VOLUME-7, ISSUE-2, FEBRUARY-2018 • PRINT ISSN No 2277 - 8160

Original Research Paper

Anesthesiology

DEXMEDETOMIDINE(0.5 µgkg)IS BETTER THAN CLONIDINE (1 µgkg) IN ATTENUATING STRESS RESPONSE TO LARYNGOSCOPY AND INTUBATION WHEN USED AS PREMEDICATION IN ADULT SURGICAL PATIENTS

Dr. Santosh Kumar Bhaskar Professor, Anaesthesiology, Chirayu Medical College and Hospital, Bhopal

Dr. Tahir Ali Khan* Assistant Professor, Anaesthesiology, Chirayu Medical College and Hospital, Bhopal *Corresponding Author

ABSTRACT

Background and Aims: The laryngoscopy and endotracheal intubation are known to have profound cardiovascular effects which may increase perioperative morbidity and mortality. The aim of the present study was to compare effects of clonidine & dexmedetomidine to attenuate stress response during laryngoscopy and endotracheal intubation. Methods: In this prospective, randomised, comparative clinical study, one hundred patients of either sex, aged between 20-60 years and American Society of Anesthesiologists (ASA) physical status I and II were included. Patients were randomly allocated into two groups of 50 patients each. Group 1 received intravenous clonidine 1µg/kg infusion whereas group 2 received intravenous dexmedetomidine 0.5µg/kg infusion, diluted in 200 ml normal saline over 10 minutes. Hemodynamic monitoring as HR, SBP, DBP, MAP and oxygen saturation were noted and compared at different time points as; Before induction, after induction, after laryngoscopy and intubation and 5 minutes after laryngoscopy and intubation. The statistical analysis was done using Microsoft excel package. Results: The mean heart rate(MHR) in the clonidine group was higher than dexmedetomidine during all observation period,which was statistically significant (P = 0.001).The mean SBP and DBP was significantly lower after intubation and 5 min postintubation in dexmedetomidine group than clonidine group. Conclusion: We conclude that intravenous dexmedetomidine, in doses used in our study, is superior to intravenous clonidine in attenuating the pressor response during laryngoscopy and intubation.

KEYWORDS : Dexmedetomidine, clonidine, pressor response, endotracheal intubation.

Introduction

Laryngoscopy and tracheal intubation are noxious stimuli that provoke a transient but marked sympathetic response, manifesting as tachycardia and hypertension.[1] This response may not be of much significance in an otherwise normal individual, but in patients, particularly those with systemic hypertension, coronary artery disease, cerebrovascular disease or intracranial aneurysms, even these transient changes can result in potentially deleterious effects.[2]

Various pharmacological and non-pharmacological methods[3] have been used to attenuate the hemodynamic responses to laryngoscopy and tracheal intubation but none of them have proved to be ideal. Hence the search for an ideal agent still continues.

Clonidine is an agonist shown to blunt the hemodynamic responses to noxious stimulation and to prevent the overall hemodynamic variability.[4]

Dexmedetomidine, a more specific and selective α-2 adrenergic agonist has sedative, analgesic and sympatholytic effects that blunt many of the cardiovascular responses seen during perioperative period.[5]

Several studies[6] have been conducted to compare the varying dose of clonidine and dexmedetomidine for reducing the stress response after larygoscopy and endotracheal intubation .The present study was undertaken to compare effects of clonidine(1 µg/kg) and dexmedetomidine(0.5 µg/kg) to attenuate stress responses during laryngoscopy and endotracheal intubation**.**

Materials and Methodology

This prospective, randomised, comparative clinical study was conducted after obtaining institutional review board approval. Written informed consent was obtained from all the patients prior to study. A total of 100 patients of ASA grade I and II,, of either sex and aged between 20 to 60 years scheduled for elective surgeries under general anaesthesia were selected for the study and randomly allocated into two groups of 50 each to be started on one of the following intravenous infusions: group 1 received 1 µg/kg clonidine in 200 ml normal saline over 10 minutes whereas group 2 received 0.5 µg/kg dexmedetomidine in 200 ml normal saline over 10 minutes. Randomisation was done by random number table to select the first group out of two groups, after that the cases were allocated by systematic way (systematic randomised allocation method).

Patients with allergy to study drugs (clonidine and dexmedetomidine), hypertension, pheochromocytoma, diabetes and other cardiovascular diseases, heart rate < 60 bpm, basal metabolic index (BMI) > 30, anticipated difficult intubation, haemodynamic instability, history of bleeding diathesis or those undergoing emergency surgeries were excluded from the study. The patients in whom duration of laryngoscopy and intubation exceeded 30 seconds, multiple attempts were taken or external laryngeal pressure was used, were also excluded from the study as all these may alter the study results. All the patients were assessed the day before surgery and a standard anesthetic technique was used in both the groups, which included oral ranitidine 150 mg, the evening before and on morning of surgery, standard monitoring with pulse oximetry, heart rate, noninvasive blood pressure, capnography and three lead electrocardiogram. Induction was done after 15 minutes of study drugs (clonidine or dexmedetomidine) administration with IV midazolam (0.03 mg/kg) followed by fentanyl (2µg/kg) and Propofol (2mg/kg). Muscle relaxation was achieved by vecuronium bromide (0.1mg/kg). Direct laryngoscopy and intubation was performed after 3 minutes by an experienced anaesthesiologist. The duration of laryngoscopy and intubation was limited to a minimum possible time and was less than 30 seconds for all the patients. Hemodynamic monitoring as HR, SBP, DBP, MAP and oxygen saturation were noted and compared at different time points as;Baseline , before induction, after induction, after laryngoscopy and intubation and 5 minutes after laryngoscopy and intubation.

Our study ended at this point and surgery was commenced. Maintenance of anesthesia was carried out with isoflurane 1 to 2 % with oxygen and nitrous oxide 50:50 ratio using controlled ventilation. At the end of Surgery, residual neuromuscular blockade was reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.1 mg/kg IV.

The data was analysed using Microsoft excel package and all variables were expressed as mean ± standard deviation. Paired t test was used for intergroup comparisons of changes from before induction value to different study periods (for each group separately). Chi-square test was used for categorical data and a P value less than 0.05 was considered statistically significant.

Results

Regarding demographic profile, there were no statistically significant differences (P > 0.05) between the two groups {**Table 1**}

Table 1:Demographic profile of patients

GROUP	CLONIDINE	DEXTMEDETOMIDINE	P VALUE
No. of Patients	50	50	-
Male	20	19	>0.05
Female	30	31	
AGE WISE DISTRIBUTION			
AGE GROUP	**CLONIDINE**	**DEXMEDETOMIDINE**	**P VALUE**
20-30	4	1	=0.102
30-40	16	16	
40-50	13	22	
50-60	17	11	
WEIGHT WISE DISTRIBUTION			
INTERVAL	**CLONIDINE**	**DEXMEDETOMIDINE**	**P VALUE**
41-50	3	9	=0.09
51-60	19	10	
61-70	28	31	
ASA WISE DISTRIBUTION			
GRADE	**CLONIDINE**	**DEXMEDETOMIDINE**	**P VALUE**
ASA-1	44	43	>0.05
ASA-2	6	7	

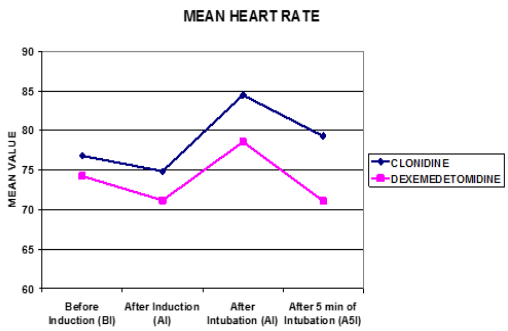

Figure 1 showing changes in mean heart rate in clonidine and dexmedetomidine group

The mean heart rate (MHR) was comparable between both the groups from before induction levels. After induction, there was a progressive fall in MHR as compared to before induction level in both the groups, which was significant, but the fall in heart rate was comparable statistically in both the groups.

Immediately after intubation, though there was an increase in MHR in both the groups, the heart rate response in clonidine group was higher when compared to dexmedetomidine group, which was statistically significant (P= 0.001). Subsequently the elevated heart rate started settling down and after 5 minutes of intubation, the difference being significant. Statistically (P = 0.001). {Figure 1}

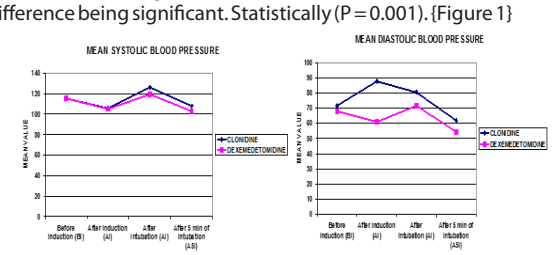

Figure 2 showing Blood pressure changes in the clonidine and dexmedetomidine group

Discussion

Dexmedetomidine is considered as a full agonist at α-2 receptors compared to clonidine which is considered as a partial agonist at these receptors. The selectivity of dexmedetomidine to α-2 receptors compared to α-1 receptors is 1620:1, whereas with clonidine it is 220:1. The selectivity is dose dependant, at low to medium doses and on slow infusion, high levels of α-2 selectivity is observed, while high doses or rapid infusions of low doses are associated with both α-1 and α-2 activities.[7]

The induction method and monitoring was done as per standardized protocol as a variable combination of drugs used for premedication, induction, relaxation and maintenance of anaesthesia can influence the sympathetic response to laryngoscopy and intubation.

The safety and efficiency of dexmedetomidine was shown by Keniya et al [6,8] who concluded that dexmedetomidine as a premedicant is effective in attenuating sympathoadrenal responses to tracheal intubation with significant anaesthetic and opioid sparing effect. Similarly, safety and efficacy of clonidine is well established for blunting stress response to intubation by Carabine, et al.[9]

All patients were induced with fentanyl followed by propofol, as several studies have shown that fentanyl attenuates the hemodynamic response to laryngoscopy and intubation [10,11], thus fentanyl would also mimic the clinical scenario more closely. As both the groups of patients received fentanyl, the occurrence of bias was eliminated.

Timing of administrating the drugs was 15 minutes prior to induction as the distribution half-life for dexmedetomidine is approximately 6 minutes and for clonidine is 6-14 minutes.[12] Side effects like hypotension and bradycardia were not observed in both the groups.

Limitations of the present study could be that we did not measure the stress mediators (catecholamine levels) in plasma and secondly, the person taking the reading (assessor) was not blinded. This could have been done by keeping the monitor in such a position, so that neither the person doing intubation reads the monitor nor the person assessing knows which drug has been used.

Conclusion

We conclude that dexmedetomidine 0.5µg /kg significantly attenuates stress response during laryngoscopy and intubation as compared to clonidine IV 1µg /kg. Future research further reducing the dose of dexmedetomidine is advocated.

References

1. King BD, Harris LC, Greifenstein FE, Elder JD, Dripps RD. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anesthesia. Anesthesiology 1951;12:556-66.
2. Fox EJ, Sklar GS, Hill CH, Villanueva R, King BD. Complications related to the pressor response to endotracheal intubation. Anaesthesiology. 1977; 47:524-5.
3. Ghaus SM, Singh V, Kumar A, Wahal R, Bhatia VK, Agarwal J. A study of cardiovascular response during laryngoscopy and intubation and their attenuation by ultrashort acting beta blocker esmolol. Indian J Anesth 2002;46:104-6.
4. Wright P.M.C., Carabine U.A., Kearney E, Howe J.P. Intravenous clonidine: Effect on the cardiovascular response to intubation. Anaesthesia Analgesia 1991;72:S1-S336.
5. Yildiz M, Tavlan A, Tuncer S, Reisli R, Yosunkaya A, Otelcioglu S. Effect of dexmedetomidine on haemodynamic responses to laryngoscopy and intubation: perioperative haemodynamics and anaesthetic requirements. Drugs RD 2006;7:43-52.
6. Panda BK, Singh P, Marne S, Atmaram A, Keniya V, Ladi S. A comparison study of dexmedetomidine Vs clonidine for sympathoadrenal response, perioperative drug requirements and cost analysis. Asian Pacific Journal of Tropical Disease 2012;1-6.
7. Gertler R, Brown CH, Silvius NE. Dexmedetomidine: a novel sedative- analgesic agent. Proc (Bayl Univ Med Cent) 2001;14:13-21.
8. Keniya VM, Ladi S, Nahpade R. Dexmedetomidine attenuates sympathoadrenal response to tracheal intubation and reduces perioperative anaesthetic requirement. Indian J Anaesth 2011;55:352-7.
9. Carabine U.A., Wright P.M.C., Howe J.P., Moore J. Cardiovascular effects of intravenous clonidine. Partial attenuation of the pressor response to intubation by clonidine. Anaesthesia 1991;46:634-7.
10. Splinter WM, Cervenko F. Hemodynamic responses to laryngoscopy and tracheal intubation in geriatric patients: effects of fentanyl, lidocaine and thiopentone.

Canadian Journal of Anesthesia 1989;36:370-76.
11. Crawford DC, Fell D, Achola KJ, Smith G. Effects of alfentanyl on the pressor and catecholamine responses to tracheal intubation. Br J Anesthesia.1987;59:707-712.
12. Davies DS, Wing AM, Reid JL, Nejll DM, Tippett P, Dollery CT. Pharmacokinetics and concentration-effect relationships of intravenous and oral clonidine. Clin Pharmacol Ther 1977;21:593-601.