Original Article

A comparative study to evaluate the effect of intranasal dexmedetomidine versus oral alprazolam as a premedication agent in morbidly obese patients undergoing bariatric surgery

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Abstract

Background: Morbidly obese patients with obstructive sleep apnea are extremely sensitive to sedative premedication. Intranasal dexmedetomidine is painless and quick acting. Intranasal dexmedetomidine can be used for premedication as it produces adequate sedation and also obtund hemodynamic response to laryngoscopy and tracheal intubation.

Materials and Methods: Forty morbidly obese patients with BMI > 35 were chosen and divided into two groups. Group DEX received intranasal dexmedetomidine 1 mcg/kg (ideal body weight) while other group (AZ) received oral alprazolam 0.5 mg. Sedation scale, heart rate and the mean arterial pressure was assessed in both the groups at 0 hour, 45 minutes, during laryngoscopy and tracheal intubation.

Results: The demographic profile, baseline heart rate, means arterial pressure, oxygen saturation and sedation scale was comparable between the two groups. The sedation scores, after 45 min, were statistically significant between the two groups i.e., 2.40 ± 1.09 in the AZ group as compared to 3.20 ± 1.79 in DEX group *P* value 0.034. The heart rate, mean arterial pressure and oxygen saturation were statistically similar between the two groups, after 45 min. The heart rate was significantly lower in the DEX group as compared to the AZ group. There was no statistical difference in the mean arterial pressure between the two groups either during laryngoscopy or tracheal intubation.

Conclusion: Intranasal dexmedetomidine is a better premedication agent in morbidly obese patients than oral alprazolam.

Key words: Intranasal, dexmedetomidine, morbidly obese, sedative premedication, obstructive sleep apnea

Introduction

Morbidly obese patients have multiple comorbidities such as obstructive sleep apnea and hypertension. Oxygen desaturation may occur in obstructive sleep apnea (OSA) patients after use of sedatives and opiates in the perioperative period. Obtunding hemodynamic response to laryngoscopy and tracheal intubation is an important anesthetic goal.

Dexmedetomidine, an alpha 2 agonist, has anxiolytic, sedative, analgesic and sympatholytic properties, which are attributes of an ideal premedication agent. The common modes of administration of dexmedetomidine are intravenous, intranasal and intramuscular. The intranasal method of administration is easy to administer apart from being painless, odourless and tasteless.[1] The onset of action of intranasal drug is within 20 minutes of its administration, as it bypasses the first pass metabolism. Oral alprazolam has been traditionally used as a premedicant drug. The intranasal administration of dexmedetomidine has not been tried in morbidly obese patients. We chose to study the effect of intranasal dexmedetomidine and compare it with oral alprazolam. Our hypothesis was that intranasal dexmedetomidine will produce better sedation without respiratory depression and also obtund the hemodynamic response to laryngoscopy and tracheal intubation.

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Materials and Methods

After obtaining written informed consent, Institutional Review Board approval and Clinical Trials Registry- India registration (CTRI/2011/06/001786), forty morbidly obese patients scheduled for elective surgery under general anesthesia

were studied. The inclusion criteria were: Patients of either sex; body mass index (BMI) greater than 35; posted for elective surgery; and hemodynamic stability. Exclusion criteria were: Refusal to consent; known allergy to alpha 2 agonists; patient with recent cardiac events like coronary stenting, acute myocardial infarction; and mentally deranged patients. Oral pantoprazole was given as premedication to all patients in the ward.

In the preoperative room, baseline monitoring in the form of sedation scale according to the Ramsay sedation scale[2] [Table 1], heart rate, peripheral oxygen saturation (SpO_2) and non-invasive blood pressure were noted by the nurse in-charge. The patients were then divided into two groups according to a random computer generated number. Patients of group DEX were given intranasal dexmedetomidine in the dose of 1 mcg/kg ideal body weight (calculated by Broca's formula) with a one ml syringe (without needle) in both the nostrils after preparing the patient. Group AZ was given oral alprazolam 0.50 mg with a sip of water. The monitoring was continued in the recovery room by the nurse, who was blinded to medication used in the study. After 45 minutes, the parameters like the sedation scale, heart rate, SpO_2 and mean arterial pressure (MAP) were noted. The patients were then shifted to the operation room (OR) where standard monitors were attached. General anesthesia was induced in both the groups by a standard technique. Intra-arterial radial artery cannulation was done in all the patients and invasive blood pressure was monitored. The hemodynamic responses (heart rate and invasive mean blood pressure) and SpO_2 at laryngoscopy and intubation was noted by the OR technician who was also blinded to the study. Three readings were noted during laryngoscopy, and during tracheal intubation. The mean of the three readings was taken for study considerations.

The primary outcome analyzed was sedation after 45 minutes. Secondary outcomes analyzed were heart rate, MAP and SpO_2 after 45 minutes and during laryngoscopy and tracheal intubation.

The statistical analysis was carried out using Statistical Package for Social Sciences 17.00 version (SPSS 17.0) for Windows. Statistical techniques included quantitative and qualitative analysis. We based our sample size estimation on the sedation score. On the basis of a pilot study conducted by us, we considered that significant sedation occurred at 45 min after doses of DEX. It was observed that mean difference of 2.58 in sedation score after 45 min with standard deviation of 0.753 and 0.500 in the respective two groups (DEX and AZ). Using alpha 0.05 and beta 0.10, we aimed to enrol 20 patients per group.

Continuous variables are presented as mean + SD. Categorical variables are expressed as frequencies. Unpaired t tests were used for comparison of continuous variables between the two groups. Repeated measurements were analysed by repeated measures ANOVA. Differences between groups were assessed with Chi-square or Fisher's exact test for categorical variables as appropriate. *P* value of <0.05 was taken as significant.

Table 1: Ramsay sedation score

Patient is anxious, agitated or restless or both
Patient is cooperative, oriented and tranquil
Patient responds to commands only
Patient exhibits brisk response to light glabellar tap or loud auditory stimulus
Patient exhibits sluggish response to light glabellar tap or loud auditory stimulus
Patient exhibits no response

Results

The demographic profile of the two groups is shown as [Table 2]. The sedation and hemodynamic parameters recorded at different time intervals is shown as [Table 3]. The BMI profiles, baseline heart rate, mean arterial pressure, SpO_2 and sedation scale was comparable between the groups.

Table 2: Demographic profile

Hemodynamic parameters	Group AZ (*n*=20)	Group IN (*n*=20)	*P* value
Weight (kg)	123.96±18.92	122.57±23.07	0.837
Height (m)	1.62±0.08	1.61±0.08	0.713
BMI (kg/m^2)	47.39±6.57	46.47±7.54	0.682

AZ=Alprazolam

Table 3: Sedation and hemodynamic parameters

Hemodynamic parameters	Group AZ (*n* = 20)	DEX Group (*n* = 20)	*P* value
Baseline			
Heart rate	76.65±12.12	79.25±18.53	0.603
MAP	89.45±16.26	94.10±17.17	0.385
SpO_2	98.65±1.66	97.90±1.99	0.205
sedation	1.70±0.57	1.40±0.50	0.086
AT 45 minutes			
Heart rate	82.95±16.99	75.05±16.48	0.144
MAP	93.40±22.77	89.0±13.46	0.462
SpO_2	98.80±2.59	97.30±3.44	0.127
sedation	2.40±1.09	3.20±1.79	0.034
At laryngoscopy			
Heart rate	86.50±14.78	75.70±13.72	0.022
MAP	86.0±24.94	87.6±18.98	0.821
At tracheal intubation			
Heart rate	92±38.32	84±14.32	
MAP	100±29.44	97±23.01	

AZ=Alprazolam; DEX=Dexmedetomidine

The sedation scores after 45 minutes were statistically significant between the two groups i.e., 2.40 ± 1.09 in the AZ group as compared to 3.20 ± 1.79 in the DEX group and the *P* value was 0.034.The heart rate, mean arterial pressure and SpO_2 was similar between the two groups after 45 minutes with no statistical difference.

During laryngoscopy and tracheal intubation, the heart rate was significantly lower in the DEX group as compared to the AZ group. There was no statistical difference in the MAP between the two groups during laryngoscopy and tracheal intubation.

The other observation made was that intranasal administration of dexmedetomidine was well tolerated. No patients complained of any local irritation or pain, smell or taste. Both groups of patients were able to walk to the washroom without any orthostatic hypotension.

An interesting observation was that dexmedetomidine group patients tolerated preoxygenation with a peak end-expiratory pressure (PEEP) of 10 cm with face mask tightly fitted on the face.

Discussion

Dexmedetomidine, an alpha 2 agonist has been shown to have favourable properties in bariatric patients[3] in view of their unique quality of sedation, where the patient can be calmly aroused to perform tasks and excellent communication when aroused and go back to sleep once the stimulus is withdrawn without any respiratory depression or drop in oxygen saturation along with analgesic quality. This is attributed to the pharmacological properties of dexmedetomidine which acts on the locus coeruleus and causes an EEG activity similar to natural sleep unlike conventional gabaminergic sedative.[3] The alpha 2 agonist property also helps decrease heart rate and blood pressure response to laryngoscopy and tracheal intubation.

The conventional modes of administration of dexmedetomidine are intravenous, intramuscular and intranasal. We chose the intranasal route in view of quick onset of action, easy to use, odourless, painless and do not require an intravenous line. The intravenous administration causes immediate sedation along with bradycardia and hypotension and therefore not suitable as a premedicant agent before surgery. The intramuscular route is not ideal as absorption is erratic. The intranasal route has been successfully used as a sedative in children for magnetic resonance imaging and computerized tomography scan in children and as premedication in children with burns.[4,5] It has also been used as premedication for dental extraction under local anesthesia.[6]

This is the first clinical trial in adult morbid obese patients with intranasal dexmedetomidine. We chose the morbid obese patient population as the dose and drug to choose for premedication is a challenging task for the anaesthesiologist. Excess sedation in these patients can cause a drop in peripheral oxygen saturation.[7] Comorbidities like obesity cardiomyopathy and hypertension can cause exaggerated hemodynamic responses during laryngoscopy and tracheal intubation. The use of dexmedetomidine can attenuate this response.

Yuen *et al.*[3] studied the use of intranasal dexmedetomidine in healthy adult volunteers, who were not for any surgery and therefore had no pre-procedure anxiety, and concluded that intranasal dexmedetomidine produces significant sedation in doses of 1 and 1.5 mcg/kg. We used the lower safe dose of 1 mcg/kg as there are no studies in morbid obese patients. We observed the patients in the preoperative room after premedication for monitoring and oxygen supplementation, if required.

The sedation score achieved in dexmedetomidine group in our study was ideal as the patients were well sedated, without any respiratory depression or drop in peripheral oxygen saturation. Dexmedetomidine group patients also tolerated preoxygenation with PEEP because of the better quality of sedation.

The heart rate response during tracheal intubation was blunted in group DEX as compared to AZ group. None of the patients required any vagolytic drug like atropine as the bradycardia was not accompanied by hypotension. There was no statistically significant blunting of the pressor response to tracheal intubation in both the groups as the dose requirement for that is possibly higher.

There were certain limitations of our study.The time given for premedication was about 45 minutes and probably a longer time could have achieved a better sedation in both the groups.

Ideally an atomised nasal spray should have been used to administer the drug instead of the syringe for better drug absorption. The dose required in obese patients is always difficult to titrate.

The hemodynamic parameters could have been studied for a longer period of time after intubation instead of just during tracheal intubation.

To conclude, intranasal dexmedetomidine in morbid obese patients, in a dose of 1 mcg/kg ideal body weight, proved to

be a better premedication agent than oral alprazolam as far as sedation is concerned. However, the dose used in the study was inadequate for attenuating hemodynamic response to laryngoscopy and tracheal intubation. More studies are needed to determine the ideal dose of intranasal dexmedetomidine as premedication.

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