


## 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

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         |

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 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 intravenous (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 adjunctive 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  $\alpha$ -2 adrenoceptor 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  $\alpha$ -2  $\beta$  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  $\mu$ gr/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  $\mu$ gr) were comparable to midazolam (3.6  $\mu$ gr), 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 adjunctive agent to LIDO in reducing patients' anxiety and improving cooperation during surgery.

## 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  $\alpha$ -error of 0.05 and  $1-\beta=0.80$ . 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:

IR.MUI.RESEARCH.REC.1399.009). Before the intervention, informed consent was obtained from all participants. The unwillingness of the patient to continue participation in the study came into consideration. All patients' information was kept confidential in this study. This study was registered in the Iranian clinical trial registry IRCT20200406046966N.

Healthy participants (ASA class I or II) of both sexes aged between 18 and 30 with asymptomatic bilateral mesioangular Class I and II position B impacted mandibular third molars indicated for surgical removal were included in the present study. To ensure that the nature of impaction was the same on both sides, radiographic evaluation using a panoramic view was done, and too easy or too challenging cases were excluded from the study. Having low blood pressure, bradycardia, unstable hypertension, and liver disorders that are contraindications for the application of DEX also came into consideration. The presence of tumors and malignant lesions and being a smoker were considered exclusion criteria. Being allergic to DEX and/or LIDO, surgical duration of more than 20 minutes, application of more than one cartridge, patients who did not come back for the second surgery, and the occurrence of medical complications during surgery were among other exclusion criteria.

Patients were allowed to rest for 10–15 minutes before starting the surgery. Considering the split-mouth and crossover study designs in all participants, patients were randomly divided into two subgroups using a computer-generated random list. In group 1 ( $n = 13$ ), the first surgery was performed under local anesthesia only (cartridge containing 1.8 mL of 2% LIDO with epinephrine 1 : 80,000), and in group 2 ( $n = 13$ ), the first surgery was performed by applying DEX in combination with local anesthesia (cartridge containing 1.8 mL of 2% LIDO with epinephrine 1 : 80,000 + 0.1 ml DEX [27]), and for the second surgery, the subjects received the anesthetic solutions in the reverse order.

As a result, since DEX has a different pH compared to LIDO local anesthetic, the pH of the local anesthetic would most likely change; as a result, it is essential to keep the preparation's consistency under control [28]. 0.1 ml of DEX (Daru Pakhsh Co., Tehran, Iran), which contains ten  $\mu\text{g}$  of the drug, was added to each LIDO cartridge (Exir Co., Tehran, Iran) using an insulin syringe. To equalize the volume and appearance of cartridges, 0.1 ml of normal saline was added to cartridges in the control group. Both solutions were prepared by an anesthesiologist with matching random codes registered on them. The observers and the attending surgeon were blind regarding the type of cartridge being used for each surgery.

The surgical procedure started 15 minutes following the local anesthetic injection. The surgeries were carried out in a fully equipped operating room with resuscitation equipment. Standardized surgical technique was applied by providing an envelope flap followed by a buccal osteotomy, tooth removal, copious rinsing, suturing, and patient instruction. The duration of surgery was recorded as the period between making the incision and placing the last stitch.

- 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 ("Modertely frightened")
- 4) I was so frightened and nervous that
- a) Treatment was difficult ("Severely frightened")
- b) The treatment did not succeed ("Severely frightened")

FIGURE 1: The SDFQ and clinical classification of patient's fear.

Patients did not take any medication before surgery. Two surgeries were performed by one experienced surgeon, separated by at least four weeks.

At the end of the surgery, patients were asked whether they were relaxed or anxious during the operation using a short dental fear questionnaire (SDFQ) as a 4-point Likert scale that shows the greater numerical value for greater fear (Figure 1) [29]. Patients' cooperation was assessed by a cooperation scale consisting of three parts (Table 2) [30], and their overall satisfaction was evaluated by a linear, non-graded 10 cm VAS assessed by a blind observer at the end of the procedure [31]. VAS scores of satisfaction of both patient and surgeon were recorded between 0 (not satisfied at all) to 10 (very satisfied) [32]. After the second procedure, the patients were asked to subjectively evaluate the two procedures in terms of anxiety and discomfort and to indicate which application was more effective or if they were equally effective in reducing their anxiety.

Statistical analysis was performed by setting the significance level at 0.05 and using SPSS (Table 1), version 22. Patients' sedation, cooperation, and patient's and surgeon's satisfaction scores were compared using the Wilcoxon and paired  $T$  test.

### 3. Results

Of the total number of 26 patients, 58% were female. The mean age of the participants was  $22.03 \pm 2.39$ .

SDFQ reports showed that patients in the "DEX + LIDO" group were 1.5 times more relaxed than those in the "LIDO alone" group, which was considered statistically significant (Wilcoxon test,  $P$  value  $< 0.019$ ) (Table 3).

The mean scores of satisfaction for both the surgeon and the patients were significantly higher in the DEX + LIDO group (Figure 2) (paired  $T$  test,  $df = 25$ ,  $P$  value  $< 0.05$ ); however, differences between patients' and surgeon's

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 |       |       |
| Interfering movements         | No interfering movement                                    | Number                     | 24         | 16    | 40    |
|                               |  | Percent                    | 92.3%      | 61.5% | 76.9% |
|                               | Minor movements, the position remained appropriate         | Number                     | 2          | 10    | 12    |
|                               |  | Percent                    | 7.7%       | 38.5% | 23.1% |
|                               | Minor movements, the patient had to be repositioned        | Number                     | 0          | 0     | 0     |
|                               |  | Percent                    | 0          | 0%    | 0%    |
|                               | Gross movements considerably interfered with the procedure | Number                     | 0          | 0     | 0     |
|                               |  | Percent                    | 0%         | 0%    | 0%    |
| Verbalized discomfort         | Not at all   | Number                     | 20         | 12    | 32    |
|                               |  | Percent                    | 76.9%      | 46.2% | 61.5% |
|                               | Some verbalization but did not indicate pain or discomfort | Number                     | 3          | 8     | 11    |
|                               |  | Percent                    | 11.5%      | 30.8% | 11.5% |
|                               | Some verbalization indicating pain or discomfort           | Number                     | 3          | 6     | 9     |
|                               |  | Percent                    | 11.5%      | 23.1% | 17.3% |
|                               | Complained frequently during the procedure                 | Number                     | 0          | 0     | 0     |
|                               |  | Percent                    | 0%         | 0%    | 0%    |
| Nonverbal signs of discomfort | Not at all   | Number                     | 21         | 11    | 32    |
|                               |  | Percent                    | 80.8%      | 42.3% | 61.6% |
|                               | Slight discomfort, occasional grimaces                     | Number                     | 1          | 11    | 12    |
|                               |  | Percent                    | 3.8%       | 42.3% | 23%   |
|                               | Moderate discomfort, feet/hands tensed, tears in eyes      | Number                     | 4          | 3     | 7     |
|                               |  | Percent                    | 15.4%      | 11.5% | 13.5% |
|                               | Marked discomfort apparent during the procedure            | Number                     | 0          | 1     | 1     |
|                               |  | Percent                    | 0%         | 3.8%  | 1.9%  |

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    |
|  | Percent %                  | 84.6       | 57.7 | 71.1  |
| I was nervous but the treatment was carried out successfully ("slightly frightened") | Number                     | 3          | 3    | 6     |
|  | Percent %                  | 11.5       | 11.5 | 11.5  |
| I was so frightened and nervous that treatment was difficult ("severely frightened") | Number                     | 1          | 8    | 9     |
|  | Percent %                  | 3.8        | 30.8 | 17.3  |
| Total  | Number                     | 26         | 26   | 52    |
|  | Percent %                  | 100        | 100  | 100   |

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].

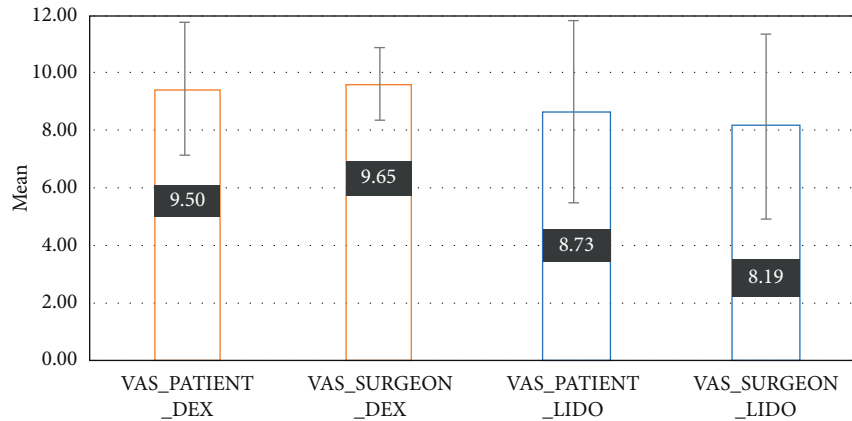


FIGURE 2: VAS scores of the patients and the surgeon.

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

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

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 palpal 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

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.<br>(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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### References

- [1] J. P. Shepherd and M. Brickley, "Surgical removal of third molars," *BMJ*, vol. 309, no. 6955, pp. 620-621, 1994.
- [2] A. Arntz, L. Dreessen, and P. De Jong, "The influence of anxiety on pain: attentional and attributional mediators," *Pain*, vol. 56, no. 3, 1994.
- [3] G. W. Bell and P. J. Kelly, "A study of anxiety, and midazolam-induced amnesia in patients having lower third molar teeth extracted," *British Journal of Oral and Maxillofacial Surgery*, vol. 38, no. 6, pp. 596-602, 2000.
- [4] H.-O. Kazancioglu, A.-S. Dahhan, and A.-H. Acar, "How could multimedia information about dental implant surgery effects patients' anxiety level?" *Medicina Oral, Patología Oral y Cirugía Bucal*, vol. 22, no. 1, pp. e102-e107, 2017.
- [5] L. Dou, M. M. Vanschaayk, Y. Zhang, X. Fu, P. Ji, and D. Yang, "The prevalence of dental anxiety and its association with pain and other variables among adult patients with irreversible pulpitis," *BMC Oral Health*, vol. 18, no. 1, p. 101, 2018.
- [6] G. Minervini, A. Romano, M. Petruzzi et al., "Oral-facial-digital syndrome (OFD): 31-year follow-up management and monitoring," *Journal of Biological Regulators & Homeostatic Agents*, vol. 32, no. 2, pp. 127-130, 2018.
- [7] G. Minervini, L. Fiorillo, D. Russo et al., "Prosthetic treatment in patients with temporomandibular disorders and orofacial pain and/or bruxism: a review of the literature," *Prosthesis*, vol. 4, pp. 253-262, 2022.
- [8] R. De Stefano, A. Bruno, M. R. Muscatello, C. Cedro, G. Cervino, and L. Fiorillo, "Fear, and anxiety managing methods during dental treatments: a systematic review of recent data," *Minerva Stomatologica*, vol. 68, no. 6, pp. 317-331, 2019.
- [9] M. Seto, H. Furuta, Y. Sakamoto, and T. Kikuta, "Sedative methods used during extraction of wisdom teeth in patients with a high level of dental anxiety," *J Korean Assoc Oral Maxillofac Surg*, vol. 37, no. 3, p. 241, 2011.
- [10] K. Ouchi and K. Sugiyama, "DEX dose dependently enhances the local anesthetic action of lidocaine in inferior alveolar nerve block: a randomized double-blind study," *Regional Anesthesia & Pain Medicine*, vol. 41, no. 3, 2016.
- [11] N. Bao, K. Shi, Y. Wu et al., "Dexmedetomidine prolongs the duration of local anesthetics when used as an adjuvant through both perineural and systemic mechanisms: a prospective randomized double-blinded trial," *BMC Anesthesiology*, vol. 22, no. 1, p. 176, 2022.
- [12] T. M. Freitas, C. David, A. G. Almeida, F. J. Pinto, J. Costa, and D. Caldeira, "Cardiovascular and respiratory safety of sedation strategies used in transesophageal echocardiography: a systematic review incorporating network meta-analysis," *Journal of Cardiothoracic and Vascular Anesthesia*, vol. S1053-0770(22)00516-X, 2022.
- [13] M. Shukry and J. A. Miller, "Update on dexmedetomidine: use in nonintubated patients requiring sedation for surgical procedures," *Therapeutics and Clinical Risk Management*, vol. 6, pp. 111-121, 2010.
- [14] C. Kaya, N. O. Celebi, S. Debbag, O. Canbay, and O. Onal, "Comparison of dexmedetomidine and remifentanyl infusion in geriatric patients undergoing outpatient cataract surgery: a prospective, randomized, and blinded study," *Medical Gas Research*, vol. 12, no. 4, pp. 146-152, 2022.
- [15] X. Zhou, W. Li, H. Wang, C. Li, and H. Jiang, "Safety and efficacy of ketamine-fentanyl-dexmedetomidine-induced anesthesia and analgesia in neonatal and aged rats," *Dose-Response*, vol. 19, no. 4, Article ID 155932582110639, 2021.
- [16] G. M. Keating, "Dexmedetomidine: a review of its use for sedation in the intensive care setting," *Drugs*, vol. 75, no. 10, pp. 1119-1130, 2015.
- [17] X. Guo, Y. Xue, W. Ji, J. Liang, and Z. Qingshi, "Effects of administration of  $\alpha(2)$  adrenergic receptor agonist into psoas major muscle on inflammatory pain induced by injection of complete Freund's adjuvant in rats," *Molecular Pain*, vol. 18, Article ID 174480692211078, 2022.
- [18] C. W. Cheung, C. L. A. Ying, W. K. Chiu, G. T. C. Wong, K. F. J. Ng, and M. G. Irwin, "A comparison of dexmedetomidine and midazolam for sedation in third molar surgery\*," *Anaesthesia*, vol. 62, no. 11, pp. 1132-1138, 2007.
- [19] A. Arhami Dolatabadi, E. Memary, M. Shojae, and H. Kamalifard, "Dexmedetomidine-fentanyl versus midazolam-fentanyl in pain management of distal radius fractures reduction; a randomized clinical trial," *Emerg (Tehran, Iran)*, vol. 6, no. 1, p. e10, 2018.

- [20] G. M. Obayah, A. Refaie, O. Aboushanab, N. Ibraheem, and M. Abdelazees, "Addition of DEX to bupivacaine for greater palatine nerve block prolongs postoperative analgesia after cleft palate repair," *European Journal of Anaesthesiology*, vol. 27, no. 3, 2010.
- [21] G. Fritsch, T. Danninger, K. Allerberger, A. Tsodikov, T. K. Felder, M. Kapeller et al., "DEX added to ropivacaine extends the duration of interscalene brachial plexus blocks for elective shoulder surgery when compared with ropivacaine alone: a single-center, prospective, triple-blind, randomized controlled trial," *Regional Anesthesia & Pain Medicine*, vol. 39, no. 1, 2014.
- [22] C. M. Brummett, E. K. Hong, A. M. Janda, F. S. Amodeo, and R. Lydic, "perineural DEX added to ropivacaine for sciatic nerve block in rats prolongs the duration of analgesia by blocking the hyperpolarization-activated cation current," *Anesthesiology*, vol. 115, 2011.
- [23] N. Nooh, S. A. Sheta, W. A. Abdullah, and A. A. Abdelhalim, "Intranasal atomized dexmedetomidine for sedation during third molar extraction," *International Journal of Oral and Maxillofacial Surgery*, vol. 42, no. 7, pp. 857–862, 2013.
- [24] T. W. V. Fan, L. K. Ti, and I. Islam, "Comparison of DEX and midazolam for conscious sedation in dental surgery monitored by bispectral index," *British Journal of Oral and Maxillofacial Surgery*, vol. 51, 2013.
- [25] T. Yoshitomi, A. Kohjitani, S. Maeda, H. Higuchi, M. Shimada, and T. Miyawaki, "DEX enhances the local anesthetic action of lidocaine via an alpha-2a adrenoceptor," *Anesthesia & Analgesia*, vol. 107, 2008.
- [26] G. Troiano, L. Laino, M. Cicciù et al., "Comparison of two routes of administration of dexamethasone to reduce the postoperative sequelae after third molar surgery: a systematic review and meta-analysis," *The Open Dentistry Journal*, vol. 12, no. 1, pp. 181–188, 2018.
- [27] S. Liu, Y. Wang, Y. Zhu, T. Yu, and H. Zhao, "Safety and sedative effect of intranasal dexmedetomidine in mandibular third molar surgery: a systematic review and meta-analysis," *Drug Design, Development and Therapy*, vol. 13, pp. 1301–1310, 2019.
- [28] R. D. Sanders, J. Xu, Y. Shu et al., "DEX attenuates isoflurane-induced neurocognitive impairment in neonatal rats," *Anesthesiology*, vol. 110, 2009.
- [29] B. GURSOYTRAK, O. KOCATURK, M. KOPARAL, and B. GULSUN, "Assessment of effect of submucosal injection of dexmedetomidine on postoperative symptoms," *Journal of Oral and Maxillofacial Surgery*, vol. 78, no. 3, pp. 366–371, 2020.
- [30] L. I. Cortinez, Y.-W. Hsu, S. T. Sum-Ping et al., "Dexmedetomidine pharmacodynamics: Part II," *Anesthesiology*, vol. 101, no. 5, pp. 1077–1083, 2004.
- [31] B. GURSOYTRAK, O. KOCATURK, M. KOPARAL, and B. GULSUN, "Comparison of dexmedetomidine and ketamine for managing postoperative symptoms after third-molar surgery," *Journal of Oral and Maxillofacial Surgery*, vol. 79, no. 3, pp. 532–536, 2021.
- [32] C. W. Cheung, K. F. J. Ng, J. Liu, M. Y. V. Yuen, M. H. A. Ho, and M. G. Irwin, "Analgesic and sedative effects of intranasal dexmedetomidine in third molar surgery under local anaesthesia," *British Journal of Anaesthesia*, vol. 107, no. 3, pp. 430–437, 2011.
- [33] V. M. Yuen, T. W. Hui, M. G. Irwin, T.-J. Yao, G. L. Wong, and M. K. Yuen, "Original article: optimal timing for the administration of intranasal dexmedetomidine for premedication in children," *Anaesthesia*, vol. 65, no. 9, pp. 922–929, 2010.
- [34] Y. Tonooka and K. Sunada, "Dexmedetomidine enhances the pulpal anesthetic effect of lidocaine: a pilot study," *Anesthesia Progress*, vol. 65, no. 1, pp. 38–43, 2018.
- [35] J. Alizargar, M. Etemadi Sh, N. Kaviani et al., "Injection of lidocaine alone versus lidocaine plus dexmedetomidine in impacted third molar extraction surgery, a double-blind randomized control trial for postoperative pain evaluation," *Pain Research and Management*, vol. 2021, Article ID 6623792, 6 pages, 2021.
- [36] V. Singh, M. Thepra, S. Kirti, P. Kumar, and K. Priya, "Dexmedetomidine as an additive to local anesthesia: a step to development in dentistry," *Journal of Oral and Maxillofacial Surgery*, vol. 76, no. 10, 2018.
- [37] Y. Ustün, M. Gündüz, O. Erdoğan, and M. E. Benlidayi, "Dexmedetomidine versus midazolam in outpatient third molar surgery," *Journal of Oral and Maxillofacial Surgery*, vol. 64, no. 9, pp. 1353–1358, 2006.