Research Article

Effect of Dexmedetomidine Added to Lidocaine Cartridge on the Level of Patient Sedation, Cooperation, and Patient and Surgeon Satisfaction during Mandibular Third-Molar Extraction Surgery: A Randomized Double-Blind Controlled Trial

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Background. Various methods have been introduced for anxiety control during third-molar extraction surgery. Dexmedetomidine (DEX) is known to have analgesic, anxiolytic, and sympatholytic properties with minimal adverse effects. This study aimed to evaluate the impact of the local injection of the combination of DEX and Lidocaine on patients’ anxiety and the surgeon’s satisfaction during third-molar extraction surgery. Methods: A total number of 26 healthy volunteers with symmetrical bilateral impacted mandibular third-molar teeth indicated for surgical removal were included in this double-blind randomized controlled trial. A single experienced surgeon performed two surgical extraction procedures within at least four-week time intervals using anesthetic cartridges containing “DEX+LIDO” or “LIDO alone” used randomly on each side for each patient. The Visual Analog Scale and the SDFQ index were used to evaluate patients’ anxiety and surgeon satisfaction during the procedure. Results. SDFQ reports showed that patients in the “DEX” group were 1.5 times more relaxed than those in the “LIDO alone” group. As a result, the level of sedation was considered statistically significant between the two groups (Wilcoxon test, P value <0.019). Wilcoxon test results also showed significant differences between the two groups regarding patients’ overall cooperation in terms of interfering movement and verbal presentation of discomfort (P value <0.05); however, this difference was not considered significant regarding nonverbal signs of discomfort (P value >0.05). Moreover, both the surgeon and the patients reported a significantly higher satisfaction rate in the DEX group (paired T-test, df = 25, P value <0.05). Conclusions. It was inferred from the outcomes of the present study that the application of DEX added to the LIDO local anesthesia cartridge could significantly benefit anxious patients with previous unpleasant dental treatment experiences. Trial Registration. This trial is registered with the clinical trial registration number: IRCT20200406046966N.

1. Introduction

Many patients experience anxiety before, during, and after surgical dental treatments due to the expected pain and discomfort. Experience of anxiety and discomfort following dental treatments, including impacted third-molar extraction surgery as the most common dental surgical procedure [1], may lead to an irrational fear of other necessary dental treatments [2]. On the other hand, the role of dental anxiety in a patient’s perception of pain, cooperation, and
satisfaction cannot be ignored [3]. Patients with a high level of anxiety who agree to be operated on under local anesthesia would eventually be unable to cooperate adequately of anxiety who agree to be operated on under local anesthesia [3]. Patients with a high level of anxiety who agree to be operated on under local anesthesia [3]. Patients with a high level of anxiety who agree to be operated on under local anesthesia, and a prolonged operating time during the procedure, which results in stress on the operator, poor surgical performance, and a prolonged operating time [4]. Also, anxious patients tend to exaggerate the intensity of their pain and fear [5].

Besides, the application of sedation methods in complex rehabilitations as well as certain conditions including temporomandibular joint disorders, bruxism, and masticatory muscle spasms enhances patients’ cooperation and the quality of treatment [6, 7]. Numerous medications and methods have been discovered, used, and studied over the years for managing dental fear and anxiety [8]. Midazolam is a well-known benzodiazepine commonly administered by the intravascular (IV) route during oral surgery for sedative purposes [9]. Since it can cause some respiratory depression alongside the absence of analgesic properties, some investigators are looking for an alternative with an easy and effective route of administration as well as additional analgesic properties and minimal adverse effects.

Achieving profound local anesthesia plays a critical role in the success of a surgical procedure [10]. Various adjuvant agents are added to local anesthetics to improve analgesic efficiency and reduce the required number of anesthetic cartridges [11]. DEX (Table 1) is a colorless medication that acts as a selective α-2 adrenoreceptor agonist, acting in various tissues, including the nervous, cardiovascular, and respiratory systems [12]. It was approved by the FDA in 1990 for sedation of non-intubated patients during surgical procedures [13]. When used as a sedative, DEX is believed to have analgesic, anxiolytic, and sympatholytic properties along with minimum respiratory and neurocognitive adverse effects [14, 15]. It is also associated with reduced blood pressure and heart rate [16]. DEX also has vasoconstrictor features by acting on α-2β receptors of peripheral blood vessels and has been shown to enhance the anesthetic effects and prolong the duration of action of LIDO (Table 1) local anesthesia as well as reduce the required dosage of anesthetic drugs [17]. Therefore, it is suggested that DEX can be helpful for anxiety control in patients undergoing dental surgery when achieving adequate patient cooperation is a challenging issue for the operator [18].

It was demonstrated that during the recovery period, the analgesic and sedative effects of DEX were longer than the combination of midazolam and fentanyl [19]. Also, DEX combined with bupivacaine, compared to bupivacaine alone, provides a better anesthetic effect due to the prolonged analgesic effect in greater palatine injection during cleft palate surgery. Moreover, the severity of the pain in the first 24 hours was reported to be less by using this combination, while sedative and hemodynamic properties were similar in both groups [20]. Furthermore, adding a small amount of DEX to LIDO and its application for nerve block injection has been demonstrated to decrease the onset time of anesthesia and increase the duration of action without causing any systemic side effects [21, 22].

Another study by Nooh et al. showed that 1.5 µg/kg inhaling DEX could significantly increase patient calmness in the first 20–30 minutes of the surgical procedure; the peak effect was in 40–50 minutes after application and eliminated after 70–80 minutes. Besides, systolic pressure and heart rate were lower in this group. The conclusion was that DEX could be considered a safe and efficient sedative for the surgical removal of impacted third-molar teeth [23].

The results of a study by Fan and colleagues showed lower blood pressure and heart rate during dental surgical procedures in patients receiving DEX; furthermore, a higher cooperation rate was reported in the DEX group in comparison to the midazolam group. No respiratory adverse effects were reported for the DEX group. Therefore, regarding predictable hemodynamic and pharmacologic properties, DEX is suggested to be a safe substitute for midazolam for sedation purposes [24].

On the contrary, Cheung and associates showed that the sedative effects of DEX (0.88 µg/kg) were comparable to midazolam (3.6 µg/kg), while blood pressure, heart rate, and anxiety in the DEX group were considerably lower than midazolam. The patient’s satisfaction in the midazolam group was not superior to the DEX group [25]. Moreover, in a systematic review, it was reported that there was no statistical difference between the two routes of intraoral submucosal and extraoral intramuscular injections of DEX regarding postoperative pain, swelling, and trismus [26].

The present study aimed to evaluate the efficacy of DEX as an adjuvant agent to LIDO in reducing patients’ anxiety and improving cooperation during surgery.

### Table 1: Table of abbreviations for common terms.

| Term                                | Abbreviation |
|-------------------------------------|--------------|
| 1 DEX                                | DEX          |
| 2 Visual analog scale               | VAS          |
| 3 Short dental fear questionnaire   | SDFQ         |
| 4 Lidocaine                         | LIDO         |
| 5 Food and drug administration      | FDA          |
| 6 Statistical package for social sciences | SPSS        |

2. Materials and Methods

Calculation of the sample size was done using the formula for comparison of two means. A minimum difference of 1.3 in the mean score of the Visual Analog Scale (VAS) (Table 1) between the “LIDO alone” and “LIDO + DEX” groups was considered statistically significant with an α-error of 0.05 and 1-β = 0.80. This randomized double-blind controlled trial study with a split-mouth and parallel design was performed on 26 patients (52 samples) with bilateral impacted mandibular third molars indicated for surgical removal who were referred to the Especial Dental Clinics of Isfahan University of Medical Sciences, Isfahan, Iran, from April to July 2020. None of the patients or the surgeon were aware of the type of anesthetic agent used for each surgery.

This study followed the Declaration of Helsinki on medical protocol and ethics, and the Regional Ethical Review Board of Isfahan University of Medical Sciences approved this study on 4th April 2020 (IRB approval code:
1) I was totally relaxed during the treatment (“Relaxed”)
2) I was nervous but the treatment was carried out successfully. (“Slightly frightened”)
3) I was nervous, the treatment could only just be carried out (“Moderately frightened”)
4) I was so frightened and nervous that
   a) Treatment was difficult (“Severely frightened”)
   b) The treatment did not succeed (“Severely frightened”)
satisfaction were not significant in each DEX and LIDO group (paired T test, df = 25, P value < 0.05) (Table 4).

Regarding patients’ cooperation, there was a significant difference between the two groups concerning interfering movement and verbal presentation of discomfort (Wilcoxon test, P values of 0.021 and 0.040, respectively). Nonetheless, nonverbal signs of discomfort did not differ significantly between the DEX + LIDO group and the LIDO alone group (Wilcoxon test, P value > 0.050) (Tables 2 and 5).

### 4. Discussion

The results of the present study showed that the surgeon’s and patient’s satisfaction was significantly higher by adding DEX to the LIDO cartridge when compared to LIDO alone. Besides, the patient’s level of sedation and cooperation was shown to be significantly higher in the DEX group.

Concerning the degree of sedation, a systematic review and meta-analysis have reported that DEX as a safe medication can provide a good sedative effect for surgical extraction of impacted wisdom teeth [27]. These results are in favor of the outcomes of our study.

On the contrary, several studies have evaluated the effect of DEX on patients’ sedation. According to Obayah et al. during the first 24 hours after surgery, no significant change in the sedation level was reported among children who received greater palatine nerve blocks using bupivacaine plus DEX and those who received bupivacaine alone [20]. Furthermore, Cheung et al. compared DEX to midazolam for sedation purposes in third-molar extraction surgery and discovered that both medications provided comparable sedation. Heart rate and blood pressure were reported to be lower in the DEX group. There was no significant difference in satisfaction or pain scores between the two groups [18].

### Table 2: Patients cooperation values were reported in three parts including interfering movement, verbalized discomfort, and nonverbal signs of discomfort.

| Patients cooperation | Local anesthetic cartridge | Total |
|----------------------|---------------------------|-------|
|                      | Dex + lido | Lido alone |       |
| No interfering movement | Number 24 | 16 | 40 |
| Minor movements, the position remained appropriate | Number 2 | 10 | 12 |
| Minor movements, the patient had to be repositioned | Number 0 | 0 | 0 |
| Gross movements considerably interfered with the procedure | Number 0 | 0 | 0 |
| Not at all | Number 20 | 12 | 32 |
| Some verbalization but did not indicate pain or discomfort | Number 3 | 8 | 11 |
| Some verbalization indicating pain or discomfort | Number 3 | 6 | 9 |
| Complained frequently during the procedure | Number 0 | 0 | 0 |
| Not at all | Number 21 | 11 | 32 |
| Slight discomfort, occasional grimaces | Number 1 | 1 | 12 |
| Moderate discomfort, feet/hands tensed, tears in eyes | Number 4 | 3 | 7 |
| Marked discomfort apparent during the procedure | Number 0 | 1 | 1 |

### Table 3: Patients’ reports on sedation using SDFQ.

| SDFQ | Local anesthetic cartridge | Total |
|------|---------------------------|-------|
|      | Dex + LIDO | LIDO alone |       |
| I was completely relaxed during the treatment (“relaxed”) | Number 22 | 15 | 37 |
| I was nervous but the treatment was carried out successfully (“slightly frightened”) | Number 3 | 3 | 6 |
| I was so frightened and nervous that treatment was difficult (“severely frightened”) | Number 1 | 8 | 9 |
| Total | Number 26 | 26 | 52 |

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These contradictory results could be explained by the different control groups studied in these experiments compared to our study. In fact, DEX is compared to midazolam as a sedative or bupivacaine as long-lasting local anesthesia was shown to be effective in pre and postoperative pain control, which can directly affect patient satisfaction when compared to LIDO as a medium-lasting agent with no considerable sedative properties.

Regarding pain evaluation, Gursoytrak et al. showed that submucosal administration of DEX added to articaine local anesthesia could be considered an effective tool for controlling postoperative symptoms including edema, trismus, and pain [29]. However, when comparing DEX to ketamine in another study with a similar design, it was demonstrated that ketamine was superior to DEX concerning postoperative pain control [31]. The outcome of our study supports the results of their first trial and the efficacy of DEX in postoperative pain control. Moreover, contradictory results with the second experiment could be justified by the fact that DEX is compared to ketamine, which as an opioid is considered the most potent medication available for pain control and is not used routinely for this purpose following surgical removal of impacted mandibular third-molar teeth. Besides, other studies have stated that LIDO plus DEX compared to LIDO alone could reduce the pain score significantly. In Cheung’s study, evaluating the effects of intranasal administration of DEX 45 minutes before third-molar extraction surgery as an adjunct to the local anesthesia, perioperative sedation, and postsurgical analgesic effects was reported to be superior in the DEX group [32]. Also, Nooh et al. reported that intranasal administration of 1.5 μg/kg atomized DEX is effective, convenient, and safe as a sedative for patients undergoing third-molar extraction [23]. Besides, DEX also provided satisfactory premedication sedation when used alone intranasally in children [33]. Also, according to Tonooka and colleagues, administration of DEX added to LIDO for dental local anesthesia in eight patients led to improved sedation levels and enhanced pulpal local anesthesia compared to LIDO alone [34]. Similar results were obtained from other clinical studies by Alizargar, Sing, and colleagues [35, 36]. These results are consistent with the outcomes of our study and support the idea that DEX, regardless of the route of administration, could provide superior results concerning the level of sedation and patients’ cooperation.

During a dental surgical procedure, the bispectral index tracked a comparison of conscious sedation using DEX and Midazolam; findings showed that patients in the DEX group had lower heart rates and blood pressure and cooperated better. However, there was no noticeable difference in bispectral index values between the two groups [24]. Furthermore, in Ustun’s study, it was reported that although both groups experienced equal levels of sedation, the cooperation scores revealed that the operator preferred DEX. In conclusion, these results suggest that DEX can provide a higher level of satisfaction for both the operator and the patient when compared to midazolam [37]. These results were consistent with our work. Regarding the patients’ cooperation, however, a thorough evaluation of different aspects of cooperation in our study, including interfering movement and verbal and nonverbal representation of discomfort showed that application of DEX led to significant improvement in the first two mentioned factors, while the nonverbal representation of discomfort was shown to be comparable between the two groups. This can be justified by the fact that nonverbal representation of discomfort in contrast to interfering movements and verbal complaints during surgery might not directly interfere with the surgeon’s satisfaction.

Table 4: Paired T-test results for VAS of patient’s and surgeon’s satisfaction.

|               | Paired differences | Mean | Sd  | df  | P value |
|---------------|--------------------|------|-----|-----|---------|
| PATIENT_DEX   | 0.76               | 1.53 | 2.56| 25  | 0.017   |
| PATIENT_LIDO  | 1.46               | 1.77 | 4.20| 25  | <0.001  |
| SURGEON_DEX   | -0.15              | 1.08 | -0.72| 25  | 0.476   |
| SURGEON_LIDO  | 0.53               | 1.79 | 1.53| 25  | 0.138   |

Figure 2: VAS scores of the patients and the surgeon.
Table 5: Wilcoxon test results comparing patients’ cooperation between case and control groups.

|                  | COOPERATION_LIDO_1—COOPERATION_DEX_1 | COOPERATION_LIDO_2—COOPERATION_DEX_2 | COOPERATION_LIDO_3—COOPERATION_DEX_3 |
|------------------|--------------------------------------|--------------------------------------|--------------------------------------|
| Z                | -2.309<sup>a</sup>                   | -2.057<sup>a</sup>                   | -1.968<sup>a</sup>                   |
| Asymp. Sig. (2-tailed) | 0.021                                | 0.040                                | 0.050                                |
access and vision to the surgical site and, as a result, could be more easily ignored.

Regarding the split-mouth design of the study, more reliable outcomes were achieved owing to the controlled confounding factors. Nevertheless, this study had some limitations. Increasing the dosage of DEX, in addition to the sample size, can lead to more comprehensive evaluations, alongside investigating other confounding factors. Selecting samples from a wider age range might help control other confounding factors.

It could be inferred from the results of the present study that in patients with a high level of anxiety and/or unpleasant previous experience, DEX added to LIDO local anesthetic is suggested to reduce stress level as well as improve patients’ cooperation. We suggest that patients’ preoperative stress levels would be measured and recorded using a questionnaire, and only patients with high-stress levels should be included in future studies so that the effect of this method on truly anxious patients can be measured.

**Data Availability**

Data are available from the corresponding author upon request.

**Ethical Approval**

IRB number is IR.MUI.RESEARCH.REC.1399.009

**Conflicts of Interest**

The authors declare that they have no conflicts of interest.

**Authors’ Contributions**

Milad Etemadi and Kimia Salimian contributed equally to this work.

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