Original Article - Prospective Study

To Evaluate the Efficiency of Dexmedetomidine in Atomized Intranasal form for Sedation in Minor Oral Surgical Procedures

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Abstract

Aim: This study aims to evaluate the efficiency of dexmedetomidine in atomized intranasal form for sedation in minor oral surgical procedures. **Materials and Methods:** A total 25 patients fitting the inclusion and exclusion criteria were selected from the outpatient Department of Oral and Maxillofacial Surgery, Saraswati Dental College and Hospital, Lucknow. The drug was administered intranasally half an hour before the surgical procedure. The volume of drug used was recorded. The readings of all the parameters of sedation began 30 min after the drug had been administered. Intranasal sedation status was assessed by Ramsay sedation score and observer's assessment of alertness/sedation scales, every 15 min throughout the procedure. **Results:** The primary outcome variable in this study is depth of sedation produced by intranasally administered dexmedetomidine. Secondary variables included respiratory rate, blood pressure (BP), heart rate (HR), and oxygen saturation (SpO_2). The statistical software used was SPSS 20.0 for Windows (SPSS, Chicago, IL, USA). Data were expressed as mean and standard deviation or number (percentages). Sedation and behavior scores were analyzed by proportions. Hemodynamic variables including HR, SpO_2, and BP and respiratory rate were analyzed by repeated measures ANOVA. When a significant result was obtained, the Tukey test was applied for *post hoc* pairwise comparisons. $P < 0.05$ was considered as statistically significant. All the parameters were recorded at a set interval of time. **Conclusion:** In conclusion, intranasal administration of 1.5 mg/kg atomized dexmedetomidine was clinically effective, convenient, and safe for the sedation of patients undergoing minor oral surgical procedures.

Keywords: Atomizer, dexmedetomidine, intranasal sedation

Introduction

In recent years, advances in technology and pharmacology have resulted in a marked increase in the number of outpatient surgeries/procedures.[1] The number of outpatients and minimally invasive surgeries have increased dramatically in recent years as a result of advancements in surgical technology, economic consideration, and better patient cooperation. Patient cooperation is of prime importance in the field of surgery, for the patient as well as the surgeon, especially under local anesthesia. The major hindrances in the patient cooperation are apprehension toward the treatment, fear, and anxiety. It is the most significant entity, second only to pain.

Many ways have been devised to attain cessation of anxiety and fear, sedation being one of the techniques. In 1845, Connecticut dentist Horace Wells[2] used nitrous oxide to extract aching tooth. In 1846, a dentist named of William T. G. Morgan[2] gave sulfur – ether compound – to the patient undergoing surgery. Oral sedation is one of the modalities commonly used. Intranasal route is the most recent advance in the administration of sedatives through noninvasive ways. The main advantages being that it is less intimidating for the patient leading to better patient cooperation, smooth conduction of the procedure, and better use of time and resources. The highly vascularized nasal mucosa and the olfactory tissue in direct contact with the central nervous system allow nasally administered

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drugs to be rapidly transported into the bloodstream and brain, with onsets of action approaching that of intravenous (IV) therapy. It provides large surface area, porous endothelial membrane, high total blood flow, the avoidance of first-pass metabolism, rapid onset, and ready accessibility.[3] Intranasal dexmedetomidine is the most recent advance in the field of sedation. A study was done in our institute on the efficacy of dexmedetomidine in sedation when given through intranasal route. The focus was on the efficacy of the drug in terms of fear and anxiety levels of the patient undergoing various minor oral surgical procedures.

Materials and Methods

After clearance from institutional ethical committee, a total of 25 patients fitting the inclusion and exclusion criteria were selected from the outpatient Department of Oral and Maxillofacial surgery, Saraswati Dental College and Hospital, Lucknow, who volunteered to participate in the study. A written informed consent was obtained from all the patients.

Inclusion criteria

The patients were randomly selected to participate in the study based on the following criteria:

- Patients requiring minor oral surgical procedure which was expected to finish within 1½ h operative time.
- Age group: 18–50 years
- Patients with American Society of Anesthesiologists (ASA) physical status I.

Exclusion criteria

The patients falling in the following category were not selected for this study:

- Medically compromised
- Immunocompromised patients
- Pregnant and lactating mothers
- Body mass index >27 kg/m^2[3]
- Alcohol consumption in excess of 28 units per week (1 unit = 30 ml)[4]
- Chronic sedative or analgesic use, including drug abusers
- Regular use of or known allergy to dexmedetomidine, paracetamol, nonsteroidal anti-inflammatory drugs, or opioids
- Patients with preoperative inflammation at the site of drug administration
- Upper respiratory catarrh, rhinitis.

Materials

a. Liquid form in a vial of 1 ml in concentration of 100 μg/ml dexmedetomidine [Figure 1]
b. Intranasal atomization device [Figure 1] along with 3 ml syringe [Figure 2]
c. Pulse oximeter
d. Cardiac multipara monitor.

Methodology

Preoperative protocol

- Complete medical history was recorded, and thorough clinical examination of patients was done
- After selection, the patients were told about the process in detail and counseled.

Figure 1: (a) The drug used with atomizer. (b) Patient about to receive the drug. (c) Patient receiving the atomizer. (d) Patient receiving the drug on the left side. (e) Patient sedated

Figure 2: (a) Patient 2 being sedated. (b) Patient sedated

- A written detailed informed consent was obtained

The following presedation assessment parameters were also recorded:

1. Respiratory rate
2. Oxygen saturation (SpO_2)
3. Local nasal examination
4. Heart rate (HR)
5. Blood pressure (BP).

Dosage

A fresh mixture of the dosage was prepared using 1 ml of dexmedetomidine and adding 0.5 ml of normal saline to make it 1.5 ml solution.

Operative protocol

The drug was administered intranasally half an hour before the surgical procedure. The volume of drug used was recorded. The readings of all the parameters of sedation began 30 min after the drug had been administered. Intranasal sedation status was assessed by Ramsay sedation score and observer's assessment of alertness/sedation (OAA/S) scales, every 15 min throughout the procedure [Tables 1 and 2]. Ramsay sedation score ranges from 1 to 6, where 1 means that the patient is anxious, agitated, or both and 6 being unresponsive. Whereas the OAA/S ranges from 5 to 1 where 5 means that the patient does not respond to mild prodding or shaking and 1 means responds readily to name spoken in normal tone. HR and SpO_2 were recorded every 5 min. Similarly, BP and respiratory rate were recorded at 10 min. We started to take the reading after 30 min from the time of the administration of drug.

Observations and Results

A randomized study was conducted that included a total of 25 patients, of which 11 were females and 14 were males. The results of the study are expressed in tables and Graphs as medians (range). The primary outcome variable in this study is depth of sedation produced by intranasally administered dexmedetomidine. Secondary variables included respiratory rate, BP, HR, and SpO_2 [Tables 1-6 and Graphs 1-8].

The statistical software used was SPSS 20.0 for Windows (SPSS, Chicago, IL, USA). Data were expressed as mean and standard deviation or number (percentages). Sedation and behavior scores were analyzed by proportions. Hemodynamic variables including HR, SpO_2, and BP and respiratory rate were analyzed by repeated measures ANOVA. When a significant result was obtained, the Tukey test was applied for *post hoc* pairwise comparisons. $P < 0.05$ was considered as statistically significant. All the parameters were recorded at a set interval of time. The primary outcome variable, i.e., the depth of sedation was measured using Ramsay sedation score and OAA/S. Table 1 shows the Ramsay sedation score.

Discussion

This study evaluated the efficacy of the intranasal administration of atomized dexmedetomidine to sedate adult patients undergoing minor oral surgical procedures. The level of sedation required was moderate as per ASA classification of sedation. The majority of patients receiving dexmedetomidine as a primary therapy experience clinically effective sedation yet were still easily arousable, a unique feature not observed with other clinically available sedatives.[5]

Site of action of dexmedetomidine is in the locus coeruleus of the central nervous system, where it induces a state similar to natural sleep. Therefore, it is not surprising that external stimulation should facilitate arousal. Previous studies utilizing intranasal sedatives have primarily involved pediatric populations or noncompliant mentally disabled adults. These studies were primarily comparative studies comparing dexmedetomidine to other sedative drugs.[6] Our study is one of these few that involve adult patients and that too in the field of oral and maxillofacial surgery.

In our study, we have used the drug in a diluted form. Some researchers attributed the failure of their studies to the use of diluted dexmedetomidine. It has been further concluded in a number of studies that a more standardized approach to preparation and delivery of the drug will increase the success rate.[7,8] Yuen *et al*. in 2012[9] conferred that if a dose of 1 μg/kg is chosen, the onset time will range from 25 to 45 min with a median duration of sedative effect of 55–100 min. Cheung

Table 1: Ramsay sedation score

	Ramsay sedation score						
	15	30	45	60	75	90	105
1. Anxious and agitated or restless, or both	2 (8.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	11 (44.00)
2. Cooperative, oriented, and calm	8 (32.00)	3 (12.00)	0 (0.00)	0 (0.00)	2 (8.00)	12 (48.00)	14 (56.00)
3. Responsive to commands only	11 (44.00)	16 (64.00)	10 (40.00)	0 (0.00)	6 (24.00)	13 (52.00)	0 (0.00)
4. Exhibiting brisk response to light glabellar tap or loud auditory stimulus	4 (16.00)	6 (24.00)	12 (48.00)	20 (80.00)	15 (60.00)	0 (0.00)	0 (0.00)
5. Exhibiting a sluggish response to light glabellar tap or loud auditory stimulus	0 (0.00)	0 (0.00)	3 (12.00)	5 (20.00)	2 (8.00)	0 (0.00)	0 (0.00)
6. Unresponsive	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)

Table 2: Observer's assessment of alertness/sedation scale

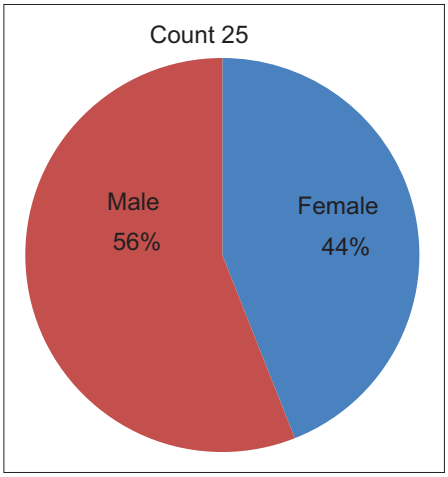
	OAA/S						
	15	30	45	60	75	90	105
5. Does not respond to mild prodding or shaking	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	1 (4.00)
4. Responds only after mild prodding or shaking	1 (4.00)	1 (4.00)	2 (8.00)	0 (0.00)	2 (8.00)	1 (4.00)	0 (0.00)
3. Responds only after name is called loudly and/or repeatedly	3 (12.00)	1 (4.00)	4 (16.00)	18 (72.00)	6 (24.00)	11 (44.00)	0 (0.00)
2. Lethargic response to name spoken in normal tone	3 (12.00)	17 (68.00)	19 (76.00)	7 (28.00)	17 (68.00)	13 (52.00)	5 (20.00)
1. Responds readily to name spoken in normal tone	18 (72.00)	6 (24.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	19 (76.00)

OAA/S=Observer's assessment of alertness/sedation

Table 3: Descriptive statistics of heart rate

Time (min)	Mean	SD	*n*
5	86.72	17.080	25
10	87.60	14.224	25
15	89.04	11.710	25
20	86.96	14.058	25
25	85.80	15.532	25
30	83.64	15.223	25
35	81.20	13.919	25
40	79.52	15.075	25
45	80.12	13.305	25
50	80.52	12.836	25
55	82.08	11.471	25
60	80.28	10.998	25
65	79.08	9.300	25
70	77.00	11.091	25
75	77.04	9.199	25
80	76.72	7.619	25
85	77.92	6.116	25
90	78.04	5.955	25

SD=Standard deviation



Graph 1: Gender distribution

et al. in their study observed that the onset of clinical sedation was at 30–45 min after intranasal administration; so, they suggested that the drug should be given 45–60 min before a surgical procedure, which in their study was third molar surgery.[4]

In our study, the sedative effect commenced only after 45 min; so, the time of delivering of the drug was set as 45 min before surgery. We observed that moderate sedation was achieved with the drug, and the sedation status of the patients was close to baseline around 90 min; all the patients were easily aroused by external stimuli. A sedative duration of 90 min was sufficiently long to perform a minor oral surgical procedure, and the short recovery period was convenient for outpatient dental sedation purposes. In our study, the vital statistics was closely monitored. These included HR, respiratory rate, SpO_2, and BP. Yuen *et al*. 2012[9] in their study used 1 g/kg and 1.5 mg/kg of dexmedetomidine intranasally and found no severe bradycardia or conduction abnormality on electrocardiogram monitoring. The observed hemodynamic

Table 4: Descriptive statistics of systolic blood pressure

Time (min)	Mean systolic blood (mm of Hg)	SD	Number of patients
10	117.32	4.516	25
20	120.48	4.691	25
30	116.96	7.419	25
40	120.12	10.549	25
50	120.56	9.548	25
60	119.92	8.129	25
80	119.24	6.240	25
90	117.64	4.769	25

SD=Standard deviation

Table 5: Descriptive statistics of diastolic blood pressure

Time (min)	Mean	SD	*n*
10	78.56	5.781	25
20	79.24	5.109	25
30	79.04	4.067	25
40	78.96	5.248	25
50	78.08	4.991	25
60	73.20	16.161	25
80	78.40	5.041	25
90	77.76	3.574	25

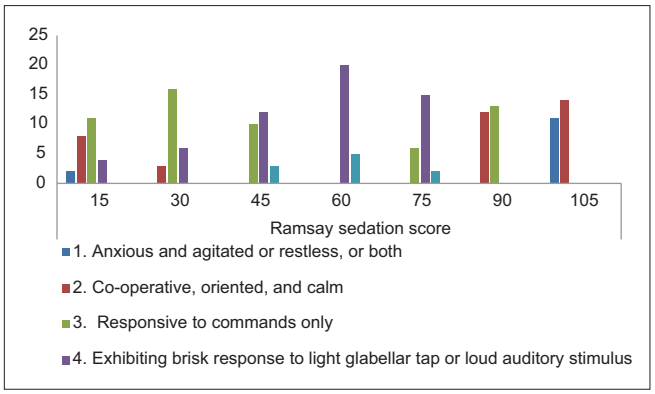
SD=Standard deviation

Table 6: Descriptive statistics of oxygen saturation

Time (min)	Mean	SD	*n*
5	98.00	0.500	25
10	97.96	0.455	25
15	98.00	0.500	25
20	98.00	1.500	25
25	98.80	0.408	25
30	98.72	0.458	25
35	98.16	0.473	25
40	97.96	0.351	25
45	98.12	0.726	25
50	97.96	0.539	25
55	97.48	0.918	25
60	97.48	0.770	25
65	97.84	0.473	25
70	97.96	0.676	25
75	97.68	0.690	25
80	97.96	0.455	25
85	97.96	0.455	25
90	98.36	0.995	25

SD=Standard deviation

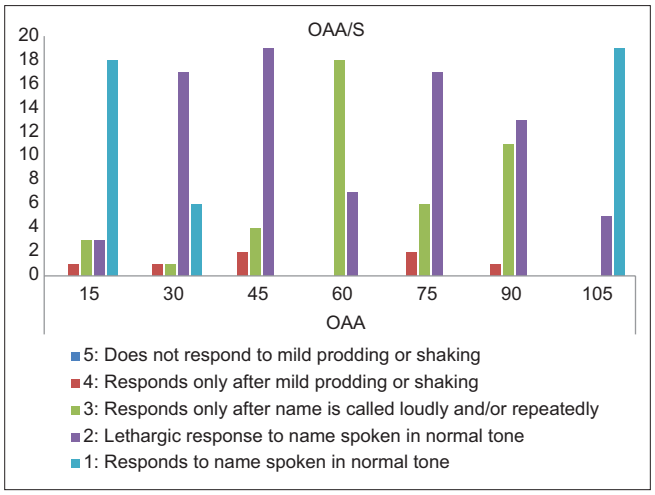
changes did not induce any subjective symptoms. Gertler *et al*. observed that dexmedetomidine does not appear to have any direct effects on the heart. Dexmedetomidine could result in cardiovascular depression, i.e., bradycardia and hypotension in IV form if given in high doses.[5] In our study, we observed that the HR ranged from 76 to 90 bpm



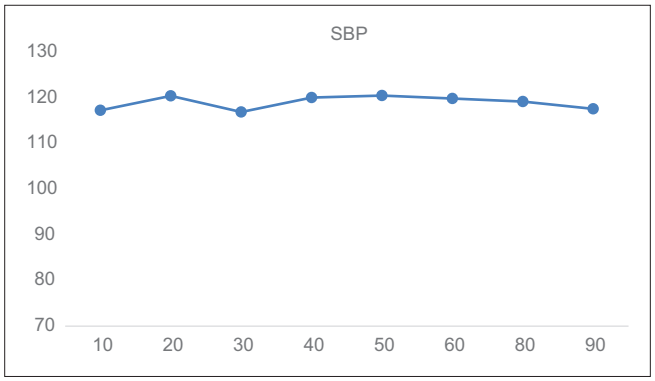
Graph 2: Results of ramsay sedation score

approximately. The baseline HR was 86 approximately. The tachycardia was attributed to the anxiety of the patient before the procedure, as we did not give any anxiolytic drug preoperatively. A few times during the procedure if there was any discomfort to the patient due to the procedure, the HR was seen to have increased insignificantly. However at no time during the procedure any intervention was required. Dexmedetomidine, as a sedative agent, can provide easily controllable sedation without respiratory depression.[10] Lack of respiratory depression due to dexmedetomidine is one of its major advantages. We, in our study, concluded that dexmedetomidine has no deleterious clinical effects on respiration when used in doses that are sufficient to provide adequate sedation and effective analgesia in the surgical population. As far as sedation with IV dexmedetomidine few studies showed a decrease up to 92%, in that case oxygen was given through face mask or nasal prongs.[10] The adverse effects of the drug on SpO_2 find a mention in a few animal studies that included rabbits.[11] Furthermore, the studies using IV dexmedetomidine to give bolus doses like 6 ug/kg/h showed significant decrease in comparison to the pretreatment levels.[12] Although in literature there was not a single study that showed that intranasal dexmedetomidine has any adverse effect on the SpO_2 at doses ranging up to 2 ug/kg. In our study, we did not observe any decrease in the SpO_2, and the need to give oxygen never rose. Furthermore, whether the SpO_2 was altered or not, oxygen cylinder was kept handy even when giving low doses of dexmedetomidine.

The adverse effects of dexmedetomidine include hypotension, hypertension, nausea, bradycardia, atrial fibrillation, and hypoxia. Overdose may cause first-degree or second-degree atrioventricular block. These are the effects seen with IV route of administration, and no such effects have been seen with the use of intranasal dexmedetomidine. The same was observed in our study as well, i.e., no adverse effects on BP were observed. Due to its significant properties as sedative and analgesic and safe respiratory profile, coupled with its ease of use and antisialagogue properties, dexmedetomidine was thought to be very useful in dental/oral procedures.[13] All



Graph 3: Results of OAA/S score



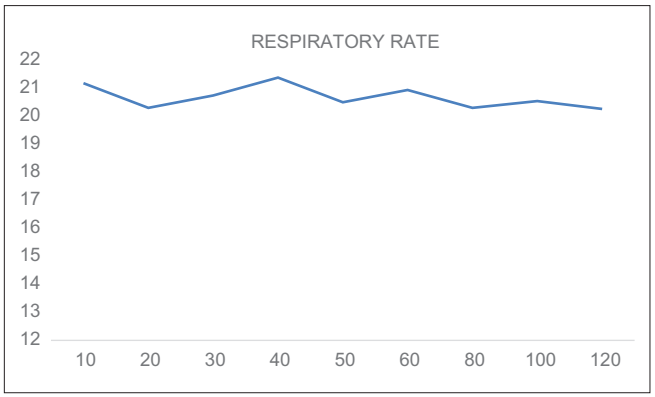
Graph 5: Systolic blood pressure variation

Measure: Systolic blood pressure

Source	Type III sum of squares	df	Mean square	*F*	Significant
Factor 1: Greenhouse -Geisser	390.220	2.534	153.985	3.172	0.038

Sum of squares and mean squares of the values recorded are a part of the calculation of the test value denoted by "*F*". "df" stands for degrees of freedom. The number of degrees of freedom is the number of values in the final calculation of a statistic that are free to vary

effects of dexmedetomidine could be antagonized easily by administering the α2-adrenoceptor antagonist atipamezole, which, like dexmedetomidine, reverses sedation and sympatholysis and has a half-life of 1.5–2 h. With the increase in the minor oral surgical procedures, there is a huge discrepancy in the anesthetist patient ratio, with patients being more than the anesthetist. To assist in this process, the American Society of Anesthesiologists developed Guidelines for Sedation and Analgesia by nonanesthesiologists.[14] This technique of using dexmedetomidine may be easily adaptable for use by properly trained nonanesthesiologists and nurse practitioners.[15]

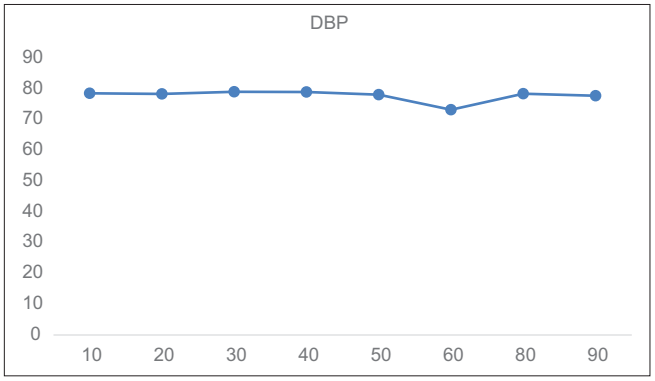


Graph 4: Respiratory rate variation

Measure: Respiratory rate

Source	Type III sum of squares	df	Mean square	*F*	*P* (significant IF <0.05)
Factor 1: Greenhouse -Geisser	33.209	4.115	8.069	1.828	0.127

Sum of squares and mean squares of the values recorded are a part of the calculation of the test value denoted by "*F*". "df" stands for degrees of freedom. The number of degrees of freedom is the number of values in the final calculation of a statistic that are free to vary



Graph 6: Diastolic blood pressure b variation

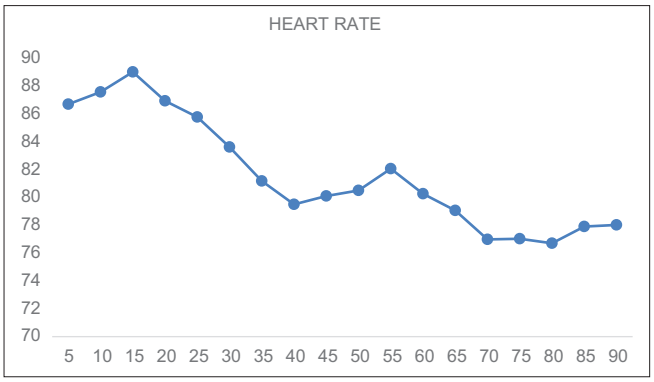
Measure: Diastolic blood pressure

Source	Type III sum of squares	df	Mean square	*F*	Significant
Factor 1: Greenhouse -Geisser	676.155	1.872	361.181	2.064	0.142

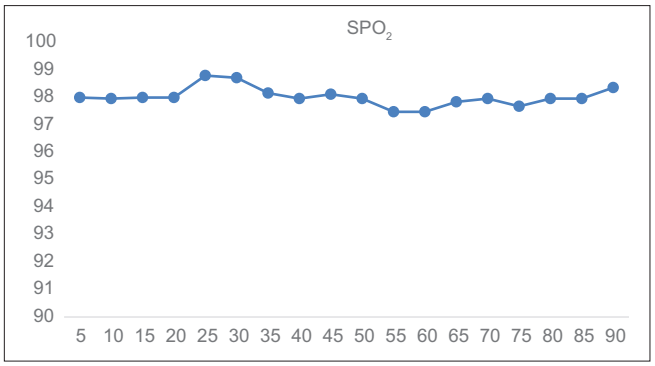
Sum of squares and mean squares of the values recorded are a part of the calculation of the test value denoted by "*F*". "df" stands for degrees of freedom. The number of degrees of freedom is the number of values in the final calculation of a statistic that are free to vary

Conclusion

In conclusion, intranasal administration of 1.5 mg/kg atomized dexmedetomidine was clinically effective, convenient, and



Graph 7: Heart rate variation



Graph 8: Oxygen saturation variation

Measure: Heart rate

Source	Type III sum of squares	df	Mean square	*F*	*P* (significant IF <0.05)
Factor 1: Greenhouse -Geisser	6905.920	3.375	2046.442	14.291	<0.001

Sum of squares and mean squares of the values recorded are a part of the calculation of the test value denoted by "*F*". "df" stands for degrees of freedom. The number of degrees of freedom is the number of values in the final calculation of a statistic that are free to vary

Measure: SpO_2

Source	Type III sum of squares	df	Mean square	*F*	Significant
Factor 1: Greenhouse -Geisser	49.938	5.383	9.278	10.151	<0.001

Sum of squares and mean squares of the values recorded are a part of the calculation of the test value denoted by "*F*". "df" stands for degrees of freedom. The number of degrees of freedom is the number of values in the final calculation of a statistic that are free to vary

safe for the sedation of patients undergoing minor oral surgical procedures.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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