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Efficacy of a Light-cured Tetracaine-based Anesthetic Gel for Rubber Dam Clamp Placement: A Triple-blind Randomized Clinical Trial

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Clinical Relevance

A light-cured anesthetic gel is an excellent alternative to decrease pain when used with a rubber dam clamp to restore noncarious cervical lesions.

SUMMARY

Objectives: To evaluate the efficacy of a new light-cured anesthetic gel for pain control in adults undergoing rubber dam isolation for the restorative treatment of noncarious cervical lesions (NCCLs).

Methods and Materials: This study was a randomized, split-mouth, triple-blind, controlled trial. The sample comprised 50 adults with at least one pair of NCCLs located in the same arch but on opposite sides. Simple randomization defined the tooth to receive the light-cured tetracaine-based anesthetic gel or the placebo gel. After cotton roll isolation, the gels were applied in the gingival tissue around the tooth with the aid of the applicator tip of a syringe, left in place for 15 seconds, and light-cured for 15 seconds. Then, a #212 clamp was positioned on the tooth. If the patient reported pain, the clamp was removed, the patient filled

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out a pain intensity form (a 0-10 visual analog scale [VAS] and a 0-4 verbal rating scale [VRS]) and an injectable anesthetic was applied before rubber dam isolation for the restorative procedure. The absolute risk, intensity of pain, and need for rescue anesthesia were analyzed by the McNemar test and the Wilcoxon signed rank test (α=5%).

Results: The odds ratio [OR] for pain (OR=3.5; 95% confidence interval [CI]=1.1 to 14.6; p=0.03) showed lower reports of pain for the light-cured anesthetic gel. One in five patients will benefit from placement of the light-cured anesthetic gel. On average, pain intensity was one VAS unit lower in those using the light-cured anesthetic gel than in those using the placebo gel. For the VRS, the pain intensity for the light-cured anesthetic gel was 0.4 units lower than the pain intensity for the placebo gel (95% CI=–0.9 to 0.07). The OR for rescue anesthesia was 2.5 (95% CI=0.7 to 10.9; p=0.18).

Conclusions: The light-cured, tetracaine-based anesthetic gel reduced the absolute risk of pain by 20% in NCCLs.

INTRODUCTION

The use of restorative treatment for noncarious cervical lesions (NCCLs) has increased, especially in the elderly population, as the occurrence of NCCLs has increased.[1,2] For instance, in the Chinese population, the occurrence of NCCLs was reported to be 63%.[3] This high proportion of patients with NCCLs increased the use of restorative treatment for these specific lesions.[4]

Restorative treatment can be performed with different restorative materials,[5-7] but adhesive systems and composite resins are the most commonly used because of their superior esthetic properties.[8] However, adhesive systems are sensitive to moisture and contaminants, such as saliva,[9] gingival fluid, and blood.[9-11] Adequate moisture control can be achieved with rubber dam isolation, which avoids external contamination and may improve the performance of restorations.[12-14]

Unfortunately, a rubber dam is kept in place by a metal clamp that also aims to retract the gingival tissue to expose the gingival margin of the NCCL. This procedure may be painful and may require the use of local anesthesia for the patient's comfort during the procedure.[15] A recent study demonstrated that approximately 70% of the patients undergoing restorative treatment of NCCLs required anesthesia for clamp placement.[11]

The problem is that approximately 18% of patients are "very much" afraid of needles,[16] which can be an obstacle for restorations of NCCLs under rubber dam isolation. Apart from that, the numbing produced by the injectable anesthesia, the pain during puncture, and its longer duration are additional disadvantages that lead patients to dislike injectable anesthesia.[17,18] The restorative procedure in NCCLs is usually performed quickly and is not painful as the procedure usually does not require cavity preparation. Therefore, topical anesthesia could be an alternative to produce analgesia for clamp placement.

Topical anesthetics have been used in dentistry to alleviate patient fears and provide pain control.[15] There are some commercially available topical anesthetics. They are suitable to replace injectable anesthesia in some dental procedures, such as probing,[19] scaling and root planning,[20-22] clamp placement in children.[23,24] and placement of mini-implants in orthodontics.[25] However, these products have a very short duration of action (10-15 minutes),[26-28] they flow to the neighboring areas causing an unpleasant anesthesia sensation, and they can be easily washed out by saliva.[23,29,30] Thus, it would be interesting to develop an anesthetic gel capable of overcoming these disadvantages and replacing injectable anesthesia.

This article presents an alternative for topical anesthesia based on a newly developed light-cured anesthetic gel. We developed a topical light-cured anesthetic gel using a more potent anesthetic salt than those used in the commercially available products. This triple-blind, randomized clinical trial evaluated the efficacy of this new light-cured tetracaine-based anesthetic gel compared with a placebo on the risk and intensity of pain in adults undergoing clamp placement for rubber dam isolation before treatment of NCCLs.

METHODS AND MATERIALS

Protocol Registration

We registered this research protocol in the Brazilian clinical trials registry (REBEC) under identification number RBR-6HXHX7. The article was written based on the CONSORT (Consolidated Standards of Reporting Trials) statement for randomised trials.[31]

Trial Design, Settings, and Data Collection Locations

We conducted a triple-blind, randomized, split-mouth, placebo-controlled clinical trial with an equal

allocation ratio. The study was performed from September 18, 2015, to November 11, 2016, in the dental clinics of the School of Dentistry of the local university.

Recruitment

The participants in the clinical trial (convenience sample) presented themselves for treatment at the School of Dentistry at the local university. No type of advertisement was done in any type of media.

Eligibility Criteria

For inclusion in the trial, participants had to be at least 18 years old and have good general and oral health. The participants had at least one pair of NCCLs, without undercuts, that needed restorative treatment to avoid excessive dental wear and to eliminate hypersensitivity. These lesions were located in the same arch, but on opposite sides, and the gingival margin had a similar size, depth, and location.

Participants were excluded if the teeth with the NCCLs were endodontically treated. Participants with gingivitis, periodontitis, dental mobility, and bruxism habits were also excluded, as were adults with a history of sensitivity or allergic reaction to ester-based anesthetics.

Sample-size Calculation

The primary outcome of this study was the absolute risk of pain caused by clamp placement. The risk of pain caused by clamp placement was reported to be 70% in an earlier study.[11] Therefore, at least 40 patients were required to detect a difference in pain risk of 30% with a power of 80% and a significance level of 5%. All calculations for determining the sample size were carried out with a freely available online program for this purpose (www.sealedenvelope.com).

The sample-size calculation did not account for potential correlation between the paired treatment outcomes. This approach resulted in a larger sample size than if the correlation coefficient between treatment outcomes was not zero. We took this approach because published within-person trials do not report this correlation coefficient; thus, we opted to be conservative.

Random Sequence Generation and Allocation Concealment

The gel to be used in each tooth was determined by simple randomization. The random sequence was generated from the same website used for sample-size calculation (www.sealedenvelope.com) by an investigator who was not involved in implementing the study.

The random sequence generated was individually placed in opaque, consecutively numbered, and sealed envelopes, which were only opened by the operator immediately before the intervention. The envelope contained the group to be used in teeth located in the quadrant with the lowest two-digit World Dental Federation (FDI) numbering system, while the opposite-side teeth received the alternative treatment.

Blinding

This was a triple-masked clinical trial, in which the patient, operator, and statistician were blinded to the group assignment. Delivery and guidance on the administration of the light-cured gels was performed by a researcher not involved in the implementation.

A single investigator prepared the topical light-cured tetracaine-based anesthetic gel following the description of the patent (BR 10 2016 007724 9).[32] The placebo gel was formulated similarly, following all the steps of the light-cured tetracaine-based anesthetic gel except for inclusion of the anesthetic salt. The light-cured gels were formulated in the Pharmacy School of the local university with the following reagents: tetracaine hydrochloride (5%), inhibitors, monomers, photoinitiators, coinitiators, dyes, and inert filler. The gels had a viscosity similar to that used in light-cured gingival barriers used for in-office bleaching. The anesthesia produced by the gel took approximately 40 minutes, reaching peak 10 minutes after application.

Both gels were transferred to dark syringes to avoid contact with light and to prevent foreknowledge of the group assignment during application. The syringes were marked only with numbered codes so that neither the operators nor the patients could identify them.

Study Intervention

One researcher was responsible for applying the gels and placing and adapting the rubber dam clamp. Another researcher was responsible for the restorative treatment. First, patients were instructed about all the steps of the treatment and the possible sensations they could experience during clamp adaptation. We made it clear that if there was any objectionable discomfort, an injectable anesthesia would be applied.

The side of the dental arch to be treated was isolated with cotton rolls and saliva ejectors, and the anesthetic gel or placebo gel was placed, with the aid of a syringe tip, in the gingival tissue around the tooth to be restored. The gel was placed 2 mm away from the gingival margin and extended approximately 2 mm beyond the gingival margin on both sides (facial and lingual). The gel was left in place for 15 seconds and then light-cured for 15 seconds with a light-emitting diode light-curing unit (Radii-cal, SDI, Bayswater, Australia) set at 1200 mW/cm^2. A #212 clamp (Duflex-SS White, Rio de Janeiro, Brazil) was positioned with a door-clamp gripper for adaptation check. At this moment, we asked the patient if he or she felt pain or discomfort. If the answer was positive, the clamp was removed, the intensity of pain/discomfort was recorded (as described in the next section), and an injectable anesthesia (2% lidocaine with epinephrine 1:100,000; Alphacaine; DFL, Rio de Janeiro, Brazil) was applied. The rubber dam was then installed and the clamp placed. Placement of the anesthetic gel did not interfere with clamp placement.

For restoration placement, the enamel surface was etched with 37% phosphoric acid for 15 seconds (Condac 37; FGM, Joinville, Brazil), followed by water washing (15 seconds) and drying with an air stream (10 seconds) keeping the dentin moist. Two coats of the two-step etch-and-rinse adhesive Ambar (FGM) were applied and the solvent evaporated with an air stream for five seconds. The adhesive was light cured for 20 seconds with the same light curing device. The composite resin Opallis (FGM) was incrementally placed and each increment light-cured for 20 seconds. The restorative steps were performed by a calibrated investigator.

Assessment of the Outcome

All outcomes were measured just after placement of the #212 clamp, as it is the most critical phase in terms of pain sensation during the procedure. The odds of having pain (yes or no) was obtained for each group and organized in a 2×2 table for paired data to allow the calculation of the odds ratio. Pain intensity was further evaluated using two different pain scales:

1. Visual analog scale (VAS)[33]: This scale is a 10-cm horizontal line labeled from 0 to 10, where 0 = no pain and 10 = unbearable pain. The patient marked the intensity of the pain with a vertical line across the horizontal line of the scale. Then, the distance in millimeters from 0 to the vertical marked line was measured with the aid of a millimeter ruler.
2. Verbal rating scale (VRS)[20,34,35]: The patient was asked to indicate the numeric value of the degree of pain using a five-point numeric rating scale in which 0 = none, 1 = mild, 2 = moderate, 3 = considerable, and 4 = severe.

Statistical Analysis

We performed the analysis following the intention-to-treat protocol, and we involved all participants who were randomly assigned.[31] We compared the odds of pain and need for rescue anesthesia for both groups using the McNemar test (α=0.05). We calculated the odds ratio (OR) of pain and the need for rescue anesthesia along with the confidence interval (CI) for the effect size. Correlation coefficients were calculated using the Spearman correlation for data on risk of pain and for rescue anesthesia.

We performed the comparison of pain intensity (VAS and VRS) using the Wilcoxon signed-rank test, as data did not follow normal distribution. Correlation coefficients for the paired data for each outcome were calculated. In all statistical tests, the significance level was set at 0.05. We performed all analyses by using the software Sigma Plot version 11.0 (Systat Software Inc, San Jose, CA, USA).

RESULTS

Characteristics of Included Participants

Clinical dental examinations were performed for a total of 120 adults; 50 met the eligibility criteria (Figure 1). Patient age ranged from 25 to 66 years (mean age, 40.4±1.0 years); the percentage of men was 40% , and the most treated teeth were the two lower first premolars (FDI two-digit notation: teeth number 34 and 44), which represented 36% of the sample.

Adherence to the Protocol and Dropouts

Treatment was performed on all participants who qualified, and no missing data were observed. Figure 1 depicts the flow diagram for the different phases of the study design.

No patient felt pain during the restorative procedure and the light-cured gel was not reapplied during any restorative procedure. The restorative procedure took approximately 20±5 minutes.

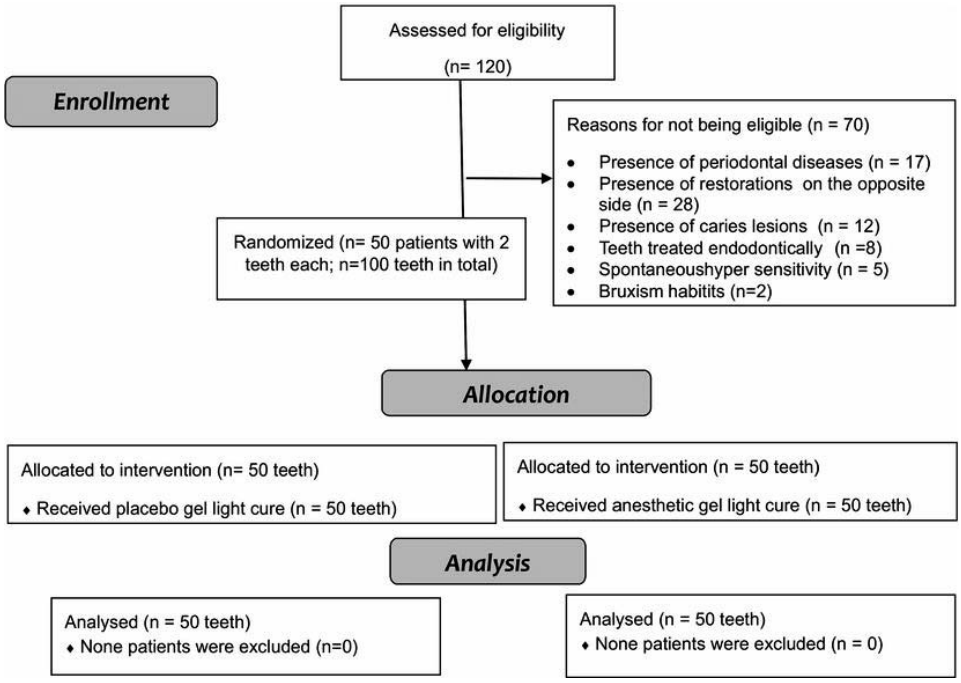

Figure 1. *Flow diagram of the split-mouth clinical trial, including detailed information regarding the excluded participants.*

Odds and Intensity of Pain

The absolute risk of pain in the side where placebo was applied was 56% (95% CI=42% to 68%); while for the anesthetic gel it was 36% (95% CI=24% to 50%) with an absolute risk difference of 20% (95% CI=0.5% to 37%). The number needed to treat was five, meaning that one patient will not report pain for every five patients being treated.

A total of 28 patients presented pain in the placebo group, and from this total, 14 patients reported pain exclusively in the side where the placebo gel was applied, immediately after the placement of the #212 clamp.

When the light-cured tetracaine-based anesthetic gel was used, the number of patients who reported pain was only 18. In comparative terms between groups, the OR for pain (Table 1; OR=3.5; 95% CI=1.1 to 14.6) was on average 3.5 times lower for the light-cured tetracaine-based anesthetic gel, and a statistically significant difference between groups was detected (Table 1; p=0.03).

The phi correlation coefficient using the Spearman test for pairs of binary data was low but significant (–0.2; p=0.04).

Pain Intensity

Pain intensity was positively correlated in both groups. The correlation was moderate for the VAS scale (Table 2, r=0.50; $p<0.0001$) and weak for the VRS scale (Table 2; r=0.43; p=0.001). The mean differences in pain intensity between light-cured tetracaine-based anesthetic gel and placebo gel groups were significant for both scales (VAS: Table 3; p=0.005 and VRS: Table 3; p=0.015). On average, pain intensity reduction was small, being one VAS unit lower in the light-cured tetracaine-based anesthetic group compared with the placebo group (95% CI=–2.3 to –0.3; Table 2). For the VRS scale, the

Table 1: *Matched Tabulation of Outcomes With the Two Treatments Along with the Odds Ratio**

Placebo Gel	Light-cured Anesthetic Gel			Odds Ratio (95% Confidence Interval)
	Positive	Negative	Total	
Positive	14	14	28	3.5 (1.1 to 14.6)
Negative	4	18	22	
Total	18	32	50	

** McNemar test (p=0.03). Correlation coefficient using the Spearman test = –0.2 (p=0.04).*

Table 2: *Means ± Standard Deviations of Pain Intensity for Both Groups Using the Two Pain Scales, as well as, mean difference and the Correlation Coefficient of the Paired Data*

Pain Scale	Means ± Standard Deviation		Mean Difference (95% Confidence Interval)	Correlation Coefficient (*p*-Value)*
	Light-cured Anesthetic Gel	Placebo Gel		
Visual analog scale (0-10 cm)	2.4±2.9	3.4±2.8	–1 (–2.3 to –0.3)	0.50 ($p<0.0001$)
Verbal rating scale (0-4)	0.8±1.0	1.2±1.1	–0.4 (–0.9 to –0.07)	0.43 ($p=0.001$)

* *Wilcoxon signed-rank test.*

light-cured tetracaine-based gel was 0.4 units lower than placebo (95% CI=–0.9 to –0.07; Table 2).

Odds of Rescue Anesthesia

In all patients who required rescue anesthesia, the injection was performed immediately after placement of the #212 clamp. In comparative terms, the OR for rescue anesthesia (Table 4; OR=2.5; 95% CI=0.7 to 10.9) was on average 2.5 times lower for the light-cured tetracaine-based anesthetic gel, but it did not reach statistical significance (Table 4; $p=0.18$). The phi correlation coefficient using Spearman test for pairs of binary data was low but significant (–0.12; $p=0.20$).

Adverse Effects

No adverse effects were observed or related by patients during this study.

DISCUSSION

This study demonstrated that the newly developed light-cured tetracaine based anesthetic gel can provide a slight reduction in the risk for and intensity of pain related to clamp placement. This finding is a result of an appropriately designed trial that followed the principles of proper randomization, allocation, and blinding of operator, patient, and statistician, thereby reducing selection and performance bias.[36]

This new light-cured tetracaine-based anesthetic gel has two main differences from topical anesthetic gels available in the market: the salt used for the anesthetic purpose and the vehicle of application. In this new light-cured anesthetic gel, we used tetracaine instead of prilocaine and lidocaine as tetracaine is more potent.[29,37] Tetracaine is an ester with higher analgesic efficacy[38] and long duration, which is related to its higher hydrophobicity that promotes a prolonged interaction with the sodium channel binding site, resulting in a higher efficacy than other anesthetics.[17,18,39]

Although we have not compared this new light-cured tetracaine-based anesthetic gel with others in the market, from a clinical standpoint, it is clear that the light-cured gel does not flow away from the applied site. This keeps the product from being diluted by saliva and keeps it in the site to be anesthetized, which is an advantage over products marketed as spray, ointment, gel, or adhesive.[30,40,41]

The purpose of this study was to assess the efficacy of the gel against a placebo. We are currently conducting a randomized clinical trial to compare this light-cured tetracaine-based anesthetic gel with other commercial products on the dental market.

Even though the use of a clamp to restore NCCLs is very common, studies that compare the pain associated with this procedure are rare. A recent article showed that 70% of patients reported pain when adapting a #212 clamp or retraction cord without any topical anesthetic. In these cases, injectable anesthesia was required most of the time.[11] The risk of pain during clamp placement in this earlier study[11] was very similar to the results of the present study; 56% of patients reported pain during clamp placement. Therefore, the performance of our new light-cured topical anesthetic gel is an interesting finding because a 20% reduction in the risk of pain was observed. It may be an alternative to replace injectable anesthesia in some cases, thereby

Table 3: *Medians and Interquartile Range of Pain Intensity for Both Groups Using the Two Pain Scales*

Pain Scale	Medians (Interquartile Range)		*p*-Value*
	Light-cured Anesthetic Gel	Placebo Gel	
Visual analog scale (0-10 cm)	1.2 (0-3.8)	3 (1.0-5.6)	0.005
Verbal rating scale (0-4)	0 (0-1)	1 (0-2)	0.015

* *Wilcoxon signed-rank test.*

Table 4: *Comparison of the Number of Patients Who Required Rescue Anesthesia in Both Groups Along With the Absolute and the Odds Ratio**

Placebo Gel	Light-cured Anesthetic Gel			Odds Ratio (95% Confidence Interval)
	Positive	Negative	Total	
Positive	10	10	20	2.5 (0.7 to 10.9)
Negative	4	26	30	
Total	14	36	50	

** McNemar test (p=0.18). Correlation coefficient using Spearman test=–0.12 (p=0.2).*

overcoming the patient's fear of needles and the numbness related to local anesthesia.

Some studies have tested the adaptation of a clamp in children undergoing rubber dam isolation for the placement of sealants[23,24,30] and have had positive results for light-cured tetracaine-based anesthetic gel, corroborating the findings of our study. It is known that because of the anatomy of NCCLs, which often present subgingival margins, there is need of gingival retraction, and retraction requires an effective gel containing a potent anesthetic salt.

From a clinical perspective, we may say that a reduction of 20% was observed in the risk of pain. This means that for every five patients needing treatment, one did not experience pain with the anesthetic gel. The number of patients that required for rescue anesthesia was not different between groups as it depends on whether the patient considers the discomfort bearable or unbearable.[22]

Finally, we should discuss the limitation of the present study. The intensity and risk of pain are subjective measures, and therefore depend on individual interpretation.[42,43] When the patient reported pain on the first side treated, there was a tendency to feel pain on the opposite side. As the gels were randomized, this bias was minimized, but probably not completely eliminated. Further well-delineated clinical studies should be conducted to compare the use of different gels for clamp adaptation in NCCLs to minimize pain.

CONCLUSION

The new light-cured tetracaine-based anesthetic reduced the risk of pain in 20% of patients. Those who experienced pain had a pain intensity that was one unit lower (VAS 0-10) than the placebo gel.

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Regulatory Statement

This study was conducted in accordance with all the provisions of the local human subjects oversight committee guidelines and policies of the State University of Ponta Grossa. The approval code for this study is 974.479.

Conflict of Interest

The authors of this manuscript certify that they have no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this article.

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REFERENCES

1. Bartlett DW & Shah P (2006) A critical review of non-carious cervical (wear) lesions and the role of abfraction, erosion, and abrasion *Journal of Dental Research* **85(4)** 306-312.
2. Wood I, Jawad Z, Paisley C, & Brunton P (2008) Non-carious cervical tooth surface loss: a literature review *Journal of Dentistry* **36(10)** 759-766.
3. Yang J, Cai D, Wang F, He D, Ma L, Jin Y, & Que K (2016) Non-carious cervical lesions (NCCLs) in a random sampling community population and the association of NCCLs with occlusive wear *Journal of Oral Rehabilitation* **43(12)** 960-966.
4. Reis A, de Geus JL, Wambier L, Schroeder M, & Loguercio AD (2018) Compliance of randomized clinical trials in noncarious cervical lesions with the CONSORT statement: A systematic review of methodology *Operative Dentistry* **43(3)** E129-E151.
5. Loguercio AD, Reis A, Barbosa AN, & Roulet JF (2003) Five-year double-blind randomized clinical evaluation of a resin-modified glass ionomer and a polyacid-modified resin in noncarious cervical lesions *Journal of Adhesive Dentistry* **5(4)** 323-332.
6. Pena CE, Rodrigues JA, Ely C, Giannini M, & Reis AF (2016) Two-year randomized clinical trial of self-etching adhesives and selective enamel etching *Operative Dentistry* **41(3)** 249-257.
7. Zander-Grande C, Amaral RC, Loguercio AD, Barroso LP, & Reis A (2014) Clinical performance of one-step self-etch

adhesives applied actively in cervical lesions: 24-month clinical trial *Operative Dentistry* **39(3)** 228-238.

8. Schroeder M, Correa IC, Bauer J, Loguercio AD, & Reis A (2017) Influence of adhesive strategy on clinical parameters in cervical restorations: A systematic review and meta-analysis *Journal of Dentistry* **62** 36-53.
9. Cobanoglu N, Unlu N, Ozer FF, & Blatz MB (2013) Bond strength of self-etch adhesives after saliva contamination at different application steps *Operative Dentistry* **38(5)** 505-511.
10. Aboushelib MN (2011) Clinical performance of self-etching adhesives with saliva contamination *Journal of Adhesive Dentistry* **13(5)** 489-493.
11. Loguercio AD, Luque-Martinez I, Lisboa AH, Higashi C, Queiroz VA, Rego RO, & Reis A (2015) Influence of isolation method of the operative field on gingival damage, patients' preference, and restoration retention in noncarious cervical lesions *Operative Dentistry* **40(6)** 581-593.
12. Brunthaler A, Konig F, Lucas T, Sperr W, & Schedle A (2003) Longevity of direct resin composite restorations in posterior teeth *Clinical Oral Investigations* **7(2)** 63-70.
13. Heintze SD, Ruffieux C, & Rousson V (2010) Clinical performance of cervical restorations—A meta-analysis *Dental Materials* **26(10)** 993-1000.
14. Raskin A, Setcos JC, Vreven J. & Wilson NH (2000) Influence of the isolation method on the 10-year clinical behaviour of posterior resin composite restorations *Clinical Oral Investigations* **4(3)** 148-152.
15. Boyce RA, Kirpalani T, & Mohan N (2016) Updates of topical and local anesthesia agents *Dental Clinics of North America* **60(2)** 445-471.
16. Armfield JM & Heaton LJ (2013) Management of fear and anxiety in the dental clinic: A review *Australian Dental Journal* **58(4)** 390-407; quiz 531.
17. Kudo M (2005) Initial injection pressure for dental local anesthesia: effects on pain and anxiety *Anesthesia Progress* **52(3)** 95-101.
18. Kumar M, Chawla R, & Goyal M (2015) Topical anesthesia *Journal of Anaesthesiology, Clinicsl Pharmacology* **31(4)** 450-456.
19. Winning L, Polyzois I, Nylund K, Kelly A, & Claffey N (2012) A placebo-controlled trial to evaluate an anesthetic gel when probing in patients with advanced periodontitis *Journal of Periodontology* **83(12)** 1492-1498.
20. Mayor-Subirana G, Yague-Garcia J, Valmaseda-Castellon E, Arnabat-Dominguez J, Berini-Aytes L, & Gay-Escoda C (2013) Anesthetic efficacy of oraqix® versus hurricaine® and placebo for pain control during non-surgical periodontal treatment *Medicina Oral, Patología Oral y Cirugía Bucal* **19(2)** 192-201.
21. Wambier LM, de Geus JL, Boing TF, Chibinski ACR, Wambier DS, Rego RO, Loguercio AD, & Reis A (2017) Intrapocket topical anesthetic versus injected anesthetic for pain control during scaling and root planing in adult patients: Systematic review and meta-analysis *Journal of the American Dental Association* **148(11)** 814-824.e812.
22. Wambier LM, de Geus JL, Chibinski AC, Wambier DS, Rego RO, Loguercio AD & Reis A (2016) Intra-pocket anaesthesia and pain during probing, scaling and root planing: a systematic review and meta-analysis *Journal of Clinical Periodontology* **43(9)** 754-766.
23. Lim S & Julliard K (2004) Evaluating the efficacy of EMLA topical anesthetic in sealant placement with rubber dam *Pediatric Dentistry* **26(6)** 497-500.
24. Yoon RK & Chussid S (2009) Topical anesthesia for rubber dam clamp placement in sealant placement: Comparison of lidocaine/prilocaine gel and benzocaine *Pediatric Dentistry* **31(5)** 377-381.
25. Valieri MM, de Freitas KM, Valarelli FP, & Cancado RH (2014) Comparison of topical and infiltration anesthesia for orthodontic mini-implant placement *Dental Press Journal of Orthodontics* **19(2)** 76-83.
26. Daneshkazemi A, Abrisham SM, Daneshkazemi P & Davoudi A (2016) The efficacy of eutectic mixture of local anesthetics as a topical anesthetic agent used for dental procedures: A brief review *Anesthesia, Essays and Researches* **10(3)** 383-387.
27. Friskopp J, Nilsson M, & Isacsson G (2001) The anesthetic onset and duration of a new lidocaine/prilocaine gel intra-pocket anesthetic (Oraqix®) for periodontal scaling/root planing *Journal of Clinical Periodontology* **28(5)** 453-458
28. Nayak R & Sudha P (2006) Evaluation of three topical anaesthetic agents against pain: A clinical study *Indian Journal of Dental Research* **17(4)** 155-160.
29. Meechan JG (2000) Intra-oral topical anaesthetics: A review *Journal of Dentistry* **28(1)** 3-14.
30. Stecker SS, Swift JQ, Hodges JS, & Erickson PR (2002) Should a mucoadhesive patch (DentiPatch) be used for gingival anesthesia in children? *Anesthesia Progress* **49(1)** 3-8.
31. Pandis N, Chung B, Scherer RW, Elbourne D, & Altman DG (2017) CONSORT 2010 statement: Extension checklist for reporting within person randomised trials *BMJ* **357** j2835.
32. Wambier LM, Farago PV, Loguercio AD, & Reis A (2016) Processo de obtenção de barreira gengival anestésica fotoativada **BR 10 2016 007724 9** 1-22 [in Portuguese].
33. Herdevall BM, Klinge B, Persson L, Huledal G, & Abdel-Rehim M (2003) Plasma levels of lidocaine, o-toluidine, and prilocaine after application of 8.5 g Oraqix in patients with generalized periodontitis: Effect on blood methemoglobin and tolerability *Acta Odontologica Scandinavica* **61(4)** 230-234.
34. Breivik H, Borchgrevink PC, Allen SM, Rosseland LA, Romundstad L, Hals EK, Kvarstein G, & Stubhaug A (2008) Assessment of pain *British Journal of Anaesthesia* **101(1)** 17-24.
35. Derman SHM, Lowden CE, Kaus P, & Noack MJ (2013) Pocket-depths-related effectiveness of an intrapocket anaesthesia gel in periodontal maintenance patients *International Journal of Dental Hygiene* **1(1)** 1-4.
36. Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, & Sterne JA

for the Cochrane Bias Methods Group & Cochrane Statistical Methods Group (2011) The Cochrane Collaboration's tool for assessing risk of bias in randomised trials *British Medical Journal* **343** d5928.

37. Giordano D, Raso MG, Pernice C, Agnoletti V, & Barbieri V (2015) Topical local anesthesia: focus on lidocaine-tetracaine combination *Local and Regional Anesthesia* **8** 95-100.
38. Milam SB & Giovannitti JA, Jr. (1984) Local anesthetics in dental practice *Dental Clinics of North America* **28(3)** 493-508.
39. Becker DE & Reed KL (2012) Local anesthetics: Review of pharmacological considerations *Anesthesia Progress* **59(2)** 90-101; quiz 102-103.
40. Koppolu P, Mishra A, Swapna LA, Butchibabu K, Bagalkokar A, & Baroudi K (2016) Comparison of efficacy among various topical anesthetics: An approach towards painless injections in periodontal surgery *Saudi Journal of Anaesthesia* **10(1)** 55-57.
41. Roh J, Han M, Kim KN, & Kim KM (2016) The in vitro and in vivo effects of a fast-dissolving mucoadhesive bi-layered strip as topical anesthetics *Dental Materials Journal* **35(4)** 601-605.
42. Chesterton LS, Barlas P, Foster NE, Baxter GD, & Wright CC (2003) Gender differences in pressure pain threshold in healthy humans *Pain* **101(3)** 259-266.
43. Renton T (2015) Pain. Part 1: Introduction to pain *Dental Update* **42(2)** 109-112, 114-106, 118-120 passim.