TWO DIFFERENT DOSES OF DEXMEDETOMIDINE IN ATTENUATING SYMPATHOADRENAL RESPONSE TO ENDOTRACHEAL INTUBATION - A COMPARATIVE STUDY

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ABSTRACT

BACKGROUND

The objective of our study was to determine whether a lower dose (0.6 microgram/kg) of dexmedetomidine is as effective as the usual dose (1 microgram/kg) for attenuating sympathoadrenal response to endotracheal intubation.

MATERIALS AND METHODS

90 patients were fixed to undergo elective surgeries under general anaesthesia, were randomly divided into 3 groups. Group A-received 0.6 microgram/kg of dexmedetomidine, group B received 1 microgram/kg of dexmedetomidine and group C received 10 ml normal saline over 10 minutes before induction. Anaesthesia was standardised in the groups and vital parameters were recorded for up to 10 minutes after intubation.

RESULTS

At 5 minutes and completion of drug infusion, group B had statistically significant fall in heart rate as compared to group A (17.3% and 27.2% vs. 5.2% and 10.3%). Maximum fall in mean heart rate was observed at 10 minutes after intubation in group A (29.1%) and at completion of drug infusion in group B (27.2%). The maximum fall in SBP in both groups was observed at 10 minutes following intubation, Group C had statistically significant higher values of HR, SBP, DBP, MAP during all time interval following ET intubation.

CONCLUSION

A lower dose of dexmedetomidine (0.6 microgram/kg) loading dose provides, significantly better attenuation of sympathoadrenal response to endotracheal intubation unaccompanied by transient increase in blood pressure and bradycardia, which is observed at higher dose of dexmedetomidine (1 microgram/kg) loading dose.

KEYWORDS

Dexmedetomidine, Endo-tracheal Intubation, Sympathoadrenal Response.

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BACKGROUND

Airway management is essential for conductance of general anaesthesia. Artificial airway devices are needed for maintaining an adequate airway for the anesthetised patients.[1] Endotracheal intubation is trans laryngeal placement of endotracheal tube via the nose or mouth. Laryngoscopy and the tracheal intubation are the noxious stimuli which provoke a transient, but marked sympathetic response manifesting as hypertension and tachycardia. The circulatory response to laryngeal and tracheal stimulation following laryngoscopy and tracheal intubation were documented by Reid and brace in 1940 and King et al in 1951 and interpreted as reflex sympathoadrenal stimulation. Increase in MAP of an average 25 mm of mercury was observed in normotensive patients following laryngoscopy and intubation under anaesthesia, with thiopental, nitrous oxide, oxygen and suxamethonium.[2]

Left ventricular failure, myocardial ischemia and cerebral haemorrhage may occur in high risk patients. Convulsions maybe precipitated in pre-eclamptic patients.[3] Post intubation sympathoadrenal responses have been associated with ST segment changes and ventricular arrhythmias. Norepinephrine levels may double and continue 4-8 mins, epinephrine levels may quadruple, Although the response may be transient, it is invariable, significant, often persistant and of great concern. Many strategies have been advocated to minimise the haemodynamic adverse responses and aimed at different levels of the reflex arc.[4]

Example

- Blockade of peripheral sensory receptors and afferent input by local anaesthetic-Topical infiltration of superior laryngeal nerve.
- Blockade of central mechanisms of integration of sensory input-Fentanyl, morphine etc.

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- Blockade of efferent pathway and effector sites-alpha agonist, beta blockers, iv lignocaine, calcium channel blockers etc.

No single drug or technique is satisfactory.[4]

Alpha 2 receptors are located in blood vessels where they mediate vasoconstriction and on sympathetic terminals where they inhibit norepinephrine release.

Alpha 2 receptors are located within central nervous system and their activation leads to sedation, reduction of tonic levels of sympathetic outflow and augmentation of cardiac vagal activity, which can result in decrease I heart rate and cardiac output. In addition, alpha 2 receptors within the spinal cord modulate pain pathways, thereby providing analgesia.[5,6,7]

Intra venous dexmedetomidine, a central alpha 2 agonist in being used in Anastasia practise as a premedicant. Advantages are sedation, analgesia anxiolysis and improved haemodynamic stability. Because of these properties, it can reduce the haemodynamic response of laryngoscopy and intubation.[6]

It has been recently introduced in India (2009). Various studies have used dexmedetomidine in the dose of 0.6 microgram/kg.[8,9] and 1 microgram/kg body weight[10,11] as intravenous bolus for attenuating haemodynamic response. There is a need to know whether 0.6 microgram/kg or 1 microgram/kg is the ideal dose for attenuation of haemodynamic response to laryngoscopy and intubation. Hence the present study is aimed at comparing the effectiveness of 2 different doses of intravenous dexmedetomidine.

Objectives

- To study whether lower dose (0.6 microgram/kg) dexmedetomidine is as effective as the usual dose (1 microgram/kg) for attenuating haemodynamic response to laryngoscopy and intubation.
- To study whether lower dose (0.6 microgram/kg) dexmedetomidine is associated with less side effects as compared to usual dose.
- To study the effect on HR, SBP, DBP, MAP associated with laryngoscopy and intubation
- To study any adverse effects associated with administration of either dose of dexmedetomidine such as perioperative hypotension, bradycardia.

MATERIALS AND METHODS

After getting written informed consent from the patients, 90 patients of ASA 1 and 2 grade adults aged 18-60 years undergoing elective surgery under GA was included in the study.

Inclusion Criteria

- Mallampatti score 1 and 2
- ASA grade 1 and 2
- Age between 18-60 years.

Exclusion Criteria

- Age less than 18 or more than 60 years
- ASA grade 3 and 4
- Patients with hypertension, cardiac, renal, hepatic or thyroid abnormalities or cerebral diseases.
- Patients with pre-operative systolic BP of less than 80 mm of mercury, diastolic BP > 60 mmHg.
- Patients with bradycardia, arrhythmias and already on beta blockers
- Patients with difficult airway and obese patients
- Pregnant patients
- Patients for emergency surgeries
- History of allergy towards any of the studied drugs.

Study Design

Analytical randomised prospective study.
An informed consent was taken in all patients.

Pre-Anaesthetic Evaluation

A careful pre-anaesthetic evaluation was done by taking history and clinical examination.

Patients pulse rate, blood pressure, respiratory rate and relevant clinical signs and symptoms were noted.

All patients received alprazolam 0.5 mg orally at night on the day before surgery.

Randomisation of the Patients

Patients were randomised into 3 groups consisting of 30 each by Non-investigator to receive dexmedetomidine 0.6 microgram/kg, 1 microgram/kg and saline by picking a lot method.

Preparation of Operation Theatre

All drugs and equipment were checked and kept ready before starting the procedure. On the day of surgery, intra-venous line obtained with 18 of 20-gauge cannula according to surgery planned. On entering the OT, pulse oxymeter, NIBP and ECG monitors were connected. A baseline heart rate Systolic, diastolic and mean arterial blood pressure were recorded.

Anaesthetic Procedure

Before 10 mins of induction.

- Group A-Received 0.6 microgram/kg of dexmedetomidine intra-venous route over 10 mins.
- Group B- Received 1 microgram/kg of dexmedetomidine intra-venous route over 10 mins.
- Group C-Received normal saline 10 ml intravenously over 10 mins.

All the patients were pre-medicated with 0.2 mg glycopyrrolate, 4 mg Emiset, given intravenously before induction. All the patients were pre-oxygenated with 100% oxygen for 3 minutes before induction. Induction was achieved with fentanyl 1 microgram/kg and propofol in incremental doses of 20 mg every 10 seconds till the verbal response is lost. Vecuronium 0.1 mg/kg was given for intubation. All patients were ventilated with 4 litres/minute

oxygen and 6 litres/min of nitrous oxide and 1% sevoflurane with the use of Bain circuit for 3 minutes and then intubated. Laryngoscopy was done with rigid laryngoscope with standard Macintosh blade. Intubation was done with appropriate sized, disposable high volume, low pressure, cuffed endotracheal tube. Oral intubation was done for all surgical procedures. Laryngoscopy and intubation was done in 15-20 seconds. No additional agents were given for the first 10 minutes post intubation, nor was any surgical stimulus given to these patients. Heart rate, Systolic, Diastolic and mean arterial pressure was recorded at the following time intervals using automatic multiparameter monitor.

1. T1-Baseline or before giving test drug.
2. T2-2 minutes after starting of test drug infusion
3. T3-5 minutes after starting test drug infusion
4. T4-Completion of test drug infusion
5. T5-After induction
6. T6-One minute after intubation
7. T7-Five minutes after intubation
8. T8-Ten minutes after intubation.

At the end of 10 minutes monitor period, surgery is commenced. Anaesthesia is maintained with oxygen, nitrous oxide, sevoflurane and vecuronium bromide of 0.02 mg/kg and IPPV. At the end of surgery reversal was done with inj. Neostigmine 0.05 mg/kg and inj. Glycopyrrolate 0.01 mg/kg iv.

Statistical Analysis- Descriptive data presented as mean + SD and in percentage. Multiple group comparisons were made by one way ANOVA, followed by unpaired 't' test for pair wise comparison. For all the tests, p value of 0.05 was considered for statistical significance.

Statistical Software- For all statistical analysis, SPSS version 22, MedCalc 9.0.1, Systat 12.0 has been used.

Microsoft excel 2013 has been used to generate master chart, tables and graphs.

RESULTS

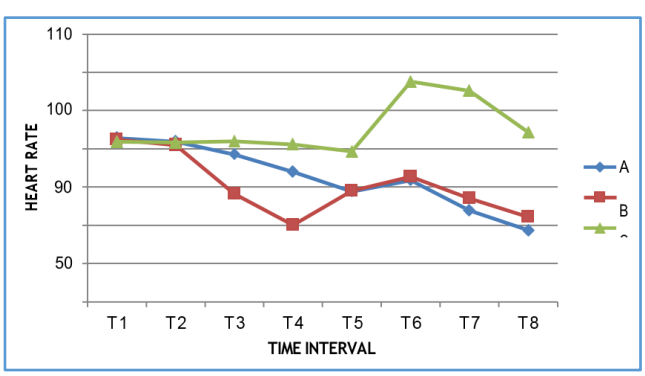

Figure 1. Comparison of Changes in Heart Rate

Mean heart rate in group A was 82.9 ± 7.38 per min, group B was 82.53 ± 7.69 per min and group C was 81.9 ± 5.98 at baseline level, which was comparable (p>0.05). At 5 minutes and at completion of drug infusion both Group A and Group B had fall in mean HR. But Group B had statistically significant fall in HR as compared to Group A. At 5 minutes, fall in HR was 5.23% in Group A, and for Group B it was 17.37%. At completion of drug infusion, fall in HR was by 10.7% and 27.26% in Group A and Group B respectively. After induction and at 1 minute after intubation, fall from baseline HR value was noted and this fall remained to be statistically insignificant between group A and group B (p>0.05). At 5 and 10 minutes after intubation, fall in HR was 22.96% and 29.15% in Group A, whereas 18.78% and 24.6% in Group B respectively which was a statistically significant difference. Maximum fall in mean HR was observed at 10 minutes after intubation in Group A and it was observed in Group B at 10 just before induction.

The difference in mean HR between group A and group C; group B and group C remains highly significant from T3 (p<0.05). Maximal increase in mean HR in control group occurred 1 minute after intubation, which was 19.2%.

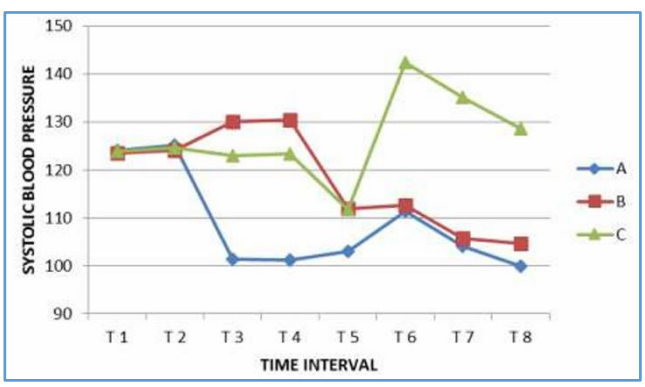

Figure 2. Comparison of Changes in Systolic Blood Pressure

The baseline mean SBP between three groups was comparable (p>0.05). There was fall of 18.37% in SBP from baseline value in group A till completion of drug infusion, while Group B showed transient rise of 5.61% from baseline value in SBP till above mentioned tome interval which was highly significant difference statistically (p <0.001). The maximum fall in SBP in both groups was observed at 10 minutes following intubation which was 19.52% and 15.27% in group A and group B respectively and this difference was also statistically highly significant (p<0.05). Neither of the group showed deviation in SBP beyond 20% of the baseline value.

The difference in mean SBP between group A and group C remains highly significant from T3 (p< 0.05). Maximal increase in mean SBP in control group occurred 1 minute after intubation, which was 14.9%.

But between group B and group C the difference in mean SBP following induction (T4) observed insignificant.

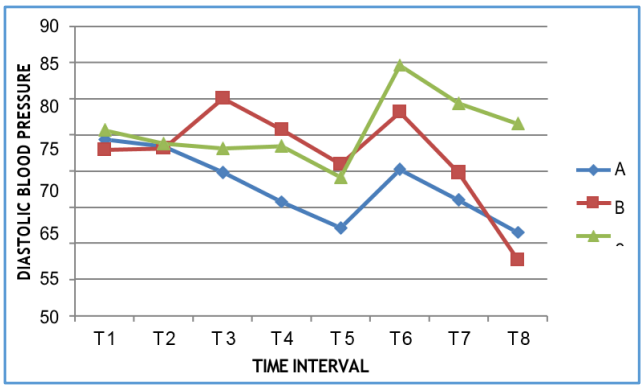

Figure 3. Comparison of Changes in Diastolic Blood Pressure

The difference in baseline mean DBP between three groups was statistically insignificant (p>0.05). Statistically significant decrease from baseline of 6.1% and 11.6% in DBP was observed in group A at 5 minutes and completion of drug infusion as compared to increase from baseline of 9.7% and 3.7% which was observed in Group B (p < 0.05).

The difference in mean DBP between group A and group C remains highly significant from T3. Maximal increase in mean DBP in control group occurred 1 minute after intubation, which was 11.9%.

But between group B and group C the difference in mean DBP following induction (T5) observed not significant.

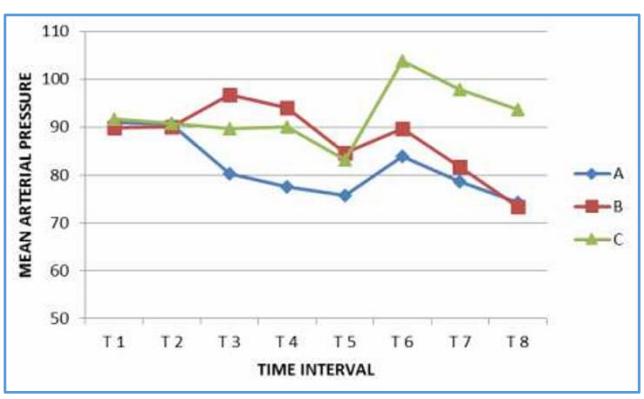

Figure 4. Comparison of Changes in Mean Arterial Pressure

The baseline mean MAP between three groups was comparable (p>0.05). There was fall of 14.7% in MAP from baseline value in group A till completion of drug infusion, while Group B showed transient rise of 4.63% from baseline value in MAP till completion of drug infusion which was highly significant difference statistically (p <0.001). The maximum fall in MAP in both groups was observed at 10 minutes following intubation which was 18.34% and 18.38% in group A and group B respectively, but this difference was statistically not significant (p>0.05). Neither of the group showed deviation in MAP beyond 20% of the baseline value.

The difference in mean MAP between group A and group C remains highly significant from T3. Maximal increase in mean MAP in control group occurred 1 minute after intubation, which was 13.2%.

But between group B and group C the difference in mean MAP following induction (T5) observed insignificant, even though mean MAP in control group had statistically higher values in all time intervals when compared to both the dexmedetomidine group.

DISCUSSION

The baseline mean HR in all the three groups are comparable without any significant statistical difference. There was a statistically significant fall in HR from base line in group B (Dexmedetomidine 1 µg/kg) at 5 minutes (T3) and completion of drug infusion (T4) as compared to group A (Dexmedetomidine 0.6 µg/kg) where the fall in HR from baseline was not significant. At this time interval the difference between mean HR in both group was also statistically significant. After induction the transient fall in mean HR observed at above time interval in group B had reversed and it remained comparable to group A.

The rise in mean HR after 1 min of intubation was greater with group B as compared to group A, but still it remained below baseline for the study groups. Mean HR remained below the baseline at 5 and 10 mins in both study groups, but the difference between the mean HR at this time interval was statistically significant. The control group had statistically significant higher values of mean HR in all time intervals when compared to study groups.

The baseline blood pressure values between three groups were comparable. In group A, fall in mean SBP by 18.3% and 18.5% at 5 mins of starting the drug infusion and completion of drug infusion respectively was observed. But in group B at above mentioned time interval a transient increase in SBP by 5.3% and 5.6% respectively was noticed, which was statistically highly significant. Following intubation; the rise in HR after 1 min, 5 mins and 10 mins of intubation was greater with group B as compared to group A but still it remained below baseline for the study groups and statistical significant difference observed only at 10 mins of intubation. The control group had statistically higher values of SBP at all time intervals compared to the dexmedetomidine groups.

In group A, fall in mean diastolic BP by 6.1% and 11.6% at 5 mins of drug infusion and completion of drug infusion respectively was observed. But in group B showed increase in diastolic BP by 9.7% and 3.7% respectively at above mentioned time interval, which was statistically highly significant, but was transient in nature, as it was followed by fall in mean diastolic BP by 2.7% after induction. An increase in diastolic BP from baseline by 7.1% was observed after 1 min of intubation, whereas in group A diastolic BP remained below baseline by 5.6%. In both group A and group B maximum fall in diastolic BP was observed at 10 mins following intubation, but in group B it was observed a fall from baseline by 21%.

A fall in mean MAP by 11.6% and 14.7% at 5 mins of drug infusion and completion of drug infusion respectively was observed in group A, whereas in group B a transient increase in MAP by 7.7% and 4.6% respectively at above mentioned time interval, which was statistically highly significant when comparing both groups. In both groups MAP started decreasing immediately after intubation, but rate of decrease was more gradual in group B. Maximum fall

in MAP observed at 10 mins following intubation but the difference between the study groups remained statistically not significant at above mentioned time interval. When comparing with control group it was found that during all time interval after intubation, control group had a statistically higher value of Systolic BP, Diastolic BP and Mean Arterial Pressure. Maximum rise in BP was observed at 1 min following intubation.

Hence group A provided stable haemodynamic condition during entire period of observation.

Aho M et al, Saraf R et al and Gandhi S et al have studied the stress response attenuating effects of dexmedetomidine at loading dose of 0.6 µg /kg in different studies and concluded that Dexmedetomidine administered before induction at a dose of 0.6 µg/kg blunted the sympathoadrenal response during endotracheal intubation.[12,13] Similarly sympathoadrenal response parameters have been studied at dose of 1 µg /kg by other researchers like Panda BK et al, Gonus N et al, Keniya V et al, Laha A et al and inferred that perioperative use of dexmedetomidine is effective in attenuating sympathoadrenal response to tracheal intubation and has a significant anaesthetic and opioid sparing effect.[11,13,14,15] Similar to our study in group B, Laha A et al observed a statistically significant transient fall in mean HR with 1µg/kg of infusion of dexmedetomidine over 10 minutes.[13] In our study at completion of drug infusion (T4) in group B the mean HR falls to 27.2% from the baseline value, which is transient and it was followed by fall in mean HR by 16.2% after induction. Transient bradycardia was observed by Gogus N et al also in their study using infusion of dexmedetomidine at 1 µg/kg over 10 minutes prior to induction.[15] Significant transient fall in HR at 1st and 5th minute after administration of single dose of 2µg /kg was observed by Lowrence et al,[16] Kenya V et al have shown decrease in HR after the infusion of 1 µg /kg of dexmedetomidine.[11]

CONCLUSION

From the present study, it can be concluded that

- In group A patients, dexmedetomidine in the dose of 0.6 microgram/kg given 10 minutes before induction effectively attenuated sympathoadrenal response to endotracheal intubation without any adverse effects.
- In group B patients, dexmedetomidine in the dose of 1 microgram/kg give 10 minutes before induction attenuated hemodynamic response to endotracheal intubation with a by phasic change in hemodynamic parameters.
- In group C patients, who were the control group, there was significant sympathoadrenal response to endotracheal intubation.

Hence it was concluded that a lower dose of dexmedetomidine 0.6 microgram/kg loading dose provides significantly better attenuation of sympathoadrenal response to endotracheal intubation unaccompanied by transient increase in blood pressure and bradycardia which is observed at a higher dose of dexmedetomidine (1 microgram/kg) loading dose.

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