ORIGINAL RESEARCH PAPER

Anaesthesiology

A Clinical Comparative Study Of Effect Of Intranasal Dexmedetomidine And Clonidine On Hemodynamic Response During Laryngoscopy In Hypertensive Adult Patients: A Double Blinded Randomized Trial.

KEY WORDS: hemodynamic responses, intranasal, dexmedetomidine, clonidine

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ABSTRACT

Induction of anaesthesia is a stressful event and can lead to major hemodynamic alterations which can be detrimental inhypertensive patients. Sedative premedication in general is considered to be an effective option for reduction of preoperativeanxiety and preventing untoward hemodynamic responses at the time of induction. Aim: We compared the efficacy of Dexmedetomidine and Clonidine in preoperative sedation and blunting of undesirable hemodynamic responses at the time of induction. Methods: Fifty four patients were randomly divided, Group D (n=27) received intranasal Dexmedetomidine 1 µg/kg and Group C (n=27) received intranasal Clonidine 3 µg/kg in the form of nasal drops 45 min before surgery. Hemodynamic parameters (HR and MAP) and sedation were observed. Results: Intranasal Dexmedetomidine was found to be more effective in producing perioperative anxiolysis, higher sedation levels and more stable hemodynamics at the time of induction. Conclusion: Dexmedetomidine via intranasal route can be considered as an alternative of conventional medications to manage selected patients with anxiety.

Introduction

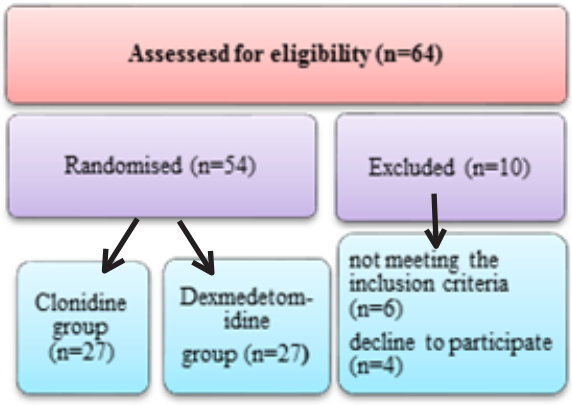
One of the main concerns of the anaesthesiologist is the appropriate management of perioperative anxiety.

Induction of anaesthesia is a stressful and anxiety provoking experience, this fear and anxiety lead to increase in catecholamine levels[1], which can be detrimental in hypertensive patients. The proper use of appropriate premedication may actually decrease anaesthetic and analgesic requirements as well as some side effects, such as postoperative emesis and untoward hemodynamic responses at the time of induction thereby ultimately provide benefits in selected surgical patients [2]. Dexmedetomidine (DEX) is a highly selective, short-acting, alpha 2-adrenoreceptor agonist. It can provide sedative, analgesic, and anxiolytic effects with minimal respiratory depression[3], which makes it a preferable choice among anaesthesiologist for use as an adjuvant for anaesthesia, as well as pre-medication for relieving anxiety or nervousness before anaesthesia. The intranasal route is a convenient and effective method of administration with high rate of patient acceptance[4]-[7]. It has been suggested that a smaller dose or routes other than rapid intravenous delivery may help minimize the hemodynamic risk of DEX.

Clonidine, another increasingly used centrally acting sympatholytic drug with predominant alpha-2 agonistic action[8],[9]. Commonly, it has been used as an antihypertensive agent, with additional sedative, anxiolytic, and analgesic properties. Patients involved in various previous studies include pediatric age group, very less study has been done with adults. Thus the present study was designed to compare the efficacy of intranasal Dexmedetomidine and intranasal Clonidine as a premedication for producing satisfactory levels of anxiolysis as well as blunting of hemodynamic responses due to laryngoscopy in hypertensive patients undergoing surgery under general anaesthesia.

Methods

After obtaining approval from ethical committee of MLN Medical College and associated hospitals a written and informed consent was obtained from the patients, the study was conducted in prospective randomized double blinded manner. This study included 54 patients of either sex between age group of 40 - 60 years of American Society of Anaesthesiologists (ASA) grade II posted for elective surgical procedure under general anaesthesia. Exclusion criteria included- patient refusal, patients of age < 40 years or >60 years, patients of age ASA grades > II, history of drug abuse, with pre-existing neurological or psychological disease, BMI >30, anticipated difficult airway, cardiac or respiratory system disease, hemodynamically unstable, previous history of allergy to the study drugs. The CONSORT flow diagram of this study is:



All patients were explained and counseled about the procedure a day before surgery and asked to take their routine morning anti-hypertensive medicine with a sip of water. Patients were randomized by computer generated random number list and randomly allocated to one of the two groups by using coded and sealed opaque envelopes for administration of study drug 45minutes prior to surgery. The drugs in coded syringes were prepared by an anaesthesia resident not involved in the study. The contents of the syringe were unknown to the person administering the drug and the anesthetist involved in the study. Baseline heart rate, SpO2 and respiratory rate were recorded before the administration of drug. Group 1- received 3 mcg/kg intranasal Clonidine hydrochloride and Group 2- received 1 mcg/kg intranasal Dexmedetomidine. The drugs were instilled in both nostrils using insulin syringe, with patient in recumbent position. We have used 0.5 ml per nostril as the maximum volume. The time of drug administration was noted, and the observer recorded SpO2, HR, MAP, and the sedation level for 45 min following drug administration. At the time of induction, an OAA/S score[10] between 1 and 4 represented satisfactory sedation and of 5 or 6 represented unsatisfactory sedation. All patients were pre-oxygenated for 3 minutes with 100 % oxygen. Anaesthesia was induced 2 mcg/kg fentanyl, 2-2.5 mg/kg Propofol and 0.1 mg/kg Vecuronium IV followed by direct laryngoscopy for tracheal intubation with appropriate sized cuffed endotracheal tube. HR and MAP were noted.

Statistical Analysis

Data was analysed using Statistical Package Of Social Sciences (SPSS, version19) software and expressed as mean ± standard deviation and Microsoft Excel 2010 version for windows. Sample size was calculated by power analysis while designing the study allowing alpha error of 5% and error of 20%. Parametric data were analyzed using the unpaired t-test. Repeated measurements data were analyzed using the paired t-test, and binary data were analyzed using Chi-square test. $P < 0.05$ was considered statistically significant.

Results

We started our study with 54 patients. The demographic profile was comparable in both groups.

Table 1: Demographic Profile

Parameters	Group C	Group D	P value
Age	49.92 ± 5.15	49.11 ± 5.65	0.291
M:F	16:11	12:15	0.275
Mean duration of surgery	106.66 ± 11.33	107 ± 11.64	0.457

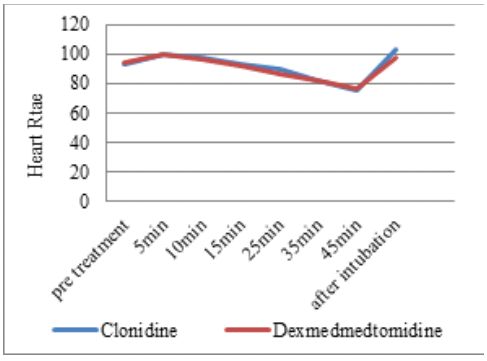


Figure 1: Comparison of mean Heart Rate among the two groups

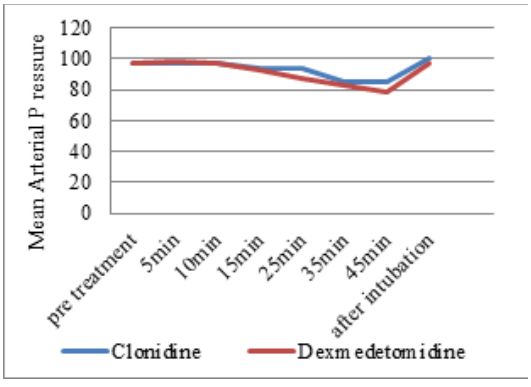


Figure 2: Comparison of Mean Arterial Pressure among the two groups

Figure 1 and 2 is in context of comparison of hemodynamic response in form of HR and MAP among the groups showing significant difference at 25 min. ($p=0.002$ for HR, $p<0.00001$ for MAP) due to faster onset of action of Dexmedetomidine.

In Figure 3 and 4 time of onset of sedation was 24.14 ± 2.9 min in Dexmedetomidine group compared with 32.92 ± 2.4 min in Clonidine group. The difference was statistically significant with earlier onset in Dexmedetomidine group. ($p<0.0001$) Nine patients in group C and twenty two patients in group D achieved satisfactory anxiolysis and sedation at the time of intubation (OAA/S score 4)[10] (Table 2) which is also statistically significant ($p = 0.0103$).

Table 2: Modified Observer's Assessment Of Alertness/ Sedation Scale

Responsiveness	Score
Agitated	6
Responds readily to name spoken in normal tone (alert)	5
Lethargic response to name spoken in normal tone	4
Responds only after name is called loudly and/or repeatedly	3
Responds only after mild prodding or shaking	2
Does not respond to mild prodding or shaking	1
Does not respond to deep stimulus	0

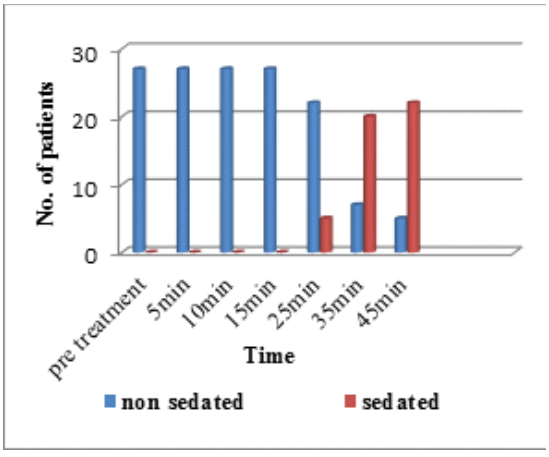


Figure 3: No. of patients sedated in Dexmedetomidine group

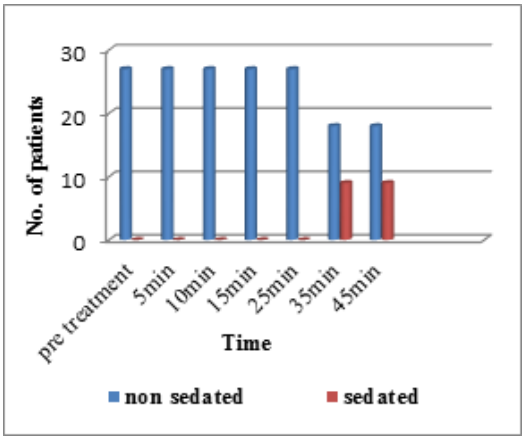


Figure 4: No. of patients sedated in Clonidine group

Hemodynamic response to laryngoscopy was blunted more in group D compared to group C with significant difference of $p= 0.009$ in HR and $p=0.0008$ in MAP

Table 3: Hemodynamic response to laryngoscopy

Parameters	Group C	Group D	P value
HR	102.55 ± 7.8	97.66 ± 7.03	0.009*
MAP	100.96 ± 3.13	96.92 ± 5.38	0.0007*

Discussion

Premedication is required to alleviate anxiety and fear as well as it allows smooth induction of anaesthesia. The patients in our study are adults with controlled hypertension and they are more prone to exaggerated unwanted hemodynamic responses during intubation. Intranasal application is a relatively noninvasive, convenient, and easy route of administration and results in a faster onset of action as well as reduces first-pass metabolism[11],12].

Another advantage with syringe nasal drops method is that it is a cost-effective drug delivery technique in experienced hands and with cooperative patients compared to atomized delivery systems. The onset of sedation and anxiolysis after Clonidine premedication was 32.92 ± 2.4 min in our study which was longer compared to findings of Mitra, et al. (2013)[13], this may be due to the use of atropine along with Clonidine in their study which has resulted in faster absorption. Similarly onset reported by Mukherjee, et al. (2010)[14] was 15.8 ± 2.6 min and by Almenrader, et al.(2007)[15] it was 23.3 ± 17.2 min, both are earlier than our study. In a study by Gupta, et al. (2017)[16] onset of intranasal Dexmedetomidine was 14.3 ± 3 min which is also earlier than our study. Previous studies have reported that intranasal DEX 1–1.5μg_kg–1 produced significant sedation within 45–60 min in healthy volunteers with similar manageable hemodynamic responses as in our study[4]-[7]. These differences may be observed due to difference in age group of patients involved in studies, other factors affecting onset may be observer related factors, nasal mucosa state and drug dosing. But inadvertent swallowing of the drug and subsequent gastric absorption are other potential drawbacks. In addition, we found that the hemodynamic response to tracheal intubation was significantly attenuated in the Dexmedetomidine premedicated patients compared to Clonidine premedication. (HR: p=0.009*, MAP: p=0.0008*). In our study, we also noted a decrease in HR and SBP at anaesthesia pre-induction in both groups. However, the reduction was mild or moderate and well tolerated without any intervention required and these findings are consistent with findings of research article of Lu c, et al (2016)[17]. No significant change was observed in SpO2 levels, no incidence of bradycardia or hypotension requiring intervention was observed at the end of 45 minutes in both the groups. Nasal irritation and stinging in addition to restlessness, euphoria, respiratory depression, hiccups and paradoxical rections[18] are major disadvantages of the intranasal administration of midazolam which is not so with Dexmedetomidine or Clonidine. This study has several limitations: Although we have chosen nasal drops via syringe as method of drug administration, but sprayed or atomized delivery technique have shown improved uptake and earlier onset when compared to our method. Other limitations of the study include lack of placebo or control group. However, these limitations should not invalidate the main conclusions from this study.

Conclusion

In conclusion, intranasal Dexmedetomidine at a dose of 1 μg/kg as premedication has demonstrated a comparable perioperative anxiolysis as Clonidine after 45 min, but with more stable hemodynamics, higher sedation levels at the time of induction, and improved patient satisfactory outcomes.

Future scope

Intranasal Dexmedetomidine can be considered as an effective premedication alternative to manage selected patients with anxiety.

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