



International journal of interdisciplinary dentistry

ISSN: 2452-5588

ISSN: 2452-5596

Sociedad de Periodoncia de Chile Implantología
Rehabilitación Odontopediatría Ortodoncia

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International journal of interdisciplinary dentistry, vol. 16, no. 3, 2023, pp. 183-186

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DOI: <https://doi.org/10.4067/S2452-55882023000300183>

Available in: <https://www.redalyc.org/articulo.oa?id=610076916002>

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RESEARCH WORK



Effect of upper lip compression on pain reduction during local anesthesia. A split-mouth randomized clinical trial.

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Work received on 07/02/2022
Revised work 14/08/2022
Approved for publication on 29/12/2022

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INTRODUCTION

One of the most uncomfortable aspects of the dental attendance is the pain associated with the dental injection, which can cause anxiety and fear⁽¹⁾. Pain as a conscious perception can be viewed from its properties, i.e., the transformation of mechanical, thermal and chemical sensory inputs into a subjective awareness of being in pain⁽²⁾.

Pain induced by the injection of local anesthetics can be reduced by complementary methods, as lip or skin pressure and vibration⁽³⁾. The theoretical base for the analgesic effect of pressure at the injection site can be explained by the gate control theory of pain proposed by Melzack & Wall⁽⁴⁾ which describes how the A-β nerve fibers transmit the information from the tactile receptors on the skin, stimulating the inhibitory interneurons that close the gate on integrating centers of the central nervous system. These neurons act by reducing the number of pain signals transmitted by C and A-δ fibers from the skin to second-order neurons that decussate and ascend to the brain^(4,5).

Previous studies using this theoretical basis have shown that the vibration on the skin of the lip or different parts of the face can reduce the intensity of the pain coming from teeth or soft tissues⁽⁶⁻⁹⁾, designing electromechanical equipment that can cause tactile stimulus, thus reducing the perception of pain in dental anesthesia⁽¹⁰⁻¹²⁾. However, there have been no reports that quantify the effectiveness of using tissue compression near the puncture site and the measurement of pain perception during local dental anesthesia administration, controlling variables as standardization of the compression instrument, masking

ABSTRACT

Objectives: To evaluate the effect of pressure on the skin of upper lip in decreasing pain perception during a local maxillary anesthetic injection. **Material and Methods:** A split-mouth crossover randomized clinical trial was designed. Seventy-one volunteer students (23.6±1.9 years old, 53.5% women) were selected. A group chosen at random had their left or right side of upper lip compressed by a wooden clothes peg as the compression instrument and 0.6 ml of lidocaine 2% with epinephrine 1:100,000 was administered at the buccal apex level of the lateral incisors tooth. Two weeks later anesthesia was administered on the opposite side of the lip according to the randomization recorded. The intensity of perceived pain level between the two injections using a 100 mm visual analog scale (VAS) and co-variable effect were compared (Wilcoxon test $p < 0.05$, RStudio). **Results:** The average of the perceived pain with and without upper lip compression was 27.6±14.5 mm (range 0-80 mm) and 36.33±17.9 mm (range 10-90 mm) respectively ($p = 0.002$). No significant differences were recorded according the covariance analysis with the sex ($p = 0.55$) and age ($p = 0.89$). **Conclusion:** The upper lip compression significantly reduces the perception of pain during a local maxillary anesthetic technique.

KEY WORDS

Pain; Trigeminal nerve; Local anesthesia; Compression; Clinical trial.

Int. J. Inter. Dent Vol. 16(3); 183-186, 2023.

participants and the dentist's abilities in the anesthetic technique⁽⁹⁾.

Considering the inherent variability in the experience of dental surgeons and the morphological and sociocultural characteristics of patients that may influence the perception of pain during the injection of dental anesthesia⁽¹⁾, the purpose of this study was to assess the effectiveness of controlled compression of the upper lip on reducing the perception of pain during a local maxillary anesthetic injection. The null hypothesis tested was that upper lip compression does not alter the perception of pain during a maxillary anesthetic injection.

MATERIALS AND METHODS

Study Design

A randomized clinical crossover clinical trial was designed. The study was approved by The local Ethics Committee on Involving Human Subjects of Faculty of Medicine of Universidad Austral de Chile (Ord no 13/01/2016) and written informed consent was obtained from all subjects. The trial was registered prior to patient enrollment at ISRCTN registry (n° ISRCTN10930940. Date of Registration: 02/01/2020) and the experimental design followed the Consolidated Standards of Reporting Trials (CONSORT)⁽¹³⁾ statement guidelines. The study was carried out in the School of Dentistry of Universidad Austral de Chile (Valdivia, Southern of Chile) from April to June 2020.

Subject and sample size

Subjects were students in the dental anesthesia course at the

university's dental school of the local university, who have not previously received dental anesthesia as part of their undergraduate training. Subjects were recruited in the order in which they reported for the screening session. The sample was calculated based on the results obtained by Nanitos et al.9 The mean Visual Analog Scale pain scale value of 22.1 mm (without intervention) and 12.9 mm (with intervention) with a standard deviation of 12.02 mm and effect size d-Cohen value of 0.7 was considered. Using the two-tailed calculation, an alpha value of 0.05 and a power of 0.8, the size per study group calculated was 30 subjects. In total, sixty participants to be assessed was estimated (G*Power. V.3.1.9.6. The G*Power Team).

Eligibility criteria

A total of 83 participants were examined by two calibrated dentists to check if the participants met the inclusion/exclusion criteria. Both researchers were calibrated using a checklist of the presence of the selection criteria measured in 20 student volunteers prior to the study, who performed the local anesthetic technique used in this study according to the recommendations of Malamed⁽¹⁴⁾, asking the level of pain perceived during the injection of the anesthetic obtaining an intraobserver reliability of Pearson's $\rho = 0.85$. The recruited students read and signed an informed consent form after a detailed explanation of the experimental protocol and the possible risks involved, with undamaged tissue, without lesions or surgical interventions on the upper lip that accepting the terms of the research. Students with a history of allergies or adverse reactions to local anesthesia, presence of dental pain because of dental or orthodontic treatment one month prior to the study or periodontal origin, infection in the puncture area, students with pharmacological treatment with non-steroidal anti-inflammatory drugs (NSAIDs), benzodiazepines or antidepressants were excluded.

Pilot study with the wooden clothes peg

The compression instrument used was a sterile wooden clothes peg (Art and CraftTM, Chile) (Figure 1a). The pressure exerted was standardized in the Solid Laboratory of the Mechanics Institute at the Universidad Austral de Chile. To do this, the pressure was measured in N/cm² of 20 wooden clothes pegs chosen at random using the INSTRON4469 and its respective software INSTRON BLUEHILL-2. In this analysis, an average pressure of 1.05 ± 0.2 N/cm² (range 0.95–1.12 N/cm²) was demonstrated. In order to control the measurement bias of the compression with the wooden clothes peg in the perception of pain or discomfort when using it on the participants' lips, a pilot study was conducted with 10 volunteers (5 men), who had the peg placed on their upper lip; they were asked to assess if the pain were it as innocuous or noxious perception. On the other hand, they were asked on a visual analog scale (VAS) from 0 mm (no pain) to 100 mm (unbearable pain). In this test, all subjects answered that stimulus was an innocuous and comfortable perception. The average pain on the VAS was 0.93 ± 1.7 mm (median = 0 mm), with no differences being observed according to the side of the lip ($p = 0.74$) or the gender of the volunteers ($p = 0.28$) (Wilcoxon test; $p < 0.05$).

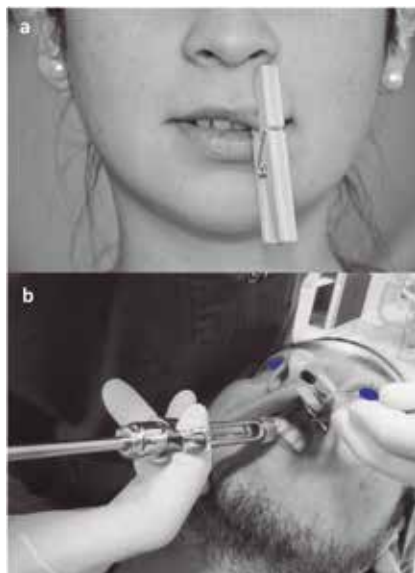


Figure 1. (a) type of wooden clothes peg used as an instrument for skin compression on the upper lip on the subject's left side and (b) method of anesthetic injection. Note the separation of the lip with mirror observing the puncture point.

Randomization sequence generation and intervention

To determine the chronological order of the injection for to control the measurement bias and placebo effect of lip compression, a randomization process within subject was performed using software available at <http://www.sealedenvelope.com> by a staff member not involved in the research protocol, who recorded the details of the allocated group on cards contained in sequentially opaque, numbered and sealed envelopes. The allocation assignment was revealed by opening the envelope immediately before the procedure, where cards containing one of two colors were used, indicating the primary intervention: red card meant anesthetic using compression with a sterile wooden clothes peg and white card meant anesthetic without compression. Thus, the concealment of the random sequence was guaranteed, in order to prevent selection bias. On other hand, in order to control different time may have an influence on the pain perception, all measurement was applied between 10:00 to 12:00 hours of the day. In preparation for the anesthetic, the volunteers rinsed with a mouthwash of 0.12% chlorhexidine (OralgeneTM, MaverPharma, Chile) and were positioned in the dental chair as described by Malamed for local maxillary anesthetic techniques⁽¹⁴⁾. One investigator (JL) prepared the carpule syringe using a 30G short needle (Septoject XL, SeptodontTM, Saint-Maur-des-Fossés, France) and a cartridge of 2% Lidocaine hydrochloride and epinephrine 1:100,000 (Xylonor 2%® Septodont, Saint-Maur-des-Fossés, France) at room temperature. For the volunteer selected for anesthesia with lip compression, the investigator responsible for the anesthetic technique is a dentist with 10 years of experience in the dental emergency service, placed the wooden clothes peg on the upper lip at the level of the left upper canine, separating the lip with the use of a dental mirror, next to the puncture site and immediately performed the anesthetic technique according to the recommendations made by Malamed⁽¹⁴⁾, placing the needle parallel to the lateral incisor and going down to one centimeter from the bottom of the vestibule, with the needle tip and their bevel oriented toward the apex of the tooth, depositing a third (0.6 ml) of the contents of the anesthesia cartridge within 15 seconds (Figure 1b). Immediately after fifteen seconds withdrawing the needle, the second investigator (JL) presented the volunteer with a card with the VAS, asking "How much pain did you perceive during the puncture and administration of the anesthesia?" and registering the value indicated. The principal investigator did not participate in the collecting or recording of the data. After two weeks (the washout period), the second injection was done on the contralateral side of the maxilla with the same technique and the complementary intervention according to the randomization sequence described.

Data analysis

To verify the effectiveness of the pressure during the anesthetic technique, the level of pain perceived by the volunteer on the VAS during the anesthetic injection with or without skin compression was considered a dependent variable. A third investigator with no previous participation and blinded in data previously recorded performed the statistical analysis of the data. The homogeneity of the results was verified by the Shapiro-Wilk test ($p < 0.05$). Then the average values and confidence interval were compared between the groups. The effectiveness of the skin pressure was determined by the 10-point difference on the Verbal Analog Scale as clinically relevant and considering a statistically significant decrease in average and standard deviation of the level of perceived pain of participants (Student's t test, $p < 0.05$). Finally, a covariance analysis was calculated for to determine effect of result in association with sex and age of the participants (ANOVA; $p < 0.05$). The data were tabulated and analyzed using R (R Core Team) with the packages *tidyverse* and *nlme*⁽¹⁵⁾.

RESULTS

The anesthetic procedures were implemented exactly as planned between april to june 2020, and no modification was performed. Eleven out of 83 subjects were not enrolled in the study because they did not fulfill the inclusion criteria and one study subject did not attend the second session of this crossover clinical trial. (Figure 2). Thus, 71 subjects with a mean age of 23.6 ± 1.9 years old (range 20-29 years; 53,5% women) were selected. Thirty-nine subjects (54.9%) received the first local anesthesia with compression. The values of the pain perception had a parametric distribution ($p = 0.22$).

The average of the perceived pain during the administration of anesthesia with skin pressure according of VAS was 27.6 ± 14.5 mm (median = 30 mm; range = 0-80 mm) and without pressure an average pain of 36.33 ± 17.9 mm (median = 30 mm; range = 10-90 mm), and there was a statistically significant difference between the two groups (Student's t test; $p = 0.002$) (Table 1). No significant differences were recorded according the covariance analysis with the sex ($p = 0.55$) and age ($p = 0.89$) of the participants.

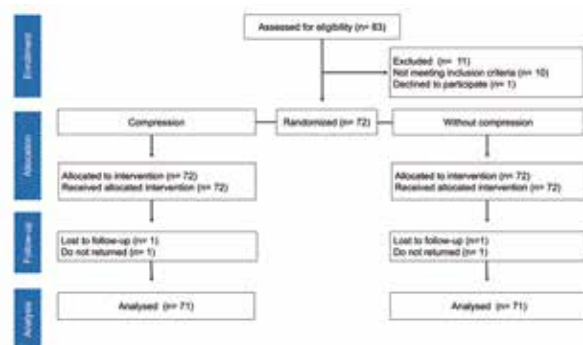


Figure 2. Participant flow diagram (CONSORT) in the different phases of the study design. The subjects participated in both study groups (crossover) with a two weeks wash-out period.

Table 1: Level of pain perceived by study group according to the visual analog scale of pain (n=71).

Visual Analog Scale of Pain Level (in millimeters)						
Group	Mean	SD ¹	Median	Min	Max	CI ² 95%
Pressure	27.6	14.58	30	0	80	24.15 - 31.03
Without pressure	36.33	17.9	30	10	90	32.09 - 40.57

1. SD: Standard deviation

2. CI: confidence interval

3. Wilcoxon test ($p < 0.05$)

DISCUSSION

The main results of this crossover clinical trial prove that the use of pressure during intraoral local maxillary anesthetic significantly reduces the perception of pain compared to the pain perceived during administration of a local anesthetic without compression.

Previous reports have demonstrated the inherent painful effect that occurs in the parenteral injection of drugs, considering important the basic understanding of physiology for pain control⁽¹⁶⁾ as well as the use of complementary techniques of local anesthetic administration and its relationship with the patient's anxiety⁽¹⁷⁾. According to our results, probably the main mechanism underlying the application of wooden clothes peg prior to the anesthetic injection is the diffuse noxious inhibitory controls (DNIC)^(18,19). This theory suggests that a spino-reticulo-spinal loop is the mechanism behind hypoalgesia. In this context, the mechanical pressure in the upper lips probably activates small diameter nociceptive afferents (fiber Aδ or fibers Aδ and C), which inhibit the wide dynamic range neurons (WDR) in upper or lower spinal segments (lateral inhibition) and facilitate the activation of serotonergic neurons from the subnucleus reticularis dorsalis (SRD) in the caudal medulla^(18,20). These results are based on previous reports that indicated that DNIC can be induced by a non-painful condition stimulus and suggests that Endogenous Analgesia (EA) does not have a direct proportional relationship with the magnitude of the perception of the conditioning pain^(21,22). The practical use of this theory acts as an analgesic mechanism to the inherent chemical and mechanical stimuli generated during the injection of the anesthetic fluid. The chemical stimuli are produced by the release of pro-inflammatory agents (such as bradykinin, serotonin, prostaglandins, ATP, among others), a product of the tissue damage caused during the penetration of the needle and the loss of continuity of the mucosa and the conjunctive tissue close to the puncture site⁽¹⁷⁾. Other mechanism that could explain de pain reduction in the present study is the Gate Control Theory⁽⁴⁾. Our results suggest that by placing a wooden clothes peg prior to the anesthetic injection, the activity in large-diameter (non-nociceptive) myelinated (A-β) primary afferents "turned on" an inhibitory interneuron, which in turn inhibited the trigeminal spinal projection neurons that transmit the injury message to the brain (Figure 3). Despite this, we hypothesized that the Gate Control Theory acts in a minor proportion than DNIC, because in the present study the application of mechanical stimulus (wooden clothes peg) is applied before the noxa and therefore it would not have the reactive capacity to block the pain transmission of the painful afferent fibers stimulated by the subsequent injection. Conversely, DNIC is an endogenous mechanism of analgesia that generates hypoalgesic effects in the medium term (minutes) due to its supraspinal action. This mechanism allows its use prior to the injurious event (anesthetic injection) and is therefore useful in

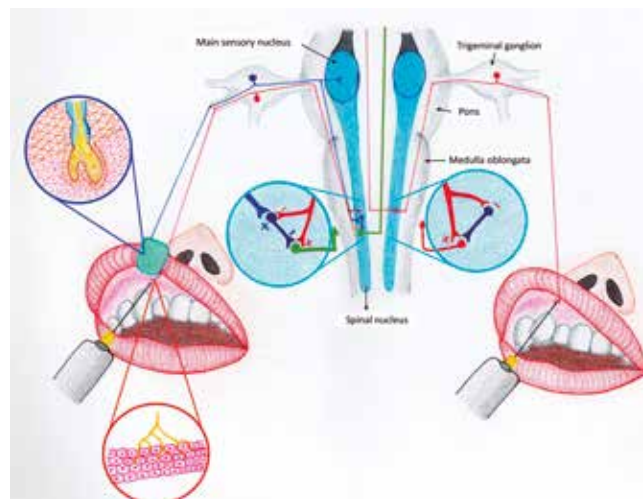


Figure 3. Pain gating in the trigeminal spinal nucleus based on that proposed by Melzack and Wall⁽⁴⁾ in the context of the trigeminal pain pathway. During needle puncture and infiltration of local dental anesthesia administration, tissue damage causes release of inflammatory mediators that stimulate nociceptors that initiate the pain pathway. Our results suggest that stimulation of cutaneous mechanoreceptor such as placing a wooden clothes peg (green) prior to the anesthetic injection stimulate in large-diameter (non-nociceptive) myelinated (A-β) primary afferents (blue axon) "turned on" an inhibitory interneuron (black neuron), which in turn inhibited the trigeminal spinal projection neurons (green axon) that transmit the injury message to the brain.

dental and medical clinical procedures.

On the other hand, mechanical nociception is dependent on the channels activated by stretching. When mechanical forces stretch or compress the tissue, the channels activated by stretching are opened and a neural discharge is initiated⁽¹⁷⁾. The hypertonic or hypotonic fluids can take the water to or from the cell and activate the channels sensitive to compression or stretching, producing pain. It has been shown that the transient receptor potential (TRP) A1 channels can be activated by mechanosensation⁽²³⁾, which in this case is produced by the injection of the volume of local anesthetic in the submucosal region of the bottom of the vestibule of the lower central incisor.

Vibration on the skin at the puncture site can significantly reduce pain perception⁽⁹⁾, as can the use of distraction devices with manual stimulation⁽⁷⁾ and with co-stimulation⁽⁸⁾. Nowadays the market offers skin vibration devices such as DentalVibe™ and the Vibraject™, which they report as being effective in the reduced perception of pain compared to a conventional anesthetic technique or in children⁽¹¹⁾, in adolescents⁽¹⁰⁾ or during the blockade of the inferior and infraorbital alveolar nerves⁽¹²⁾. However, other reports do not refer to increased benefits, rather comparing the use of topical anesthetic and topical anesthetic accompanied by vibration⁽²⁴⁾, or the use of vibration compared to an electrical injection device⁽²⁵⁾. This disparity in the results may be explained by pain being perceived as a result of a neurophysiological process, which is influenced by several sociodemographic, cultural and psychological factors in an individual⁽¹²⁾ as well as the technique and manner of using the anesthetic, because the sensitivity of the nociceptors depends not only on the chemical nature of the injected anesthetic, but also on the mechanical effect that occurs according to the site, the speed and the volume of the injection⁽²³⁾. In addition, the frequency and type of vibration of the device applied to each subject, the operator's ability and, fundamentally, the acquisition of the vibration instruments by the dentist and the patient's tolerance to its use must also be considered.

The main limitations of our study are related to the anesthetic technique. The fast speed of the selected injection has been previously described^(1,14-16) it was used because it is the method habitually used in public dental services where there is heavy demand. Although there are reports that recommend a slower injection speed⁽¹⁴⁾, the injection speed was chosen to determine whether the decreased pain was due to the lip compression or not. Another point to consider is the anatomical site to anesthetize, which can influence the perception of pain. The puncture site used in this study is justified by the participation of volunteer students making access to the puncture site easier, the location of the wooden clothes peg and the heightened sensitivity in the oral region, because it is one of the zones with the greatest density of receptors for feeling and pain⁽²⁶⁾ compensate by the lack of visual perception of the subject at the

site of the needle puncture⁽²⁷⁾ which makes it possible to discriminate with greater accuracy two points of stimulus and the activation of the gate control theory of pain during skin and nociceptive stimulus in this oral region.

Despite these limitations, our study describes the perception of significantly less pain with the use of an instrument to compress the upper lip during local maxillary anesthetic administration. The reason for the use of the wooden clothes peg is to verify the effect of upper lip compression with a domestic instrument, with a constant compression, easily acquired and which allows its common use for the replication of the design presented.

In conclusion, the use of skin compression on the upper lip during local maxillary anesthetic administration significantly reduced the perception of pain during the needle puncture and injection of the anesthetic compared to the use of conventional local maxillary anesthetic. Future studies will need to verify the effect of skin compression with this instrument on other anesthetic techniques and using other complementary methods for pain control such a warming anesthetic cartridges⁽²⁸⁾ in patients with acute dental pain.

ACKNOWLEDGMENTS

We wish to thank all the volunteer students in the School of Dentistry at the Universidad Austral de Chile for participating in this study.

This research is original and has not been published, simultaneously submitted, or already accepted for publication elsewhere. In addition, all authors have contributed to this research according to the purpose of the

manuscript: conception and study design (PCA, CC, RM); Data acquisition and literature search (PCA, SL, JL); Data analysis and interpretation (CC); drafting of article, critical revision, final approval on the content of the manuscript (PCA, SL, JL, CC and RM).

CLINICAL RELEVANCE

Scientific rationale for the study: One of the most uncomfortable aspects of the dental clinic is the fear and anxiety caused by the pain associated with the dental injection. There have been no reports that quantify the effectiveness of using skin or tissue compression near the puncture site for to improve a less pain perception during local anesthesia administration. Our hypothesis is that upper lip compression decreases pain perception during a maxillary anesthetic injection

Main result: The average of the perceived pain with skin upper lip compression during local dental anesthesia administration was significantly lower than without lip compression.

Practical implications: The skin of upper lip compression significantly reduces the pain perception during local dental anesthesia administration.

CONFLICT OF INTEREST AND FUNDING SOURCE DISCLOSURE

The authors declare that they have no conflicts of interest with commercial brands or companies of dental materials used in this research.

The financing was private and made with the authors' own economic resources.

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