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Effectiveness of *Acmella oleracea* for topical anesthesia on buccal mucosa

Lucas Cerutti de Andrade[a], Isabella Welter Rotta[b], Sandro Revay Chaves[b], Denise Tiemi Uchida[c], Zilda Cristiani Gazim[c], Fabiana Borges Padilha Ferreira[c], Ezilda Jacomassi[c], Daniela de Cassia Faglioni Boleta-Ceranto[d]

Abstract

Objective: The present study aimed to determine the effectiveness and safety of *Acmella oleracea* ointment used as topical anesthetic for buccal mucosa.

Methods: The topical agent was applied to dried buccal mucosa. Next, a short needle was inserted in the mucobuccal fold above the maxillary canine eminence and then immediately removed. Each volunteer served as his/her own control. Pain was measured with a visual analogue scale and by heart rate.

Results: A one-way analysis of variance followed by a Kruskal-Wallis test showed no statistically significant differences in the effectiveness of the two *Acmella oleracea* ointment concentrations studied compared to the benzocaine 20% ($P<0.05$) control.

Conclusion: *Acmella oleracea* ointment was effective and safe in reducing the pain from needle insertion in the methodology used in the present study.

Keywords: *Acmella oleracea*; benzocaine; pain; topical anesthetic

[a] School of Dentistry, Paranaense University, Cascavel, PR, Brazil
[b] Dentist graduated from Paranaense University, Cascavel, PR, Brazil
[c] Department of Pharmacy, Paranaense University, Umuarama, PR, Brazil
[d] Department of Basic Sciences, Division of Physiology, Paranaense University, Cascavel, PR, Brazil

Efetividade de anesthesia tópica a base de *Acmella oleracea* sobre a mucosa bucal

Resumo

Objetivo: O presente estudo objetivou determinar a efetividade de uma pomada a base de *Acmella oleracea* para anestesia tópica da mucosa bucal e sua segurança.

Métodos: A mucosa bucal dos voluntários foi seca e os agentes anestésicos foram aplicados. Em seguida, uma agulha curta foi inserida no sulco vestibular acima da eminência canina e imediatamente removida, cada voluntário foi controle de si mesmo. A medida de dor foi feita através de uma escala analógica visual e pela variação da frequência cardíaca.

Resultados: Análise de variância seguida pelo teste de Kruskal-Wallis mostrou que não houve diferença estatisticamente significante no índice de dor quando comparadas as duas concentrações da pomada de *Acmella oleracea* e o controle Benzocaína 20% ($P<0,05$).

Conclusão: A pomada de *Acmella oleracea* foi efetiva e segura em reduzir a dor provocada pela inserção da agulha de anestesia na metodologia utilizada no presente estudo.

Palavras-chave: Anestesia tópica; *Acmella oleracea*; benzocaina; dor

Correspondence:
Daniela de Cassia Faglioni Boleta-Ceranto
dcboleta@unipar.br

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Introduction

Early humans sought to understand pain, and pain management has been the focus of centuries of research [1]. Anatomical and physiological studies performed by Descartes (1606-1650) first confirmed the existence of nerves that are able to receive sensorial information at the periphery and transmit it to the brain. Descartes found that specific nervous pathways conducted pain to the brain. Therefore, much discussion occurred until pain could be defined as follows: "A sensorial experience, emotionally unpleasant, associated to a real or potential tissue damage or described as if the damage was present" [2].

In dentistry, pain is one of the most common symptoms, and it is therefore of the utmost importance to dentists. Pain sensation can be described as acute, burning, continuous, spasm, silent or pulsating, and it varies according to human emotions. Pain control is one of the most important aspects of dentistry practice.

Medication, including analgesics and anesthetics, is necessary to control pain. Anesthetic salts are formed by combining weak alkaloids and strong acids. Anesthetic salts are used both for their stability and water-soluble properties, which allow diffusion through interstitial fluids to the action site. Anesthetic solutions suppress neural transmission and block the afferent nervous fibers transmission of pain signals to the brain [3].

For an anesthetic to reach the action site a minimally invasive maneuver is necessary in the surrounding tissues; this maneuver can cause pain because of the needle insertion. The sensation may vary based on the patient's former pain experiences. To minimize the pain caused by the needle puncture, some artifices, such as using a topical anesthetic, can be used. Through topical analgesia, nerve endings free from accessible structures (e.g., intact mucosal membrane, rubbed skin or ocular cornea) are incapable of stimulation when an appropriate solution is applied directly at the superficial area.

Some substances are frequently used as anesthetics. The continuous search for alternative and natural treatments make the study of these substances interesting even when they are used as topical anesthetics, which is important to ensure a treatment with the minimum amount of pain possible.

According to the literature, a plant popularly known as Jambu or watercress from Pará (*Acmella oleracea*) is cultivated in the north of Brazil and used as an Amazonian cookery seasoning; it also has cicatrizing and analgesic properties to treat oral lesion [4,5].

The leaves and inflorescence (capitula) are used as household medicine in the northern region of the country to treat oral and throat diseases. When chewed, the leaves and flowers generate a tingling sensation to the lips and tongue. This sensation is caused by the action of spilanthol, an isobutylamide compound that promotes local anesthetic action and is used for tooth ache [4].

A literature search revealed many of the pharmacological properties of *Acmella oleracea*, including its use and efficiency as a local analgesic when applied directly to the oral mucosa [5]. However, no studies have investigated the use of spilanthol ointments, the active ingredient of the plant, as a topical anesthetic for buccal mucosa, which would simplify the application of infiltrative anesthesia. This dearth of research thereby justified the present study, the objective of which was to analyze the effect of an *Acmella oleracea* anesthetic ointment on oral mucosa and to evaluate its safety as topical anesthetic.

Methods

This study was performed at Paranaense University Dentistry Clinic, Cascavel-PR, Brazil, and approved by the National Research Ethics Committee Protocol Number 0681.0.375.000-09. The sample consisted of 29 healthy adult volunteers ranging in age from 18 to 24 years (average 19.8 years), 60% female and 40% male. Prior to participating in the study, a medical history was obtained from each subject. Patients with histories of anesthetic sensitivity or recent oral trauma, or taking central nervous system suppressive medications, or with endocrine, metabolic or hormonal diseases and pregnant patients were excluded from the study [6]. Each participant signed an informed consent form [7]. All patients were approached by the same researcher to explain the study conditions to ensure that the volunteer felt secure with the researcher, and this fact would not influence the perception of pain. *Acmella oleracea* ointment was prepared in different concentrations. A pilot study was performed to determine the best concentrations for analysis. The researcher evaluated a maximum of five volunteers per day, depending on availability. The patients were scheduled for 15-min session. The volunteers were analyzed in two individual sessions spaced one week apart in a double-blind study. In the first session, each volunteer served as his/her own control and randomly applied benzocaine (control) on one side; five minutes later, 15% or 30% Acmella ointment was applied to the other side. The order of the drug administration, each combination and the side of first needle insertion were randomized. The test site was the mucobuccal fold above the maxillary canine eminence [6]. The mucobuccal mucosa was dried with a 2×2 gauze on both sides of the mouth, and the topical agents were applied with a sterile cotton tip applicator. All agents were left in place for three minutes. Next, a twenty-seven gauge short needle was inserted into the mucosa just past the bevel and then immediately removed. No local anesthetic solution was deposited into the tissue. After a five-minute rest period, the same procedure, with the other topical agent, was repeated on the opposite side. One investigator applied the topical agents to the mucobuccal fold, and a second one performed all the insertions. For pain measurement, the volunteers were instructed to use a 100 mm visual analogue scale, drawing a vertical line at a point between no pain and unbearable pain (Fig. 1); the line corresponded to the amount of pain felt during the needle insertion procedure [8]. The ratings were performed after both insertions.

Fig. 1. Visual Analogical Scale.

The heart rate was monitored on all participants using a pulse oximeter (Onyx® Modelo 9500, Minneapolis MN, USA) throughout the procedure. The participants' heart rates were recorded at baseline, before the procedure began, while the topical agents were being applied, at the time of the first and second needle insertions, and during the rest periods following each insertion [6].

The essential oil of watercress from Pará (*Spilanthes acmella* (L. Murray) flowers was obtained through the hydrodistillation process of summit fresh flowers [9] harvested at the Medicinal plant nursery of Paranaense University- Unipar, Umuarama campus, northeast of Paraná, Brazil. Fertile branches were deposited in Unipar Educacional Herbarium (HEUP), under number 2227. The essential oil was incorporated as an ointment with polyethyleneglycol 4000 (20%) and polyethyleneglycol 400 (75%) (10), and incorporated in 15% and 30% concentrations. Benzocaine 20% (Benzotop®, DFL, Rio de Janeiro, RJ, Brazil) was used as a positive control.

The results were submitted to a one way analysis of variance (ANOVA) test followed by a pairwise comparison with Duncan's Multiple Range and Tukey's test. Differences were considered significant at the 5% level.

Results

The average pain score after using *Acmella oleracea* ointment 15% was 46.3 (37.5 for men and 49.7 for women), 13.7 (4.5 for men and 18.6 for women) for *Acmella oleracea* ointment 30% and 25.3 (34.3 for men and 21.9 for women) after Benzocaine 20%, as shown in Table 1. The lower rate indicates less pain perception, thus, more effectiveness of the topical anesthetic.

Table 1. Average VAS pain scores comparing the groups. Values are given as mean ± standard error.

Acmella 15%	*Acmella* 30%	Benzocaine
46.3±9,6	13.7±3,9	25.3±8,2

A one-way ANOVA, followed by the Kruskal-Wallis test, showed that there was not a significant difference in the effectiveness of the two *Acmella oleracea* ointment concentrations studied compared to the benzocaine (P=0.026) control. However, significant differences were found when the two concentration studied (15% and 30%) were compared to one another (P=0.009) (Fig. 2).

To analyze the effect of pain on a physiologic variable, the heart rate was measured at baseline, while the topical agents were applied, at the time of the first and second needle insertion and during the rest period following each needle insertion. An ANOVA, followed by Tukey's test, demonstrated significant differences (P<0.05) between some of these observational periods (Fig. 3). The magnitude of differences between the heart rates average during these periods was 5.5 beats per minute.

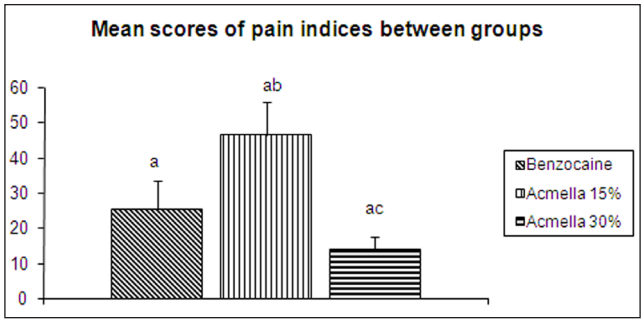

Fig. 2. Average (± E.P.M) pain rate of male and female volunteers after needle insertion under topical anesthetics effect. Averages of different letters statistically distinguish each other according to Tukey test.

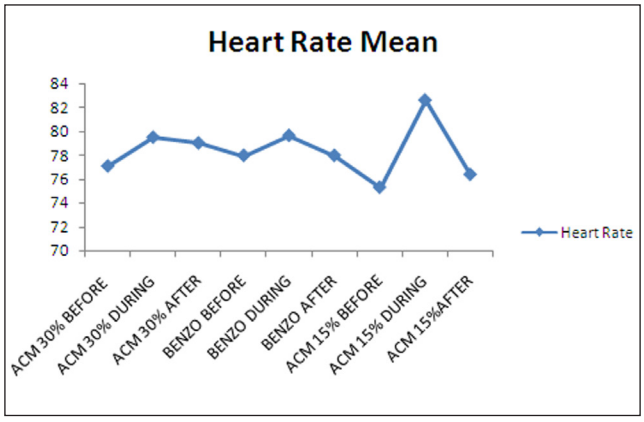

Fig. 3. Average heart rate of volunteers before, during and after the needle puncture in different treatments.

Discussion

The results of the present study showed that the anesthetic effect produced by both the 15% and 30% *Acmella oleracea* ointments was not statistically significantly different compared to the benzocaine control, which demonstrated its effectiveness in blocking the pain produced by the anesthetic needle puncture. However, the efficiency of topical anesthetics has been questioned by some authors, who doubt its real pharmacological action and reinforce its psychological effect, which must be considered. Martin et al. [11] observed that if patients thought they were receiving topical anesthetics, they presented with less pain because they had less anxiety about the injection. The same author also mentions that the most important aspect of the topical anesthetic use may not be its clinical efficiency but

the psychological effect on the patient, who is aware of the professional effort to avoid pain. Kincheloe et al. [12] observed that patients with high pain expectations described greater pain rates than those with lower expectations and that local anesthetics had no effect over the experienced pain.

Pain and anxiety are greatly related during dental treatment. Because many nerve fibers are involved in both factors, they can become superimposed, thereby affecting research results. The murine study developed by Boleta-Ceranto et al. [13] demonstrated that injecting an algesic agent in the orofacial region can alter the anxiety rate in animals, which could influence in the pain. Therefore, it is not possible to confirm or deny that anxiety can affect the nociception, particularly in humans, when many factors (e.g., environment, physiological, psychological) greatly influence pain interpretation. In the present study, we did not evaluate the emotional state of the volunteers, their expectations of pain in using local anesthetics, or any possible trauma they may have experienced in dental treatments; these factors could interfere with the pain index.

The existence of some type of dental treatment phobia is common, particularly to the anesthetic procedure because it involves needle puncture. During stressful situations the autonomic nervous system responds with an adrenergic discharge, which is originated by the sympathetic activation and adrenal hormone release. The heart rate (HR) parameter is directly altered by the adrenalin discharge. The heart rate was monitored during all procedures and registered before, during and after the needle puncture. During each period, independent of the treatment, an increase of the HR was detected, but it soon returned to its basal rate. Therefore, the only statistically significant alteration occurred when the 15% *Acmella oleracea* ointment was used as a topical anesthetic. Although no significant difference in pain rate was revealed by the volunteers through the visual analogical scale, comparing benzocaine and the *Acmella* 15% ointment, there was a difference related to the HR, which demonstrates that the needle puncture had an algesic effect when using the 15% ointment. There was no significant difference when comparing the alteration of HR after Benzocaine and 30% *Acmella oleracea* ointment use, which indicated its effect as a topical anesthetic once more.

In spite of the care taken in the present study to minimize any interference during the tests, it was not possible to control all factors that could interfere in the results, mainly, the emotional and hormonal alterations of the volunteers. This issue was relevant in this study because the majority of participants were women, and the volunteers' menstrual cycles were not evaluated; hormonal alterations can alter pain perception in the orofacial region [14,15].

The differences in the characteristics of the different regions of the oral mucosa must be noted. The keratinized and non-keratinized tissue areas and the anesthetic effectiveness in these areas must be considered. Nusstein et al. [16] observed no significant difference between using or not using topical anesthetics (20% Benzocaine) to anesthetize the inferior alveolar nerve and the upper molars regions; however, the topical anesthetic was effective in the maxillary lateral incisors region. Hersch et al. [17] observed that lidocaine obtained better results in reducing mucosa pain in the inferior premolar tooth region compared to the same region on the maxillary dental arch. Nakanishi et al. [18] and Meechan et al. [19] agreed about the lack of efficiency of 20% benzocaine in reducing pain during the needle puncture at the pterygomandibular raphe and upper first molar regions. The present study opted to use the mucobuccal fold above the maxillary canine eminence region because of its easy access, following Rosivack et al.´s methodology [6], although the disagreement with results from other previously mentioned studies might be attributed to the different methodologies used.

This study followed the same puncture procedures, using only the needle's bevel, as that used by Nusstein et al. [16], Rosa et al. [20] and Rosivack et al. [6] to evaluate the topical anesthetics efficiency, acknowledging that once the needle's bevel penetrated, the anesthetic salt would be injected into the tissues and its action in the region and the effectiveness of the topical anesthetic would no longer be necessary. However, considering that the anesthetic salt's effect is not immediate, the analgesia of the topical anesthetic would not be efficient if the needle penetrated beyond the needle's bevel, but this issue can be analyzed in future studies.

Because of the different techniques and anesthetics used, it becomes difficult to perform a quantitative comparison among works regarding the level of pain upon puncture. Table 2 compares the results for the pain index of this study with another study using the same methodology and anesthetic control (benzocaine).

During all procedures, no adverse reaction caused by the *Acmella oleracea* ointment was reported, which suggested that its use was safe.

Table 2. Comparing the results for the pain index of this study with another study using the same methodology and anesthetic control.

Autors	Anesthetics	Women	Men	Mean Pain Score
Rosa et al., 1999	Lidocaine	19.2	14.6	16.9
	Lidocaine placebo	26.8	40.5	33.65
	Benzocaine	26.8	40.6	19.6
	Benzocaine placebo	25.35	25.2	25.35
Present study	*Acmella oleracea* 15%	49.7	37.5	46.3
	Acmella oleracea 30%	18.6	4.5	13.7
	Benzocaine	21.9	34.3	25.3

In addition to the needle puncture, other methods can be used to evaluate the effectiveness of topical anesthetic action. Donaldson et al. [21] observed the effectiveness of topical anesthetic through the gingival sulcus probing procedures, a common procedure in dental clinic routines, which could also be used to evaluate the efficiency of the *Acmella oleracea* ointment.

Conclusion

Based on the study results, *Acmella oleracea* ointment use was safe and effective in reducing needle insertion pain in the methodology used in the present study.

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