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A Public Health Perspective on Sedation Dentistry in Bangladesh: Use of Clonidine

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Authors' contributions

This work was carried out in collaboration among all authors. Author OG designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors SI and MSI managed the analyses of the study. Author MSI managed the literature searches. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Background: Since more than 40 years ago, people have been using the alpha-2 adrenergic agonist clonidine to treat hypertension. The FDA authorized the use of clonidine in October 2008 as a premedication drug before sedation. This study's main objective is to discover if clonidine may be used as a pre-operative sedative in mild sedation dentistry and, if so, at what dosage level is safe to do so.
Methods: A large inner city dental clinic that offers free dental treatment to those in need participated in this clinical, cross-sectional research of its patients. Information was gathered from treatment records completed between March 2012 and April 2012. Examined were the relationships between the research sample's characteristics and the usage of clonidine at two dosage levels (0.1 mg and 0.2 mg compared to controls). The hemodynamic changes (such as systolic, diastolic, mean arterial pressure, and pulse) in patients receiving clonidine 0.1 mg, clonidine 0.2 mg, and the control group were compared using an analysis of variance with the Duncan Multiple Range Test.
Results: Pre-sedation systolic and diastolic blood pressure readings were lower in the clonidine 0.2 mg group compared to the 0.1 mg group and the control group. According to the findings, the control group's mean systolic blood pressure was considerably higher during the first intraoperative period than the 0.2 group's. Mean systolic blood pressures for the 0.2 mg clonidine dose group

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were substantially lower at pre-sedation and the first intraoperative periods in comparison to the 0.1 mg group and the controls after adjusting for age, BMI, and Versed dosage. After model correction, there was no discernible difference in the three groups' diastolic blood pressures.
Conclusion: The use of clonidine did not significantly reduce the quantity of sedatives required, according to this study's findings. When compared to the 0.1 mg group and the controls in the adjusted model, the mean systolic blood pressures for the 0.2 mg clonidine dose group were significantly lower at the pre-sedation and the first intraoperative times; however, there were no significant differences across the measurement times for the effect of clonidine on diastolic blood pressure.

Keywords: Public health; sedation dentistry; clonidine; Bangladesh.

1. INTRODUCTION

The most used sedatives in dentistry are benzodiazepines, which may be taken on their own or before venous cannulation to provide mild sedation [1]. Benzodiazepines come in a wide range of options, including diazepam, triazolam, midazolam, and lorazepam [1,2,3]. There are other medication classes for preoperative dental sedation, including as GABA agonists (zolpidem, zaleplon), antihistamines (hydroxyzine, diahydramine), and anticonvulsants [1]. Triazolam [Halocin] is the most often used benzodiazepine in dental procedures [4]. Triazolam offers benefits for safety, such as a short-acting sedative effect, but it may also briefly impair memory [but not at dosages of 0.5 mg or less] [5,6]. Triazolam has drawbacks similar to other benzodiazepines in that it relaxes the muscles that support the airway, which may result in respiratory depression and upper airway blockage [7]. Additionally, despite taking an oral sedative, triazolam generates high blood pressure and tachycardia, suggesting individuals are in a high adrenergic state [7].

Since more than 40 years ago, clonidine, an alpha-2 adrenergic agonist, has been used to treat hypertension [8,9-12]. The FDA granted clonidine approval in October [2008] for use as a premedication drug before sedation [13]. In addition to lowering post-operative shivering and nausea and vomiting, clonidine lowers anesthetic needs [14,15-18]. In addition, clonidine has a sympatholytic action, provides post-operative analgesia, and does not, unless overdosed, induce respiratory depression [19,20-22]. Additionally, clonidine doesn't result in amnesia [19].

2. METHODS

This research was clinical and cross-sectional. A large inner city dental clinic that offers free dental treatment to those in need participated in this clinical, cross-sectional research of its patients. Information was gathered from treatment records completed between March 2012 and April 2012. Many of the patients were excellent candidates for mild sedation dentistry since they experienced a great degree of dental anxiety and worry. Patients had the option to participate or not in the trial after reviewing the permission form and any potential negative effects of clonidine. These patients' sedations and treatments were given as a part of a yearly course that was offered to certify working dentists across the state and area to administer intravenous sedation in their dental offices.

As part of the check-in procedure, each patient's vital signs were obtained in the waiting area. The research had 101 individuals. 23 (14 female, 9 male) of the 104 patients treated throughout the time period gave their permission and satisfied the inclusion requirements for clonidine medication. Hypotension (blood pressure less than 100/70) and/or bradycardia were considered exclusion criteria (heart rate less than 60 beats per minute). Additionally, patients were disqualified if they had any of the following conditions that are contraindicated for taking clonidine: kidney disease, heart disease (including coronary artery disease, irregular heartbeat, recent heart attack), depression, blood circulation disorders (including Reynaud's disease, stroke), pregnancy, or alcohol use.

One patient was eliminated owing to being unable to gain intravenous access, leaving only 80 controls and 103 participants in total. The remaining 81 patients served as controls and did not receive clonidine medication. Body mass index, gender, and age were extracted from the medical records. The American Society of Anesthesiologists (ASA) physical state categorization was used to group the patients. This technique of categorization is used to assess patients' health status prior to surgery

(20). Smokers who smoked at least half a pack of cigarettes per day (ppd) for 1 to 30 years were the main determinant of ASA II status. A history of depression, drug and/or alcohol misuse, heart disease, pulmonary disorders (COPD, bronchitis/emphysema), hypertension, asthma, diabetes mellitus (type II), and pulmonary problems (bronchitis/emphysema) were additional medical factors that affected ASA status.

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2.1 Statistic Evaluation

Using SAS, all statistical analyses were carried out. In order to investigate the relationship between the research sample's characteristics and clonidine usage, descriptive statistics, such as Chi-square tests, were used. The hemodynamic changes (such as systolic, diastolic, mean arterial pressure, and pulse) in patients receiving clonidine 0.1 mg, clonidine 0.2 mg, and the control group were compared using an analysis of variance with the Duncan Multiple Range Test. The patients were examined and compared at four different times:

1. The pre-assessment visit, which usually takes place one week before the sedation and dental procedures;
2. The pre-sedation assessment, which took place in the dental operating room 30 to 1 hour after the clonidine group's administration of the medication;
3. The beginning of the sedation and dental procedure; and
4. The intra-operative visit. The patient's vital signs, oxygen saturation, and degree of consciousness were monitored during the intraoperative procedure and reported every five minutes.

Depending on the kind of dental work done, the length of the intraoperative anesthesia and treatment might be anything from one and two and a half hours. The course of therapy includes periodontal, endodontic, and significant oral surgery.

The quantity of sedation was compared between the two clonidine dosages to see whether there was a discernible difference in the decrease of sedation between them. To determine the efficacy of clonidine on the level of sedation, these dosages were compared to those of the control group. The Duncan's Multiple Range Test was used to analyze these comparisons and determine if there are any significant mean differences. The results of these analyses were used to create a simple regression model.

Backward elimination was used to improve the model by determining which variables should be maintained and included in the basic regression model. These findings led to the elimination of gender, ASA, and Fentanyl dosages. Age, BMI, and dosages of Versed were kept in the model.

3. RESULTS AND DISCUSSION

Prior to venipuncture, the first four patients who received clonidine 0.2 mg had substantial hemodynamic alterations. From the moment they started using clonidine 0.2 mg, there were noticeable differences in BP, MAP, and pulse changes. Additionally, two of the four patients who received oral clonidine 0.2 mg had their doses of flumazenil (Romazicon) 0.2 mg reversed at the conclusion of their dental operation owing to excessive sedation (as determined by the dentist who administered the medication).

One patient got 5 mg of midazolam intravenously, while the other received 4 mg and 25 mcg of fentanyl intravenously. Even though no further adverse effects, such as PONV, fainting, light headiness, sleepiness, dry mouth, or complaints from the patients, were detected after this initial day of use, it was decided to cut the dosage in half for the remaining patients who chose to receive these pre-operation sedatives.

Primary Results of the 101 research participants, 49.5% of whom were men and 50.5% of whom were women. There were 23 individuals in the clonidine group, four of whom received a dosage of 0.2 mg, while the other 19 people received a dose of 0.1 mg. The control group, which was made up of 80 people, had 53 percent more men than women. The study's patients were mostly between the ages of 44 and 56 (42% of the total). Underweight (16.5-28.5), normal (18.5-25), overweight (25.30), obese (30-35), and severely obese were the five categories used to classify body mass index (35-40). More than half (54%) were obese, severely obese, or both.

Table 1. Study population demographics

Characteristics	Overall N=102 N (%)	Clonidine 0.1 mg N=19 N (%)	Clonidine 0.2 mg N=4 N (%)	Control N=80 N (%)	P-value#
Sex					
Female	50 (49.5)	10 (20)	4 (8)	36 (72)	0.05
Male	51 (50.5)	9 (17.7)	0 (0)	42 (82.3)	
Age					
18-30	19 (18.81)	1 (5.2)	1 (5.3)	17 (89.4)	0.49
31-43	29 (22.7)	6 (21.4)	2 (7.1)	20 (71.4)	
44-56	42(41.5)	9(21.4)	1 (2.4)	32 (76)	
>=57	12 (11.9)	3 (25)	0 (0)	9 (75)	
BMI [1]					
16-18.5	8 (7.8)	0(0)	0 (0)	8(100)	0.033
18.5-25	39 (37.8)	10 (25.6)	3 (7.7)	26 (66.7)	
25-30	24 (23.3)	2 (8.33)	0 (0)	22 (91.7)	
30-35	27 (26.2)	5 (18.52)	0 (0)	22 (81.5)	
35-40	5 (4.8)	2 (40)	1 (20)	2 (40)	
ASA Status ~					
I	16 (15.5)	1 (6.25)	0 (0)	15 (93.7)	0.27
II	74 (71.8)	17 (23)	4 (5.4)	53 (71.6)	
III	12 (11.6)	1 (8.3)	0 (0)	11 (91.7)	
IV	1 (0.8)	0 (0)	0 (0)	1(100)	

1 Body mass index
~ American Society of Anesthesiologist physical status classification
 # P-value refer to Likelihood Ratio Chi-Square test.
Effective sample size =101; Frequency missing =2

Table 2. Comparison of hemodynamic changes (N=103)

Blood pressure	Clonidine 0.1 mg	Clonidine 0.2 mg	Control
Pulse	N=19	N=4	N=80
Map*			
Initial	152^{a} / 89^{a} 81^{ab}	121^{b}/83^{a} 92^{a}	135^{ab} / 80^{a} 77^{b}
Pre-sedation	133^{A} / 80^{a} 75^{a} 97^{a}	97^{B} / 66^{b} 85^{a} 77^{b}	126^{A} / 77^{a} 78^{a} 93^{a}
First intra -	117^{AB} / 73^{A}	102^{B} / 69^{A}	121^{A} / 73^{A}
Operative	78^{a} 98^{a}	77^{a} 77^{b}	78^{a} 94^{a}
Final intra-	131^{A}/81^{A}	96^{B} / 67^{B}	126^{A} / 77^{AB}
Operative	74^{A} 89^{A}	80^{A} 80^{A}	78^{A} 89^{A}

** MAP=Mean arterial blood pressure*

The symbols letters A B' and AB indicate significant differences in means according to Duncan's Multiple Range Test; means with the same letters are not significantly different from each other

Table 2. compares the measurements of systolic and diastolic blood pressure, pulse, and mean arterial pressure (MAP) at different clonidine doses (0.2 mg, 0.1 mg, and control). When compared to the control group, mean systolic pressures for the clonidine 0.2 mg and 0.1 mg dosages are initially significantly different, according to Duncan's Multiple Range Test. The pre-sedation time systolic and diastolic blood pressures of the clonidine 0.2 mg group were lower than those of the 0.1 mg group and the control group. The findings indicate that during the first intraoperative period, the systolic mean of the 0.2 group was considerably lower than that of the control group.

The systolic and diastolic blood pressures in the 0.2 mg group were lower than those in the 0.1 mg group at the last intraoperative measurement, and they were also lower than those in the control group. In terms of pulse, the 0.2 mg group's initial pulse was noticeably greater than that of the control group but not that of the 0.1 mg group. In compared to the 0.1 mg group and the controls, the mean arterial pressure was considerably lower in the 0.2 mg group during pre-sedation and the first intraoperative measurement.

4. CONCLUSION

A randomized, double-blind approach was used in the bulk of earlier research that looked at the use of clonidine as a pre-sedative in dentistry. Clonidine was found to be a reliable pre-sedative with minor adverse effects in the majority of these investigations. In these trials, clonidine was used to lower systolic, diastolic, and mean arterial blood pressures (MAP), as well as pulse rates. Since the study's design did not randomly assign patients to various treatment groups and only 23 of the patients took clonidine, it is difficult to compare the findings (and only 4 at the highest dose groups). The dosage was reduced to 0.1 mg in the other individuals as a result of the reporting of changes in blood pressure, Map, and pulse rate in the first four patients. In general, earlier investigations did not find any negative effects at this dosage. The comparison with earlier investigations is hampered by these restrictions.

The use of clonidine did not significantly reduce the quantity of sedatives required, according to this study's findings. When compared to the 0.1 mg group and the controls in the adjusted model, the mean systolic blood pressures for the 0.2 mg clonidine dose group were significantly lower at the pre-sedation and the first intraoperative times; however, there were no significant differences across the measurement times for the effect of clonidine on diastolic blood pressure.

CONSENT

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

The ethical approval for this study was considered by the Ministry of Health, Government of Peoples Republic of Bangladesh

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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