



Anesthetic Success Rate of Inferior Alveolar Nerve Block for Mandibular Molars with Symptomatic Irreversible Pulpitis in Women Taking Antidepressants

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Article Type: Original Article

Received: 18 Nov 2021

Revised: 08 Jan 2022

Accepted: 12 Feb 2022

Doi: 10.22037/iej.v17i2.34921

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Introduction: This study sought to evaluate the success rate of inferior alveolar nerve block (IANB) during the endodontic management of mandibular molars with symptomatic irreversible pulpitis in women taking selective serotonin reuptake inhibitor (SSRI) antidepressants. **Materials and Methods:** Ninety adult female patients over 18 years of age who were diagnosed with symptomatic irreversible pulpitis of a mandibular molar were recruited in this study. The patients were equally assigned to SSRI user group (including citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline), who had taken an SSRI, and non-SSRI user group, who had not taken any SSRIs at all. All patients in both groups received 3.6 mL of 2% lidocaine with 1:80,000 epinephrine using conventional IANB injection. Access cavity was prepared 15 min after the injection. Lip numbness was necessary for all patients. Success was determined as no or mild pain upon access cavity preparation and/or instrumentation based on the Heft-Parker visual analog scale recordings. Data were analyzed using the chi-square test, Mann-Whitney U test, and *t*-test. **Results:** The success rate was 55.6% for SSRI users and 44.4% for non-SSRI users, and no statistically significant difference was observed between the two groups ($\chi^2=1.1$, $P=0.292$). **Conclusions:** Based on the results of this study, taking SSRI antidepressants could not affect the anesthetic success rate of IANB for mandibular molars with symptomatic irreversible pulpitis in women.

Keywords: Anesthesia; Antidepressants; Inferior Alveolar Nerve Block; Pulpitis; Selective Serotonin Reuptake Inhibitors

Introduction

The inferior alveolar nerve block (IANB) is the most routinely used technique to achieve local anesthesia in mandibular molars [1]. However, clinical studies have reported a failure rate of 44%-81% for the IANB in mandibular molars with irreversible pulpitis [2-4]. Some reasons have been reported for the local anesthetic failure, including anatomic causes, acute tachyphylaxis, inflammation, local tissue acidosis and central sensitization [5, 6]. In addition, as a prominent feature of depression, anxiety is considered a potential cause of IANB failure in patients who report pain after receiving local anesthetics [6].

Anxiety and depression have been evaluated in adults and commonly women show more prevalence than men [7]. Depression occurs when small amounts of serotonin neurotransmitter is available in nerve synaptic spaces. As a mediator of endogenous analgesic mechanisms in descending pain pathways, serotonin facilitates nerve signal transmission, mood regulation, sleep and a variety of brain functions [8].

Selective serotonin reuptake inhibitors (SSRIs) are believed to be the first line of treatment for anxiety and depressive disorders as a relatively new generation of antidepressants [9]. SSRIs inhibit the reuptake of serotonin (5-hydroxytryptamine or 5-HT) from synaptic spaces into the presynaptic cells increasing the



concentration of serotonin in the synaptic space and stimulate serotonergic functions within the central nervous system. SSRIs include citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline and are the most widely prescribed class of antidepressants around the world. **Table 1** presents the adult therapeutic dosages for SSRIs [10]. Benzodiazepines have virtually been replaced by SSRIs worldwide [11].

Given the impact of anxiety on the failure of IANB [6], it is hypothesized that anti-anxiety medications may increase the success rate of IANB. However, a review on literature provides conflicting results regarding the effects of a single dose of these medications such as benzodiazepines, on the success of IANB in patients without anxiety disorder [12-14]. To the best of our knowledge the success rate of IANB in patients with anxiety disorder treated with SSRIs remains unexplored. However, it would be appropriate to evaluate the effect of taking SSRIs on the success of the IANB in patients with anxiety disorder. Therefore, this study aimed to evaluate the anesthetic success rate of the IANB for mandibular molars with symptomatic irreversible pulpitis in women treated with SSRI antidepressants. The null hypothesis was that taking SSRIs would not increase the anesthetic success rate of the IANB for mandibular molars with symptomatic irreversible pulpitis in women.

Material and Methods

In this study, ninety adult female patients with an age range of 20-54 were recruited and assigned to SSRI and non-SSRI user groups. The SSRI users consisted of 45 women taking SSRIs referred from a psychiatric center to the "Clinic of the Endodontic Department, Isfahan University of Medical Sciences" for endodontic treatment. The patients took SSRIs at their therapeutic dose (**Table 1**) under the supervision of a psychiatrist to control their anxiety disorder. The therapeutic dose had already adjusted for each patient by the psychiatrist. The SSRIs used in this group were citalopram ($n=20$), fluoxetine ($n=12$), escitalopram ($n=7$), paroxetine ($n=4$), and sertraline

($n=2$). Similarly, the non-SSRI users consisted of 45 women who were not taking and had not taken SSRIs at all and were referred to the same dental clinic for endodontic treatment.

The inclusion criteria for the study were (i) women over 18 years, (ii) absence of any periapical radiolucency on intraoral radiographs (*i.e.* periapical radiography) except for widened periodontal ligament with intact lamina dura, (iii) active pain [moderate, or severe pain according to the Heft-Parker visual analog scale (HP-VAS)]. in a mandibular molar, (iv) prolonged sensibility to the cold test using the corresponding spray (Endo-Frost; Roeko, Coltene Whaledent, Langenau, Germany) [4], (v) bleeding at access cavity preparation, (vi) taking any type of SSRI (citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline) at its usual therapeutic dose (**Table 1**) for at least six weeks before the study (for the SSRI user group), and (vii) the ability to understand the use of pain scales (HP-VAS). However, the exclusion criteria for the study included (a) being allergic to local anesthetics, (b) pregnancy, (c) taking any medication that might influence pain assessment (except SSRI medications for the SSRI user group); such as analgesics, sedatives, anti-anxiety drugs and antidepressants [6, 14], (d) a history of significant/severe medical condition (except for Anxiety for the SSRI user group), (e) presence of active pathosis at the injection site and (f) inability to provide informed consent.

Study protocol was approved by the Ethics Committee of the Isfahan University of Medical Sciences (no: 394867) and registered in ClinicalTrials.gov (no: NCT02884596). Furthermore, the study was undertaken according to the ethical principles of the World Medical Association Declaration of Helsinki. All patients completed a written informed consent form to participate in the study.

The patients provided their medical histories to a designated dental assistant, who assigned the patients to a single operator for the IANB injection. The operator was blinded to the groups. The patients' dental anxiety was determined by the "Corah Dental Anxiety Scale" [15]. It is a reliable tool for use in dental offices or research projects. This scale is a simple four question survey with five possible answers. Each answer has a score, and the total score shows the dentist how anxious the patient is [15, 16]. The patients recorded their severity of initial pain using the Heft-Parker visual analog scale (HP-VAS). This scale is a 170-mm marked line divided into four sections with specific terms describing each pain level. No, mild, moderate and severe pain levels are indicated by 0-mm, 1-54-mm, 55-113-mm, and 114-170-mm divisions, respectively [17].

Before each injection, the mucosa was dried. Then, a topical anesthetic agent (20% benzocaine; Ultradent Products Inc,

Table 1. Usual adult therapeutic dosages for SSRI drugs

SSRIs	Dosage (mg/day)
Citalopram	20-60
Escitalopram	10-30
Fluoxetine	20-60
Fluvoxamine	100-300
Paroxetine	20-60
Sertraline	50-200

*SSRI=selective serotonin reuptake inhibitor

South Jordan, UT, USA) was applied to the injection site with a cotton tip applicator and left in place for 60 sec. Two 1.8-mL cartridges of 2% lidocaine with 1:80,000 epinephrine (Persocaine-E; Daroupakhsh, Tehran, Iran) were administered to each patient via the standard IANB technique. All injections were administered using a standard dental injection syringe and a 27-G 31-mm needle (CK Dental, Kor-Kyungji-do, Korea). Profound lip numbness was set as a criterion for acceptable anesthesia technique. If profound lip numbness was not achieved within 15 min, IANB was considered missed, and the patient was excluded from the study. Two patients were excluded from the study due to the lack of lip numbness and were replaced by 2 other patients. A single operator, who was blinded to the groups, carried out the injection procedures.

Fifteen minutes after the primary injection and achieving profound lip numbness, each tooth was isolated using rubber dam and access cavity preparation was initiated. The operator who prepared the access cavity was also blinded to the groups. The same operator performing the injections instructed the patients to rate any pain experienced during endodontic access preparation and/or instrumentation. If a patient felt pain, the treatment was immediately suspended and the patient recorded the pain intensity via HP-VAS. No or mild pain (HP-VAS ≤ 54 mm) was defined as successful anesthesia, whereas moderate or severe pain (HP-VAS > 54 mm) was defined as the failure of IANB anesthesia. Supplemental local anesthesia was administered for patients reporting moderate or severe pain, and the endodontic treatment continued.

Statistical analysis

With a sample size of 45 patients per group, the statistical test would detect a difference of 20% between the two groups with a two-sided alpha risk of 0.05 and a power of 80%. Data were analyzed by SPSS version 20 (IBM Corporation, Armonk, NY, USA). Comparison between the SSRI and non-SSRI user groups for the success rate of the IANB injection was carried out using the chi-square test. The initial pain and the anxiety were analyzed by the Mann-Whitney U test. Age was analyzed by *t*-test. Statistical significance was set at $P < 0.05$.

Table 2. Baseline variables for SSRI and Non-SSRI user groups

Variable	SSRI Users	Non-SSRI Users	P-value*
Total subjects (all women)	45	45	
Age (year)	23-54	20-51	0.331
Initial pain [†]	112 (21.9)	110 (19.0)	0.651
Corah anxiety scale [‡]	12.3 (2.4)	11.4 (2.9)	0.134

*SSRI=selective serotonin reuptake inhibitor; [†]There were no significant differences between the two groups ($P > 0.05$); [‡]Mean (standard deviation)

Results

Ninety adult women, with an age range of 20-54 and a mean of 37 ± 8 years, were recruited in this study. Tables 2 and 3 present the baseline variables and distribution of teeth for SSRI and non-SSRI user groups. There was no significant difference between the two groups in the success rates of the anesthesia ($\chi^2 = 1.1$, $P = 0.292$).

Discussion

The results of the current study showed that taking SSRI antidepressants did not affect the anesthetic efficacy of IANB for mandibular molars with irreversible pulpitis in women. Only women were included in this study because the prevalence of anxiety is much higher in women than in men, which might be due to social or biological reasons [8, 18]. In addition, when compared with men, women have lower pain thresholds, greater ability to describe pain and present a higher incidence of clinical conditions that cause pain [19]. Moreover, the frequency of endodontic treatment is higher in women than in men [20]. In this study, SSRIs were used among other antidepressants because they are the most widely used class of antidepressants worldwide [21]. Patients taking any type of SSRIs were included because the mechanism of action for this specific group of antidepressants is similar and is different with other group of antidepressants [11]. Moreover, only patients who had begun taking an SSRI at its therapeutic dose for at least six weeks before the study was included because there is a delay in the therapeutic response to SSRIs and a period of 3-6 weeks is necessary for their antidepressive effects to appear [22, 23]. However, the maximum time for taking SSRIs was not considered a criterion.

There were no significant differences between the SSRI and non-SSRI user groups in the efficacy of the three initial variables (age, initial pain and anxiety), making the effects of the variables minimal between the two groups. Moreover, all the teeth had (i) a lingering response (more than 1 to 2 sec) to the cold test, (ii) vital coronal pulp tissue during access cavity preparation, and (iii) initial moderate or severe pain on HP-VAS, which showed they had symptomatic irreversible pulpitis [2].

Table 3. Distribution of teeth in SSRI and Non-SSRI user groups

Tooth	SSRI Users	Non-SSRI Users
First molar	23 (51%)	24 (53%)
Second molar	20 (44%)	21 (47%)
Third molar	2 (4%)	0 (0%)

*SSRI=selective serotonin reuptake inhibitor

“Corah’s Dental Anxiety Scale” was used in the present study because it is a simple and reliable scale to assess dental anxiety [18].

The Corah’s Dental Anxiety Scale were 12.3 ± 2.4 and 11.4 ± 2.9 in SSRI and non-SSRI user groups, respectively, which shows the anxiety was not different between the groups. However, according to the Corah’s Dental Anxiety Scale, these numbers categorized as moderate anxiety, which show all patients have a moderate anxiety at the beginning of the study. Because patients had toothache, moderate anxiety was predictable for them at baseline.

The success of IANB was determined by measuring pain scores during access cavity preparation and/or initial file placement into the root canals using the HP-VAS; however, electric pulp test was not performed. This was based on the findings of Nusstein *et al.* [24], who used an electric pulp tester to measure pain intensity in teeth with irreversible pulpitis. They reported that after initial administration of anesthesia, 42% of patients with a negative response to electric pulp testing still had pain during endodontic access and consequently, needed another injection. Furthermore, the present study exhibited a success rate of 44.4% for IANB in the non-SSRI user group, which was higher than those reported in previous studies by Kreimer *et al.* [25], Fullmer *et al.* [26] and Oleson *et al.* [27]. The differences in results might be attributed to the differences in the study populations, operators, designs, and volumes of anesthetic solutions.

The monoamine hypothesis has been the prominent hypothesis of depression over the last several decades, suggesting that an imbalance in monoaminergic neurotransmission causes depression. It consists of the catecholamine and serotonin hypotheses. At its simplest, the serotonin hypotheses proposes that diminished activity of serotonin pathways plays a causal role in the pathophysiology of depression and abnormal decrease in the levels of serotonin results in clinical symptoms and signs of depression and anxiety [23, 28]. SSRIs directly bind to the serotonin-transporter protein and inhibit serotonin reuptake, making them effective drugs for the treatment of anxiety, which are considered the potential factors for the failure of IANB [6]. Moreover, the treatment of depression and anxiety is defined as the prevention of central sensitization [29]. In addition, SSRIs have little anti-inflammatory [29] and analgesic effects [30]. Considering the effect of anxiety on the failure of IANB [4], it was theorized that the success of IANB would be better in women taking SSRIs. Although the results of the present study showed that the success rate of IANB was a little higher in the SSRI user group than that in the non-SSRI user group, the difference was not significant.

Conclusions

Under the study conditions, taking SSRIs could not affect the anesthetic success of IANB in mandibular molars with irreversible pulpitis in women. Further clinical studies in this area in both men and women are recommended.

Acknowledgments

This study was supported by Isfahan University of Medical Sciences Research Grant# 394867. The authors deny any conflicts of interest.

Conflict of Interest: ‘None declared’.

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Please cite this paper as: Khademi A, Memarzadeh B, Saatchi M, Aggarwal V, Shafiee M, Minaiyan M, Omranifard V. Anesthetic Success Rate of Inferior Alveolar Nerve Block for Mandibular Molars with Symptomatic Irreversible Pulpitis in Women Taking Antidepressants. *Iran Endod J*. 2022;17(2): 52-6. Doi: 10.22037/iej.v17i2.34921.

