case		Control		Z	p
	Count	Percent	Count	Percent		
Grade I	6	17.1	23	65.7	4.58**	0.000
Grade II	19	54.3	12	34.3		
Grade III	10	28.6	0	0.0		

#Mann Whitney U Test

Fig 4. Comparison of sample based on sedation

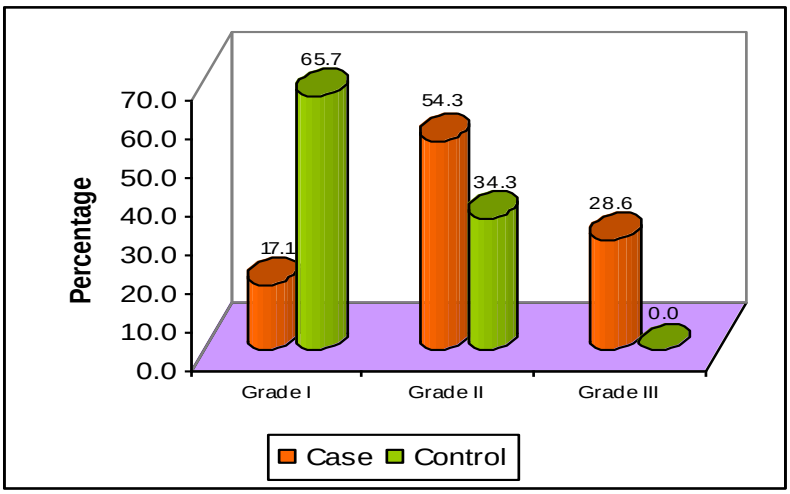

Table: 9 Case

	Mean	Std Deviation	P
IOP at baseline	13.52	1.97	0.062
Peak	15.55	2.11	

Table 10 Control

	Mean	Std Deviation	P
IOP at baseline	13.44	2.12	0.000
Peak	18.93	1.49	

Table:11 Difference between peak IOP (T5) and baseline

	Mean	Std Deviation	P
Case	2.02	2.38	<0.005
Control	5.59	1.66	

Discussion

The intraocular pressure and haemodynamic stress response to laryngoscopy and intubation is supposed to be initiated by sympathetic responses which starts within 5 seconds of laryngoscope pressing the base of tongue. It reaches a peak at about 2 minutes after intubation. Then it starts to fall and reaches the baseline value between 5 to 10 minutes after intubation. In the present study, an attempt has been made to determine the efficacy of intravenous dexmedetomidine 0.6 µg /kg 15 minutes before succinyl choline and intubation in attenuating these stress responses. The intraocular hypotensive effect of dexmedeto-midine in the present study is consistent with previous several researches on alpha-2 agonists. Dexmedetomidine infusion as a premedicant was effective in reduction of the IOP significantly. The drug was also found to reduce the IOP by 34% after a single i.v. dose of dexmedetomidine 0.6 mg/kg-1[10]. On the contrary, when Lee and colleagues infused dexmedetomidine as a supplement to isoflurane anaesthesia, they found no IOP lowering effect. However, the loading dose of dexmedetomidine used in their study was lower than that in the present study. No previous study examined the effect of dexmedetomidine on the succinylcholine induced ocular hypertension. The effect of dexmedetomidine on the IOP may be caused by a direct vasoconstrictor effect on the afferent blood vessels of the ciliary body, which results in reduction of aqueous humour production.[11] Moreover, it could increase outflow of the aqueous humour caused by a reduction of the sympathetically mediated vasomotor tone of the ocular drainage system.[12] Additionally, its associated haemodynamic response could contribute to the IOP lowering effect.[13] In the present study, HR and MAP increased significantly after intubation in the control group. On the contrary, in patients who received dexmedetomidine premedication, this response was attenuated. Several previous studies have reported the blunting effect of dexmedetomidine on this sympathetic response to laryngoscopy and intubation.[14],[15],[16] This could be due to the centrally mediated sympatholytic effects of alpha-2 agonists and by its decreasing norepinephrine release via peripheral presynaptic alpha-2 receptors. The dose of dexmedetomidine premedication administered in the present study (0.6 µg kg-1) was based on a previous clinical study [17] where the selected dose resulted in a significant reduction in IOP and prevented the rise in the IOP in response to intubation. In addition, the pressor response to laryngoscopy and endotracheal intubation was also significantly attenuated. Higher doses of dexmedetomidine were associated with an additional reduction in arterial pressure and HR without any further decrease in IOP [18],[19]. Some authors find that the use of succinylcholine in open ocular trauma is controversial and an alternative anaesthetic management based on the use of non-depolarizing neuromuscular blocking agents, despite its slower onset, was suggested. Various methods have been tried to speed up this onset, including priming, administering the non-depolarizing relaxant before the induction agent and high dose regimen. Despite these strategies non-depolarizing neuromuscular blocking agents can still result in non-ideal intubation conditions: increases in the IOP from mask application and longer time with insecure airway and prolonged paralysis. Despite this debate about the use of succinylcholine in open globe injury, most authors still agree on its use in difficult airway cases with salvageable eye situations.[20]

Limitations of the study

A limitation of this study is that the effect of dexmedetomidinc on the IOP changes after succinylcholine and intubation cannot be isolated from its action on the haemodynamics since both effects are parallel and a causal relationship cannot be denied. However, this limitation should not decline the potential advantage of using dexmedetomidiue as alternative agent to obtund the IOP changes of succinylcholine and intubation.

Conclusion

Premedication with intravenous Dexmedetomidine under the dose given in the present study design attenuates the rise in intraocular pressure following succinylcholine and intubation .The attenuation of haemodynamic stress response to laryngoscopy and intubation is an additional advantage .Hence dexmedetomidine could be used as a premedicant in situation where an increase in intraocular pressure following succinylcholine and intubation is prejudicial for patients.

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