



Research Article

EVALUATION OF THE ANESTHETIC EFFICACY AND PAIN CONTROL OF BUFFERED 4% ARTICAINE IN MANDIBULAR MOLAR TOOTH PREPARATION

©Göknil ALKAN DEMETOĞLU*, ©Hüseyin ŞEKER¹

¹Department of Prosthodontics, Faculty of Dentistry, Adnan Menderes University, Aydın, TURKIYE

*Correspondence: goknil.alkan@adu.edu.tr

ABSTRACT

Objective: This study aimed to evaluate whether buccal infiltration anesthesia with sodium bicarbonate-buffered articaine provides comparable or superior anesthetic efficacy to traditional inferior alveolar nerve block (IANB) in mandibular molar preparations, while minimizing complications and enhancing patient comfort.

Materials and Methods: A randomized clinical trial was conducted with 75 healthy adult participants requiring mandibular molar prosthetic treatment. Patients were randomly assigned to three groups: Group M: IANB with 4% articaine + 1:100,000 epinephrine; Group I: Buccal infiltration with the same articaine formulation; Group SB: Buffered buccal infiltration (2% articaine + 0.84% sodium bicarbonate + 1:200,000 epinephrine). Pain was measured using Visual Analog Scale (VAS1: during treatment, VAS2: next day), and heart rate was monitored before and during the procedure.

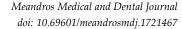
Results: VAS1 scores were significantly higher in Group I (p < .001), indicating more pain during treatment. Group SB had significantly lower VAS2 scores, reflecting reduced postoperative discomfort. No significant differences in heart rate were found across groups.

Conclusions: Buffered articaine with sodium bicarbonate used for buccal infiltration in mandibular molars showed anesthetic efficacy comparable to IANB, with less pain and fewer complications. This approach may serve as a safer and more comfortable alternative to nerve block anesthesia in routine prosthetic procedures. **Keywords:** Buffered articaine, buccal infiltration, inferior alveolar nerve block, mandibular molars, pain control

Received: 17 June 2025 Revised: 15 July 2025 Accepted: 24 July 2025 Published: 22 September 2025



Copyright: © 2025 by the authors. Published by Aydın Adnan Menderes University, Faculty of Medicine and Faculty of Dentistry. This article is openly accessible under the Creative Commons Attribution-NonCommercial





INTRODUCTION

Although infiltration anesthesia is commonly used for dental procedures in the maxilla, it may be insufficient for posterior mandibular procedures due to the dense cortical bone structure of the mandible. The inferior alveolar nerve block (IANB) represents the most commonly employed anesthetic technique for achieving mandibular molar anesthesia during dental procedures. complications such as pain, trismus, facial nerve paresis, and lingual nerve injury may ocur (1). Moreover fear of pain associated with dental injections is a primary factor contributing to patients avoiding dental visits and canceling scheduled appointments. Effective management of pain and related anxiety is essential during the administration of local anesthesia. Research indicates that 50% of adult patients fail to attend their dental appointments due to pain-related anxiety (2,3).

The acidic pH of local anesthetic (LA) solutions enhances their solubility and ensures prolonged stability (4). Research has explored the effect of increasing the pH of LAs on reducing injection pain by buffering these solutions with sodium bicarbonate (5-7). It has been proposed that alkalizing LAs with sodium bicarbonate not only minimizes injection discomfort but also accelerates the onset of anesthesia. This effect is attributed to an increase in the dissociation rate of the anesthetic molecules, subsequently enhancing the concentration of the nonionized, active form that can efficiently penetrate the nerve membrane and reach the intraneuronal region (5-7).

The majority of studies on the buffering of LA solutions in dentistry focus on lidocaine and the IANB technique (8). In contrast, articaine—one of the most commonly used anesthetics in dental practice-differs significantly from other amide LAs due to its unique thiophene ring structure, which has not been extensively investigated. The distinct physicochemical characteristics of articaine, including enhanced lipid solubility and strong protein binding, are associated with its superior anesthetic potency (9,10). Commercial articaine formulations for dental use typically contain epinephrine at concentrations of 1:100,000 or 1:200,000 and are maintained at a low pH for the reasons previously discussed. This prompts a critical inquiry: Could buffering improve the anesthetic efficacy of articaine? Enhancing the diffusion characteristics of buffered articaine may present a promising alternative for achieving effective infiltration anesthesia in mandibular molars, potentially minimizing the reliance on IANB (11,12).

Most studies about buffered local anesthetics in the literature have focused on the anesthesia of teeth that will undergo surgical and endodontic treatment(3,8-11). In most of these studies, the buffering effect of bicarbonate on the acidic environment has been emphasized since there is infection in the teeth. As far as the researchers know, this study is the first to investigate the effectiveness of bicarbonate for prosthetic purposes. In addition, the aim of this study is to observe the effectiveness of infiltration anesthesia in the lower jaw by adding bicarbonate and to increase the comfort of the patient and the physician by performing infiltration anesthesia with less risk of complications. This study hypothesizes that bicarbonatebuffered buccal infiltration anesthesia (BBIA) provides comparable anesthetic efficacy to traditional mandibular block anesthesia for mandibular molars during tooth preparation.

MATERIALS AND METHODS

This randomized clinical study was designed to compare the efficacy of three different anesthetic techniques in patients undergoing mandibular molar preparation. The study protocol was approved by the institutional ethics committee and Turkish Medicines and Medical Devices Agency (TITCK) and written informed consent was obtained from all participants prior to their inclusion in the study.

The required sample size was determined based on a previous report (13) by using G*Power analysis (G*Power, v. 3.1.9.2, Düsseldorf, Germany) with a large effect size of 0.4. Seventy-five healthy subjects were included in this study. The inclusion criteria were:

- 1. Healthy patients of both genders over the age of 18 years.
- 2. Periodontally healthy, caries-free and vital lower molars with crown or bridge indication

The exclusion criteria were:

- 1. Subjects taking any medication such as analgesics, narcotics, sedatives, or antidepressants or alcohol consumption that may affect anesthetic assessment.
- 2. Female patients during pregnancy or lactation
- 3. Third molars or previously prepared teeth

Patients were informed about study and randomly divided into three groups;

Group 1 (M): Mandibular nerve block anesthesia with 4% articaine containing 1:100,000 epinephrine

Group 2 (I): Buccal infiltrative anesthesia (BIA) with 4% articaine containing 1:100,000 epinephrine



Group 3 (SB): Buccal infiltrative anesthesia with a buffered formulation consisting of 4% articaine with 1:100,000 epinephrine mixed with 1.68% sodium bicarbonate.

All anesthetic solutions were prepared by the same operator (H.Ş.) immediately prior to tooth preparation under sterile conditions. The buffered solution was prepared by discarding 0.9 mL of the original articaine solution and replacing it with 0.9 mL of the diluted sodium bicarbonate, resulting in a final solution of 2% articaine with 1:200,000 epinephrine and 0.84% sodium bicarbonate. Before administering local anesthesia, each patient's baseline pulse rate was recorded using a fingertip pulse oximeter (P1). It was placed on the right index finger of the patient. Anesthesia was then performed according to the group assignment, and tooth preparation was initiated approximately five minutes later. After the start of the preparation, a second pulse rate measurement was taken to assess changes possibly associated with pain or discomfort during the procedure (P2).

Upon completion of the procedure, patients were asked to rate the intensity of pain experienced during the intervention using a Visual Analog Scale (VAS [VAS1]). Additionally, patients were recalled the following day for placement of the provisional restoration, during which they were again asked to rate any delayed postoperative pain using the VAS (VAS2). The VAS scale ranges from 0 to 10. 0 represents no pain, while 10 represents the worst possible pain.

All injections and tooth preparations were applied by the same experienced clinician (G.A.D.). The injection rate was maintained at approximately 1 mL/min, with using the 26-gauge needle in accordance with clinical guidelines. In addition, a double-blind approach was adopted, meaning neither the patient nor the clinician knew whether sodium bicarbonate had been added to the anaesthetic solution.

RESULTS

Seventy-five participants (39 women and 36 men) aged between 18 and 76 years (mean: 48.83 years) were included in the study, Table 1 lists the age and gender information of the groups.

Table 1. Age and gender information of the groups

	Age (Mean \pm SD)	Gender (Female/Male)
M	49.56 ± 14.46	14 (56%) / 11 (44%)
I	53.36 ± 16.43	14 (56%) / 11 (44%)
SB	43.56 ± 14.82	11 (44%) / 14 (56%)

Table 2 shows the mean VAS1 and VAS2 scores for each group. VAS1 scores were highest in the I group (p < .001). The difference between SB and M was non-significant (p = .230). For VAS2, the M and SB groups had the highest and lowest scores, respectively (p < .05).

Table 2. Mean ± SD VAS scores of the group values

	VAS1	VAS2
M	0.96 ± 0.98 a	3.92 ± 2.16 c
I	4.72 ± 2.59 b	1.60 ± 1.26 b
SB	1.72 ± 1.28 a	0.64 ± 0.81 a

The mean heart rate before and during tooth preparation is listed in Table 3. No statistically significant differences in heart rate were observed between the groups.

Table 3. Mean ± SD heart rate before and during tooth preparation

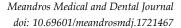
	P1	P2
M	76.72 ± 5.59 a	77.44 ± 5.77 a
I	78.16 ± 9.77 a	78.80 ± 8.73 a
SB	77.68 ± 7.98 a	78.16 ± 7.90 a

DISCUSSION

This study tested the hypothesis that provides comparable anesthetic efficacy to the conventional mandibular block technique for mandibular molars during tooth preparation, and the findings support this hypothesis by demonstrating that BBIA is a clinically effective and patient-friendly alternative.

Oral anesthesia is frequently associated with pain, primarily attributed to the acidic nature of anesthetic solutions (13). The concept of alkalinizing local anesthetics by adding sodium bicarbonate was first introduced by Louis Bignon in 1892 (14).

The reduction in pain associated with the infiltration of buffered local anesthetics may be attributed to the elevation of the solution's pH toward the physiological range (7.0–7.4), thereby minimizing tissue irritation caused by more acidic formulations (15). In a study by Gupta et al., the mean pain score on the visual analog scale (VAS) was reported as 3.4 for non-buffered anesthetics (NBA) and 0.44 for buffered formulations (16). Similarly, Arora et al. demonstrated a statistically significant difference in injection pain between buffered and NBA groups (P = 0.025) (17). Christoph et al. reported a highly significant reduction in pain (P < 0.000001), with NBA anesthesia being 2.8 times more painful than its buffered counterpart (18).





Moreover, Bunke et al. and Senthoor et al. both observed a significant reduction in pain upon administration of buffered local anesthetics (P < 0.05 and P < 0.1, respectively) (19,20). According to Kattan et al., buffering increases the likelihood of achieving successful anesthesia by 2.29 times (15). Gorrela et al concluded that buffered anesthetics not only reduce injection pain but also lead to faster onset and prolonged duration of action (15).

In the present study, pain experienced during tooth preparation was evaluated using a visual analog scale (VAS). The mean VAS score was 1.72 in the Group SB, 4.72 in the Group I, and 0.9 in Group M. While no statistically significant difference was found between Group SB and Group M, the Group I demonstrated a significantly higher pain score, indicating a less effective pain control compared to the other two techniques. Saber et al. conducted a CBCT study analyzing the relationship between the roots of mandibular posterior teeth and surrounding anatomical structures (21). According to their findings, buccal bone thickness increased in the posterior direction, while the mandibular canal was found to be closer to the tooth roots. Notably, the highest buccal bone thickness was observed in the distal roots of second molars. However, despite this anatomical variation, our study did not reveal any significant differences between the first and second molars in any of the groups.

According to a systematic review conducted by Kattan et al., buffered local anesthetic solutions demonstrated superior efficacy compared to their non-buffered counterparts in providing anesthetic efficacy in both arches for teeth affected by pulpal pathology. The application of buffered anesthetics was linked to a 2.29fold increase in the probability of achieving successful anesthetic outcomes (22). In their study on mandibular posterior teeth with symptomatic irreversible pulpitis, the authors compared the anesthetic efficacy of buffered and non-buffered 2% lidocaine with 1:80,000 epinephrine. They found that buffering did not improve the success rate of the inferior alveolar nerve block in these patients (23). Saatchi et al. reported that a BIA with 0.7 mL of 8.4% sodium bicarbonate significantly increased the success rate of lidocaine-based inferior alveolar nerve blocks (IANBs) in mandibular first molars with symptomatic irreversible pulpitis (24).

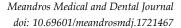
Previous studies involving bicarbonate-buffered local anesthetics have primarily focused on endodontic or surgical procedures (3,8-11,23,24). Consequently, it remains unclear whether the target teeth or surrounding tissues in those studies were affected by infection at the

time of anesthetic administration, which may influence anesthetic efficacy. In contrast, the present study specifically evaluated the effectiveness of bicarbonate-buffered BIA during tooth preparation in clinically healthy teeth and surrounding tissues. BBIA demonstrated significantly superior outcomes compared to its NBA counterpart. In a subset of patients (n=3) who received only NBA, insufficient anesthesia was achieved, resulting in intraoperative pain that necessitated additional mandibular nerve block administration. Although there was no statistically significant difference between Group SB and Group M in terms of anesthetic success, both groups achieved adequate anesthesia and reported low pain scores on the VAS scale.

Compared to lidocaine, articaine provides superior anesthetic outcomes when employed as a BIA for mandibular first molars (25). In their study involving asymptomatic subjects with normal pulps, Shurtz et al. found that buffered articaine offered no significant benefit over non-buffered articaine in terms of anesthetic success, onset time, or injection pain during primary BIA of the mandibular first molar (25).

BIA is suggested to enhance both the onset and efficacy of anesthesia (26,27). This improvement is attributed to the adjustment of the solution's pH closer to the anesthetic's pKa (26,27), which increases the proportion of the nonionized form available to penetrate the nerve sheath, thereby facilitating a faster onset and higher success rate (26). Consequently, buffering a 4% articaine solution may potentially improve the anesthetic effectiveness of BIA in the mandibular first molar regionIn alignment with these studies, the buffered articaine used in our study also demonstrated successful outcomes in achieving effective anesthesia.

Contrary to a previous study reporting that women experienced greater dentin hypersensitivity than men before and after tooth preparation (28), no significant gender-related differences were observed in the current study. Further studies are needed to explore this issue from a gender perspective. In the evaluation of post-anesthetic comfort using VAS2, a statistically significant difference was found among all groups. Patients in Group SB reported the highest comfort scores, whereas Group M was rated as the least comfortable. This may be attributed to the numbness of the tongue typically associated with mandibular anesthesia, which can negatively affect patient comfort.





In their study investigating ethnic differences in pain perception and the use of local anesthesia during tooth drilling, Moore et al. reported that Chinese dentists often refrained from administering anesthesia, as they described the drilling sensation as suan or "sourish," whereas injections were perceived as more "painful." In the present study, the bicarbonate-buffered group demonstrated the lowest scores in post-preparation discomfort assessment, indicating the highest level of patient comfort (29). While techniques such as the application of topical anesthetics prior to injection may help reduce the discomfort that patients often associate with the term "painful," this strategy may be less effective in mandibular anesthesia. This is likely due to the deeper tissue penetration required for mandibular nerve blocks, which may limit the efficacy of topicals in enhancing patient comfort during this procedure.

The correlation between pain and alterations in vital signs—specifically tachycardia and hypertension—is a well-established concept in internal medicine (30). In clinical rehabilitation settings, heart rate (HR) is often employed as an additional objective indicator of pain, based on the assumption that elevated pain levels are accompanied by an increase in HR (31).

Although studies examining the physiological response to pain in small groups of healthy individuals have reported an increase in HR following exposure to noxious stimuli (31), other studies have indicated that the relationship between pain and HR may vary among individuals (32). Dayoub et al. reported no correlation between selfreported pain scores and HR in patients presenting to the emergency department (30). Similarly, in the present study, where the relationship between pain and heart rate was also assessed, no statistically significant difference was found between the pre- and post-tooth preparation pulse measurements. In their study, Tousignant-Laflamme et al. (31) reported that experimentally induced pain in healthy individuals increased HR by 11%, and a significant correlation was found between HR and pain intensity (r = 0.50, P < .001). In the current study, however, HR measurements taken before and during the procedure did not reveal any statistically significant differences. This discrepancy may be attributed to methodological differences; whereas Tousignant et al. applied a continuous 2-minute painful stimulus to the participants' right hand, in the present study, the tooth preparation was halted as soon as the patient reported pain, resulting in a relatively shorter exposure to nociceptive stimuli. Furthermore, Tousignant et al. noted that a positive relationship between heart rate and pain perception was

found only in male participants, suggesting that heart rate may not be a clinically relevant indicator of pain perception in female patients. However, in the present study, no statistically significant difference was found between male and female participants in any of the groups. This study has certain limitations that should be acknowledged to better contextualize the findings. Firstly, the relatively small sample size may restrict the generalizability of the results to broader populations. Secondly, pain perception was assessed using the Visual Analog Scale (VAS), a subjective method that can be influenced by individual pain thresholds, anxiety levels, and prior dental experiences. Moreover, the short followup period and exclusion of patients with complex medical conditions may further limit the applicability of the conclusions. To address these issues, future studies with larger and more diverse patient populations are needed, ideally incorporating pharmacokinetic analyses to objectively evaluate the efficacy and safety of buffered anesthetic solutions.

CONCLUSION

Buffered buccal anesthesia during molar preparation represents a safe, straightforward, and clinically effective technique that can be routinely implemented to improve patient comfort and procedural experience. Due to its ease of administration and reduced risk of adverse effects compared to more invasive techniques such as mandibular nerve block, it presents a favorable alternative for both clinicians and patients in routine dental practice.

Acknowledgments

Not aplicaple.

Authorship contributions

Concept: GAD. Design: GAD, HŞ. Data collection or processing: GAD, HŞ. Analysis or Interpretation: GAD, HŞ. Literature search: GAD, HŞ. Writing: GAD, HŞ. Approval: GAD, HŞ.

Data availibity statement

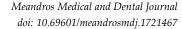
The data supporting this study's findings are available from the corresponding author upon reasonable request.

Declaration of competing interest

The authors declare no conflict of interest.

Ethics

The study was reviewed and approved by the Clinical Research Ethics Committee and of Aydın Adnan Menderes University and TITCK in the meeting held on





July 20, 2023, under protocol number 2023/17 and 24-AKD-54 respectively.

Funding

No funding was received for this manuscript.

REFERENCES

- 1-Ogle OE, Mahjoubi G. Local anesthesia: agents, techniques, and complications. Dent Clin North Am. 2012 Jan;56(1):133-48, ix.
- 2-Shahidi Bonjar AH. Syringe micro vibrator (SMV) a new device being introduced in dentistry to alleviate pain and anxiety of intraoral injections, and a comparative study with a similar device. Ann Surg Innov Res 2011;5:1.
- 3-Abou Agwa T, Sakka S, Al-Jundi A, Gazal G. Effect of adding sodium bicarbonate 8.4% to local anesthesia on pain during upper canine infiltration. Saudi J Anaesth. 2024 Oct Dec;18(4):504-508.
- 4- Becker DE, Reed KL. Local anesthetics: Review of pharmacological considerations. Anesth Prog 2012;59:90-101.
- 5-Davies RJ. Buffering the pain of local anaesthetics: a systematic review. Emerg Med (Fremantle). 2003;15(1): 81-
- 6. Guo J, Yin K, Roges R, Enciso R. Efficacy of sodium bicarbonate buffered versus non-buffered lidocaine with epinephrine in inferior alveolar nerve block: a metaanalysis. J Dent Anesth Pain Med. 2018;18:129-142.
- 7-Subburu, Nandini, Sama Venkata Naga Mounika, and Lakshmi Manasa Pappu. "Efficacy of 7.5% Sodium Bicarbonate Buffered 2% Lidocaine with 1: 80,000 Epinephrine in Exodontia." Sch J Dent Sci 4 (2023): 54-59.
- 8- Manta, K., Dabarakis, N., Lillis, T., & Fotopoulos, I. (2023). Anesthetic efficacy of buffered 4% articaine for mandibular first molar infiltration: A crossover clinical trial. Journal of dental anesthesia and pain medicine, 23(3), 135.
- 9-Almadhoon HW, Abuiriban RW, Almassri H. Efficacy of 4% articaine buccal infiltration versus inferior alveolar nerve block for mandibular molars with sympromatic irreversible pulpitis: a systematic review and meta-analysis. J Evid Based Dent Pract 2022; 22: 101712.
- 10- Miglani S, Ansari I, Patro S, Mohanty A, Mansoori S, Ahuja B, et al. Efficacy of 4% articaine vs 2% lidocaine in mandibular and maxillary block and infiltration anaesthesia in patients with irreversible pulpitis: a systematic review and meta-analysis. PeerJ 2021; 9: e12214. 11- Dhake P, Nagpal D, Chaudhari P, Lamba G, Hotwani K, Singh P. Buffered articaine: infiltration for primary molar extractions: a randomized controlled study. J Dent Anesth Pain Med 2022; 22: 387-94.

- 12- Amorim KS, Fontes VTS, Gercina AC, Groppo FC, Souza LM. Buffered 2% articaine versus non-buffered 4% articaine in maxillary infiltration: randomized clinical trial.Clin Oral Investig 2021; 25: 3527-33.
- 13- Gupta S, Kumar A, Sharma AK, Purohit J, Narula JS. "Sodium bicarbonate": An adjunct to painless palatal anesthesia. Oral Maxillofac Surg 2018;22:451 5.
- 14- Bignon A. On the anaesthetic properties of cocaine. Bull Gen Ther Med Chirurg Obstet Pharma 1892;122:170 2. 15. Gorrela H, Srujana T, Arthi S. Buffered versus Nonbuffered Local Anaesthesia in Minor Oral Surgery A Comparative Study. Ann Maxillofac Surg. 2024 Jan-Jun;14(1):15-20.
- 16- Arora G, Degala S, Dasukil S. Efficacy of buffered local anaesthetics in head and neck infections. Br J Oral Maxillofac Surg 2019;57:857 60.
- 17- Christoph RA, Buchanan L, Begalla K, Schwartz S. Pain reduction in local anesthetic administration through pH buffering. Ann Emerg Med 1988;17:117 20.
- 18- Bunke J, Sheikh R, Hult J, Malmsjö M. Buffered local anesthetics reduce injection pain and provide anesthesia for up to 5 hours. J Plast Reconstr Aesthet Surg 2018;71:1216 30.
- 19- Senthoor P, Janani K, Ravindran C. A prospective, randomized double blinded study to evaluate the efficacy of buffered local anesthetics in infected and inflamed pulp and periapical tissues. J Maxillofac Oral Surg 2020;19:246
- 20- Saber SE, Abu El Sadat S, Taha A, Nawar NN, Abdel Azim A. Anatomical Analysis of Mandibular Posterior Teeth using CBCT: An Endo-Surgical Perspective. Eur Endod J. 2021 Dec;6(3):264-270.
- 21- Kattan S, Lee SM, Hersh EV, Karabucak B. Do buffered local anesthetics provide more successful anesthesia than nonbuffered solutions in patients with pulpally involved teeth requiring dental therapy?: A systematic review. J Am Dent Assoc. 2019 Mar;150(3):165-177.
- 22- Saatchi M, Khademi A, Baghaei B, Noormohammadi H. Effect of sodium bicarbonate-buffered lidocaine on the success of inferior alveolar nerve block for teeth with symptomatic irreversible pulpitis: a prospective, randomized double-blind study. J Endod. 2015 Jan;41(1):33-5.
- 23- Saatchi M, Farhad AR, Shenasa N, Haghighi SK. Effect of Sodium Bicarbonate Buccal Infiltration on the Success of Inferior Alveolar Nerve Block in Mandibular First Molars with Symptomatic Irreversible Pulpitis: A Prospective, Randomized Double-blind Study. J Endod. 2016 Oct;42(10):1458-61.
- 24- Shurtz R, Nusstein J, Reader A, Drum M, Fowler S, Beck M. Buffered 4% Articaine as a Primary Buccal Infiltration of the Mandibular First Molar: A Prospective,



Randomized, Double-blind Study. J Endod. 2015 Sep;41(9):1403-7.

25- Whitcomb M, Drum M, Reader A, et. al. A prospective, randomized, double-blind study of the anesthetic efficacy of sodium bicarbonate buffered 2% lidocaine with 1:100,000 epinephrine in inferior alveolar nerve blocks. Anesth Prog 2010; 57: pp. 59-66.

26- Al-Sultan AF, Fathie WK, Hamid RS. A clinical evaluation on the alkalization of local anesthetic solution in periapical surgery. Al-Rafidain Dent J 2006; 6: pp. 71-77. 27- Yadav K, Sofat A, Gambhir RS, Galhotra V. Dentin hypersensitivity following tooth preparation: A clinical study in the spectrum of gender. J Nat Sci Biol Med. 2014 Jan;5(1):21-4.

28- Moore R, Brødsgaard I, Mao TK, Miller ML, Dworkin SF. Perceived need for local anesthesia in tooth drilling among Anglo-Americans, Chinese, and Scandinavians. Anesth Prog. 1998 Winter;45(1):22-8. PMID: 9790006; PMCID: PMC2148943.

29- Dayoub EJ, Jena AB. Does Pain Lead to Tachycardia? Revisiting the Association Between Self-reported Pain and Heart Rate in a National Sample of Urgent Emergency Department Visits. Mayo Clin Proc. 2015 Aug;90(8):1165-6. 30- Tousignant-Laflamme Y, Rainville P, Marchand S. Establishing a link between heart rate and pain in healthy subjects: a gender effect. J Pain. 2005 Jun;6(6):341-7.

31-Donaldson GW, Chapman CR, Nakamura Y, Bradshaw DH, Jacobson RC, Chapman CN. Pain and the defense response: structural equation modeling reveals a coordinated psychophysiologi-cal response to increasing painful stimulation. Pain. 2003;102(1–2):97–108.