Original Article

# Clonazepam for the Management of Anxiety Associated with Oral Surgery: A Randomized Double-blind Controlled Trial

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**ABSTRACT**

**Statement of Problem:** Anxiety is one of the most common challenges which affect both the patient and the surgeon throughout dental procedures. Thus, there has been growing interest in the application of sedatives in dentistry.

**Purpose:** This study evaluated the efficacy of clonazepam in reducing anxiety prior to oral surgery.

**Materials and Method:** The participants of this, randomized controlled trial, study included 60 patients who referred to the Department of Oral and Maxillofacial Surgery, Shiraz University of Medical Sciences. They were randomly allocated to either a single 2 mg dose of Clonazepam or a placebo one hour prior to the surgery. The participants and the outcome assessors were blind to the intervention. Levels of anxiety were recorded using Visual Analogue Scale (VAS) and measuring blood pressure (BP), pulse rate and arterial oxygen saturation percentage. After collecting the data, the Chi-square test was run and then the data was analyzed.

**Results:** The participants in the treatment and control groups were matched for age, sex, education, marital status and employment status ( $p > 0.05$). All anxiety determinants (VAS, BP, pulse, and oxygen saturation rates) changed significantly one hour after the administration of clonazepam ( $p < 0.05$).

**Conclusion:** Clonazepam is an effective anxiolytic drug with minimal side effects which can be used to reduce anxiety in dental patients.

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## Introduction

Going to a dentist is one of the most unpleasant experiences most people have, placing it among the top five most stressful situations in life. Given its high prevalence, patients tend to avoid dental visits unless they have reached an intolerable level of pain, which is associated with worsening their oral condition [1]. Studies indicate that there is direct correlation between anxiety associated with dental procedures and the seriousness of oral diseases [2-3]. Among dental procedures, treatments involving different aspects of oral surgery cause the highest level of anxiety [4]. Some of the symptoms associated with dental anxiety include tachycardia, elevated blood pressure, and perspiration, the management of all of these makes it more complicated for the dental team to provide the required level of care [5]. Thus, studies have indicated a growing trend towards the application of anxiolytic and sedative agents in order to provide a relaxing condition for the patient throughout dental procedures [6]. Most cases of dental anxiety can be easily treated with oral sedatives [7]. Like all the other techniques, oral sedation has its own limitations and may be ineffective in severely anxious patients. Additionally, respiratory depression is always a chief concern when applying oral sedatives, thus the patient's vital signs require

careful monitoring throughout the procedure [8].

Benzodiazepines are among the most widely used anxiolytic and sedative agents. They influence the activity of the major inhibitory neurotransmitter and gamma-aminobutyric acid (GABA). Furthermore, they raise the stimulatory threshold of the neurons in the central nervous system [9].

Some of the most common benzodiazepines which are used in dentistry include Diazepam, Midazolam and Triazolam [8]. Clonazepam is also a long-acting benzodiazepine which is primarily used to control seizure attacks. It has also been prescribed for cases of panic disorder [10-12]. However, there is still little information on the efficacy of Clonazepam for anxiety control in patients undergoing dental procedures. Therefore, this study was an attempt to assess the anxiolytic effects of Clonazepam before oral surgery.

## Materials and Method

This study was carried out in the Department of Oral and Maxillofacial Surgery, Shiraz University of Medical Sciences, Shiraz, Iran. After obtaining the approval of the Research Protocol in the Ethics Committee of the University (CT-90-5558) and explaining all aspects of the study to the patients, 60 individuals volunteered to participate in this randomized double-blind clinical trial. Non-smoking, non-alcoholic healthy adults (≥ 8 years of age) with no history of systemic condition or drug abuse were included in the study and those taking any kind of medication, pregnant women, or those in their menstrual cycle were excluded from it.

Information regarding the participants' age, gender, education, occupation, marital status, and dental history was initially recorded in a standard questionnaire. Then a random-number table, with numbers from 1-60 which indicated the total number of the participants, was used to randomly allocate each of the participants to either of the treatment or control groups. Participants with odd numbers received the placebo and even numbers received a single 2 mg dose of Clonazepam (Sobhan Daru, Tehran, Iran) one hour prior to the surgery. The participants and the examiner were blind to the treatment groups. In order to determine the level of anxiety, patients were asked to use a Visual Analogue Scale (VAS) and determine their levels of anxiety from 0 to 10 (Fig. 1) [13-15].

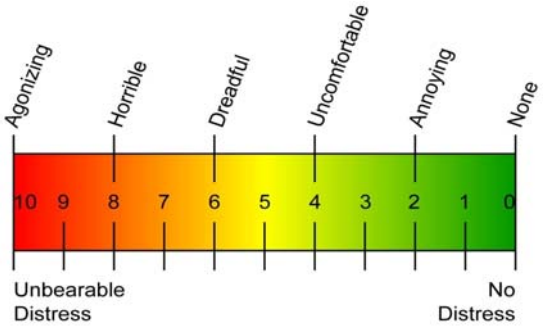


**Figure 1** VAS scale

VAS and other anxiety indices including the levels of blood pressure, pulse rate and oxygen saturation percentage were recorded before taking the medication and one hour after the surgery. Patients were monitored throughout the surgery procedures for blood pressure, pulse rate and oxygen saturation. Then the data was entered in SPSS, version 17, and the Chi-square test was run to analyze the data.

## Results

In the present study, males and females were equally distributed among the two groups. Most of the patients were married (85%), unemployed (46.6%) and had no academic degree (80%). Table 1 summarizes the demographic characteristics of the participants (in terms of their gender, marital status, education, and employment status). The average age of the treatment and control groups were 38.20 ± 10.67 and 36.43 ± 11.00, respectively. Statistical analysis revealed that

**Table 1** Participants' gender, marital status, education and employment status in the control and treatment groups

| | Gender | | Marital status | | Education | | Employment | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Male (%) | Female (%) | Single (%) | Married (%) | Non-Academic (%) | Academic (%) | Unemployed (%) | Self-Employed (%) | Student (%) | Contract worker (%) |
| Control | 16 (26.6) | 14 (23.3) | 4 (6.6) | 26 (43.3) | 24 (40) | 6 (10) | 11 (18.3) | 12 (20) | 1 (1.6) | 6 (10) |
| Treatment | 14 (23.3) | 16 (26.6) | 5 (8.3) | 25 (41.6) | 24 (40) | 6 (10) | 17 (28.3) | 7 (1.16) | 2 (3.3) | 4 (6.6) |
| Total | 30 (50) | 30 (50) | 9 (15) | 51 (85) | 48 (80) | 12 (20) | 28 (46.6) | 19 (21.1) | 3 (5) | 10 (16.6) |

the groups were matched for all the mentioned demographic variables ( $p$ >0.05). The results of the Chi-square test revealed that VAS scores decreased significantly in the treatment group one hour after taking Clonazepam ( $p$ <0.001, Figure 2).

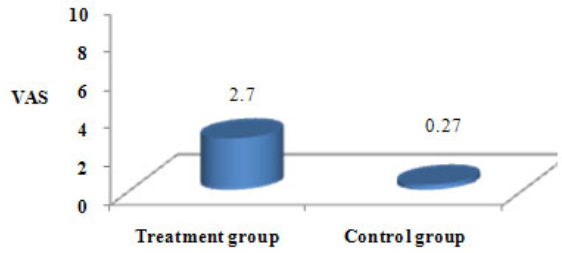


**Figure 2** VAS score variations among the control and treatment groups

Figures 3, 4 and 5 represent the differences in the blood pressure, pulse rate, and oxygen saturation percentage one hour after the taking Clonazepam or the placebo. Statistical analysis revealed that the blood pressure level, the pulse rate, and the oxygen Saturation percentage decreased significantly in the treatment group ( $p$ <0.001).

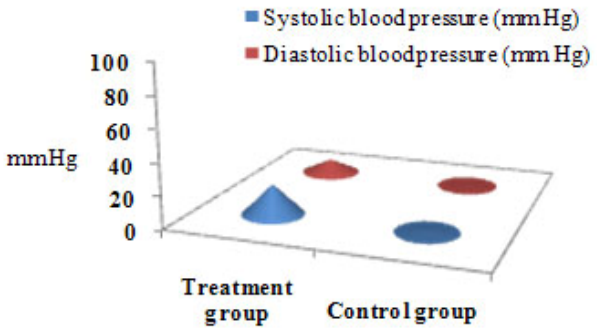


**Figure 3** Blood pressure variations among the control and treatment groups

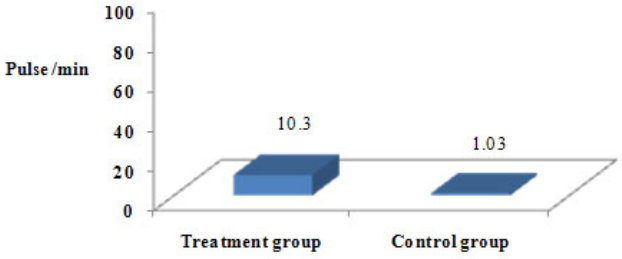


**Figure 4** Pulse rate variations among the control and treatment groups

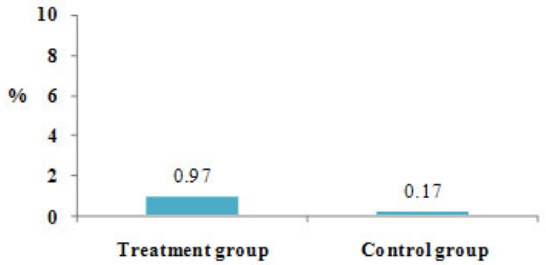


**Figure 5** Percentage of oxygen saturation variations among the control and treatment groups

## Discussion

Dental anxiety is a complex phenomenon which is under the influence of personality characteristics, past traumatic dental experiences and dentally anxious family members [16]. Various scales have been proposed to assess dental anxiety [17-19]. In this study, Visual Analogue Scale (VAS) was used. In addition the participants' blood pressure, pulse rate, and oxygen saturation percentage were measured to determine levels of anxiety associated with oral surgery.

Clonazepam is a benzodiazepine drug with anxiolytic, anticonvulsant, and muscle relaxant properties [20]. Because of their minimal adverse effects, rapid onset and accelerated recovery, numerous studies have recommended the use of benzodiazepines to reduce anxiety among children and adults [21-26]. Midazolam and Diazepam are among the most common anxiolytic agents given to children [27]. Triazolam has also been shown to have promising sedative effects in pediatric patients [28]. The recommended dose of the drug depends on numerous factors. The dentists need to decide what they are going to achieve (sedation, anxiety control, amnesia), what kind of patient they are dealing with (in terms of age, gender, level of cooperation, levels of anxiety, etc.) and what the most -appropriate means of administration is (IV, oral, rectal) [27, 29].

The results of this study, as it was indicated through VAS and measuring blood pressure level, pulse rate and the oxygen saturation percentage demonstrated that administration of Clonazepam before oral surgery can significantly reduce anxiety levels. In 2008, Chen et al. evaluated the anxiolytic effects of Mirtazapine and observed a mean variation of 2.5 in the VAS scores [25].The mean VAS score variation in the present study was 2.7±0.98 which was slightly higher than Chen's.

Coldwell et al. evaluated the amnestic and anxiolytic effect of three doses of Alprazolam in patients in need of oral surgery. Their findings indicated that the effective anxiolytic doses (50 mg and 75 mg) were associated with memory impairment and they recommended the use of alternative anxiolytic agents [30]. In the present study, however, none of the participants complained about any adverse effects or drug reactions after taking Clonazepam. Since the operator's experience can also be an important factor in increasing levels of anxiety, it is recommended that future studies be extended to more professional dental care settings.

Variations among the clinicians in terms of experience, differences in the nature of the dental procedures, and inherent inaccuracy in measuring levels of anxiety are some of the limitations of this study. The number of participants, however, consistent clinical atmosphere and the use of multiple anxiety assessment techniques were among the advantages of the present study.

## Conclusion

Despite the limitations of this study, Clonazepam seems to be an effective anxiolytic agent which has minimal side effects and it can be used to reduce anxiety associated with oral surgeries.

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