INDIRECT PULP PROTECTION AFTER SELECTIVE CARIES REMOVAL: A PRELIMINARY 6 MONTHS RANDOMISED CONTROLLED TRIAL

Proteção pulpar indireta após a remoção seletiva de tecido cariado: acompanhamento de 6 meses de um ensaio clínico randomizado controlado

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ABSTRACT

This randomized controlled clinical trial evaluated the effectiveness of using indirect pulp protection with calcium hydroxide liner or universal adhesive over a period of 6 months in deep caries on permanent teeth after selective removal to soft dentin. The sample consisted of 68 patients with 55 molars and 21 premolars with deep caries lesion (with radiographic involvement ≥ 50% dentin deep caries), (median age 27 [distribution 7-54 years]), with signs of pulp vitality (positive response to cold test, absence of spontaneous pain, negative sensitivity to percussion tests, absence of radiographic imaging suggestive of periapical lesion) and absence of cuspid loss. After selective removal to soft dentin, the test group received a universal adhesive (n = 38), whereas the control group indirect pulp protection with Calcium hydroxide (n = 38). All teeth were restored with composite resin. The successful outcome for pulp vitality was assessed after six months. The results were submitted to the Kaplan-Meier survival analysis and the Log Rank test. The baseline variables were analyzed for their distribution in the two treatment groups by x² test and showed a similarly distributed between groups. Success rates to pulp maintenance vitality were 95.5% for the control group and 96.7% for the test group (P = 0.986). Two cases of failure were recorded, one pulp necrosis (control group) and one pulpitis (test group). There is no difference between the use of calcium hydroxide or only universal adhesive in indirect pulp protection after selective removal to soft dentine followed by composite restoration at six months of follow-up, showing a high rate of success for both treatments.

Keywords: Dental caries. Calcium hydroxide. Clinical trial.
RESUMO

Este ensaio clínico controlado randomizado avaliou a eficácia da proteção pulpar indireta com cimento de hidróxido de cálcio ou apenas adesivo universal na remoção seletiva de dentina amolecida em dentes permanentes após 6 meses de tratamento. A amostra consistiu de 68 pacientes com 55 molares e 21 pré-molares com lesão profunda de cárie (envolvimento radiográfico ≥ 50% da dentina), (mediana de idade 27 [distribuição 7-54 anos]), com sinais de vitalidade pulpar (resposta positiva ao teste frio, ausência de dor espontânea, sensibilidade negativa aos testes de percussão, ausência de imagem radiográfica sugestiva de lesão periapical) e ausência de perda cúspidea. Após remoção seletiva do grupo teste recebeu adesivo universal (n = 38) e o grupo controle cimento de hidróxido de cálcio (n = 38) como proteção pulpar indireta. Todos os dentes foram restaurados com resina composta. Os resultados de vitalidade pulpar foram avaliados após seis meses e submetidos à análise de sobrevivência de Kaplan-Meier e ao teste Log Rank. As variáveis explanatórias iniciais foram analisadas quanto à sua distribuição nos grupos de tratamento pelo teste x² e mostraram distribuição similar. O sucesso na manutenção da vitalidade pulpar foi de 95,5% para o grupo controle e 96,7% para o grupo teste (P = 0,986). Duas falhas foram registradas, uma necrose pulpar (grupo controle) e uma pulpite (grupo teste). Resultados sugerem que não há diferença entre o uso de hidróxido de cálcio e/ou apenas adesivo universal após remoção seletiva de dentina amolecida e restauração de resina composta em 6 meses de acompanhamento, com alta taxa de sucesso nos dois tratamentos.

Palavras-chave: Cárie dentária. Hidróxido de cálcio. Ensaio clínico.

INTRODUCTION

The treatment of deep caries lesion has advocated liners on the pulp floor to maintain pulp vitality. Most studies showed calcium hydroxide lining as the most commonly liners in indirect pulp protection to reduce the number of residual viable bacteria, remineralize dentine, induce reactionary dentine, isolate the pulp, and protect pulpal cells from noxious stimuli2. However, data regarding clinical outcomes in permanent teeth are sparse3. The expected effects of liners might depend on which removal strategy for carious tissue is performed2.

Selective removal to soft dentin (SRSD) is strongly recommended because it provides higher successful outcomes for deep lesions5. In the permanent dentition, there is only one randomized clinical trial (RCT) conducted with lesions reaching the inner half of dentin showing a success rate of 80% over 5 years of monitoring6. The advantage of SRSD is to prevent pulp exposure – it is recommended to keep a thick layer of demineralized soft carious dentin over the pulp once low success rate is observed in direct pulp capping5-6. In a pulp exposed during caries removal, only 9% of the analyzed patients were assessed as successful, which indicates that the prognosis is highly dubious and follows conventional pulp-capping procedures – direct pulp capping or partial pulpotomy7.

Indirect pulp protection has been referred in deep caries lesion. Calcium hydroxide liner is used as capping material for the indirect pulp protection technique, in both permanent and primary teeth8. Based on a recent meta-analysis of three randomized clinical trials with primary teeth, current evidence does not support strong recommendations to use calcium hydroxide cement to maintain pulpal vitality after SRSD and before cavities restoration3. On the other hand, the application of an adhesive restorative system in the irreversibly infected dentin has not affected the pulp vitality in primary teeth8-10. Studies in primary teeth show that carious dentin was partially demineralized and contained mineral crystals within the tubules, and the hybrid layers of caries-affected dentin were thicker and more porous than the ones in sound dentin11. Adhesive system on carious dentin resulted in an altered hybrid layer with no signs of demineralization that could suggest a lesion progression12.
The evolution of adhesive systems as self-etching and universal adhesive, different from etch-and-rinse adhesives, not require a separate etching step, as they contain acidic monomers that simultaneously ‘condition’ and ‘prime’ the dental substrate. In general, self-etch adhesives have the advantage to demineralise and infiltrate the tooth surface simultaneously at the same depth, theoretically ensuring complete penetration of the adhesive\textsuperscript{13}. With increasing depth, the acidic monomers are gradually buffered by the mineral content of the substrate, loosing their ability to further etch dentin\textsuperscript{14,15}. The use of a self-etching primer would prevent carious dentin over-etching\textsuperscript{10}.

The aim of this study was to compare the outcomes of Calcium hydroxide liner or only Universal Adhesive in pulp indirect protection performed on deep caries lesion after SRSD regarding conservation of pulp vitality in 6 months follow-up period.

The null hypothesis of this study is that there is no difference regarding the maintenance of pulp vitality in permanent teeth using or not a liner material over demineralized dentin.

**Materials and methods**

This is a parallel randomized controlled clinical trial conducted in the Federal University of Rio Grande do Sul (UFRGS), Porto Alegre, RS, Brazil (registration number at http://www.ensaiosclinicos.gov.br RBR – 65ntbc). The clinical treatments were carried out by three operators (R.S.A., A.R., R.F.) and the follow-up of six-month by two researchers (R.S.A, A.R.), who were updated and trained before the beginning of the clinical procedures by an expert researcher (J.J.J.).

All participants and parents/legal guardians read and signed an informed consent form for this study. The study was approved by the Federal University of Rio Grande do Sul Ethics Committee (protocol nº 1.016.220). The experimental design of the study followed CONSORT statement.

**Sample**

Subjects were recruited from School of Dentistry of the Federal University of Rio Grande do Sul, local public schools and health public services in Porto Alegre-RS, Brazil. Subjects with uncompensated systemic diseases affecting their caries experience were not included from the sample. The experimental unit of this study was the tooth. This sample was composed of 68 patients presenting 76 deep carious lesions (radiograph depth reaching half or more of the dentine thickness). This study is a secondary outcome of a RCT that aimed to evaluate composite restorations placed after selective removal to soft dentin or stepwise excavation. The first 76 deep caries lesions treated in the large RCT were included in the present study. Sample size calculation was performed using www.openepi.com and showed that 37 patients were needed in each group to detect a 30% difference in the success rate between indirect pulp protection with calcium hydroxide liner or universal adhesive at a two-sided alpha level of 5% (type I error) and 80% power (type II error of 20%).

In the present study, the comparison between different indirect pulp protection materials was evaluated 6-month follow-up. Teeth that received SRSD were randomized for test or control groups. The control group received calcium hydroxide liner (Dycal®, Dentisply, Brazil) (CH n = 38), while the test group received universal adhesive system (Universal Single Bond®, 3M Espe, Brazil) (UA n = 38), followed by adhesive restoration in one session. Details of the study design can be seen in Figure 1.
**Inclusion criteria**

Patients presenting premolars and/or permanent molars exhibiting primary occlusal and/or occlusal-proximal deep caries lesion (depth reaching half or more of the dentine thickness, diagnosed by bite-wing radiographic) with signs of pulp vitality measured by absence of spontaneous pain, negative sensitivity to vertical and horizontal percussion, positive response to cold test (refrigerated gas; -50 °C Endo-ice, Maquirá®, Brazil), absence of periapical lesions assessed by radiographic examination (VistaScan® Dürr dental).

**Exclusion criteria**

Patients presenting premolars and/or permanent molars exhibiting cuspal loss, caries beneath the gingival margin and poor prognosis for teeth with advanced periodontal disease.

**Calibration**

The calibration of the operators for the dental examination was performed through clinical examination of 10 patients. The inter-examiners Kappa obtained was 0.83 and the intra-examiner Kappa value was ≥ 0.8 for the three operators.

**Randomization and Blinding Procedures**

Selected teeth were randomly assigned for two experimental groups to indirect pulp protection: calcium hydroxide liner (control group) or universal adhesive system (test group). The randomized sequence was generated through the website randomization.com. Allocation concealment was secured by keeping the randomization sequence in separated sequentially numbered dark envelopes. Inside the envelopes, a carbon paper was kept and, just before the envelope opening, the participant or his/her legal guardian signed the front part of the envelope, also the date was registered. The randomization procedure was performed after the SRSD was concluded. The envelopes were opened by a person who was not involved in the study.

The evaluators and participants were blinded to the indirect pulp protection material, as well as the statistician.

**Clinical and Radiographic Procedures**

All the patients received local anesthesia and rubber dam isolation. The treatments were performed as follows:

- Access to the lesion by using rotatory instruments as diamond points (if necessary).
- Remove to hard tissue from peripheral enamel and dentine by using rotatory instruments as low-speed metal burs or high-speed diamond points and hand excavator to check the hardness criteria.
- Selective removal to soft dentin, formerly defined as removal of the superficial necrotic and demineralized dentine with hand excavators\(^6\). Soft carious tissue was left over the axio/pulp wall to avoid exposure and “stress” to the pulp\(^2\).
- Cleaning with distilled water and drying with sterile filter paper.
- Group Randomization: randomization was performed to indirect pulp protection: Control group (Dycal®, Dentisply, RJ, Brazil) or Test Group (Universal Single Bond®, 3M Espe, SP, Brazil).
All cases received:

- Selective enamel etching 37% (fosforic acid, Condac 37 – FGM, Brazil), 20s and washing for 20s.
- Universal adhesive system (Single Bond Universal®) applied with microbrush in enamel and dentin walls and rubbed it in for 20s.
- Gently air-dry the adhesive for approximately 5s for the solvent evaporate.
- Light cure for 20s (Bluephase, Ivoclar-Vivadent, Brazil).
- Nanoparticulate composite (Filtek Z350®, 3M Espe, Brazil) performed by increment-mental technique.
- Light cure for 20s in each 2mm increment (Bluephase, Ivoclar-Vivadent, Brazil).
- Occlusal adjust, finishing and polishing with diamont points (nº 1190 F, KG So-rensen, Cotia, SP, Brazil) and Sof-Lex Espiral (3M, SP, Brazil).

Standardized radiographs using a positioner (Jon®, Brazil). Digital radiographs (VistaScan Perio: Germany) were obtained with phosphate storage plates with VistaScan Perio (Dürr Dental, Germany) and Astex Odontomax (São Paulo, Brazil), radiographic apparatus operating at 70 kVp, 7mA and time exposure time of 0.6 seconds.

**Clinical and Radiographic Evaluations**

The radiological exams were performed during screening (periapical and bitewing radiography), right after the restoration (bite-wing radiography), and after 6 months (periapical and bitewing radiography).

Clinical evaluations of the pulp vitality were carried out by a trained dentist who wasn’t the operator of the case and was blinded to the liner material.

This study was conducted following an intention-to-treat analysis; protocol deviations were included in the study sample. Cases of restoration failure, pulpitis, secondary caries, necrosis, periapical lesion, were treated and analyzed within the arm to which they had been randomized.

**Outcome**

This study considered success the maintenance of pulp vitality, defined as: positive response to cold test (-50 °C refrigerate test, Maquira, Brazil), absence of spontaneous pain, negative sensitivity to percussion tests, absence of digital radiographic imaging suggestive of periapical lesion.

**Statistics Analysis**

Baseline variables were recorded: age of subjects, gender, schooling, plaque index (< 20%; ≥ 20%), gingival bleeding index (< 20%; ≥ 20%) DMF-T (dichotomized according to the sample median < 9 or ≥ 9), DMF-S (dichotomized according to the sample median < 13.5 or ≥ 13.5), number of surfaces involved in the filling (dichotomized in one surface or two or more surfaces according to the distribution of this variable in the study sample); type of the tooth (molar or premolar), indirect pulp material (calcium hydroxide liner or universal adhesive system). The distribution of these variables between the groups was analyzed by qui-square test. Due to the reduced number of failures, correlation analysis between explanatory variables and outcome could not be performed. The success rate of the indirect pulp protection procedures was analyzed by Kaplan-Meyer survival test. The statistical significance of the data was determined at P < 0.05. All analyses were performed using the Statistical Package for Social Science (SPSS) software, version 21.0.
RESULTS

Patients with mean age of 27 (min 7 and max 54 years, medium 27 years) (20.5 percentile 25% and 36 percentile 75%). The sample consisted mostly of women (60%) and high school incomplete and complete (48,6%) (Table). Due to loss of follow-up, a total of 70 treatments were evaluated after 6 months of intervention (mean of 189, min 169 and max of 200 days) (Figure 1). A total of 70 treatments evaluated, 36 (51,42%) received calcium hydroxide liner (CH) followed by universal adhesive (UA) and 34 (48,58%) received only universal adhesive (UA), prior to adhesive composite restorations. Among the 68 subjects included in the study, 60 (88.2%) were given one treatment and 8 (11.8%) were given two treatments.

The survival analysis indicates rates success of 95.5% for the CH group and of 96.7% for the UA group (Kaplan-Meier test, Figure 2). The log-rank test has not revealed a significant difference among treatment groups (P = 0.986), which leads to a null hypothesis. Control group has presented one failure due to necrosis and test group has presented one failure due to irreversible pulpitis.

Moreover, no significant differences were noticed between the groups regarding base-line characteristics such as gender, schooling, plaque index, gingival bleeding index, number of restored surfaces, presence of antagonist, group of teeth, DMF-T and DMF-S (Qui-square test, see Table). Significant difference has been found in the age variable. Test group (UA) included older subjects (P = 0.008).

Visible Plaque Index (VPI) and Gingival Bleeding Index (GBI) have presented high values for both groups: 57.1%-60% of the patients presenting indexes over 20% respectively.

Most treated teeth were molar n = 55 (72.37%), whereas n = 21 (27.63%) were premolar teeth, and a multi-surface filling (two or more surfaces) composed n = 42 (55.2%) of the sample, whereas n = 34 (44.8%) were received one surface filling.

Table 1

| Variables        | CATEGORIZATION       | Total (100) | CH (51.42) | UA (48.57) | P value |
|------------------|----------------------|-------------|------------|------------|---------|
|                  | n (%)                | 36 (100)    | 36 (100)   | 34 (100)   |         |
| AGE              | <27y                  | 34 (48.6)   | 23 (63.9)  | 11 (32.4)  | >0.008  |
|                  | ≥27y                  | 36 (51.4)   | 13 (36.1)  | 23 (67.6)  |         |
| GENDER           | female                | 42 (60)     | 25 (59.5)  | 17 (40.5)  | >0.097  |
|                  | male                  | 28 (40)     | 11 (39.3)  | 17 (60.7)  |         |
| SCHOOLING        | Elemetary school in/complete | 23 (32.9) | 10 (27.8)  | 13 (38.2)  | >0.323  |
|                  | High school in/complete | 34 (48.6) | 17 (47.2)  | 17 (50)    |         |
|                  | Higher education in/complete | 13 (18.6) | 9 (25)     | 4 (11.8)   | >0.967  |
| VPI*             | <20                   | 30 (42.9)   | 16 (44.4)  | 14 (42.1)  | >0.782  |
|                  | ≥20                   | 40 (57.1)   | 20 (55.6)  | 20 (58.8)  |         |
| GBI*             | <20                   | 28 (40)     | 14 (38.9)  | 14 (41.2)  | >0.845  |
|                  | ≥20                   | 42 (60)     | 22 (61.1)  | 20 (38.8)  |         |
| PULP VITALITY    | yes                   | 68 (97.1)   | 35 (97.2)  | 33 (97.1)  | >0.967  |
|                  | no                    | 2 (2.9)     | 1 (2.8)    | 1 (2.9)    |         |
### Table 1 (cont.)

| Variables | CATEGORIZATION | Total 70 (100) | CH 36 (51.42) | UA 34 (48.57) | P value |
|-----------|---------------|----------------|---------------|---------------|---------|
| DMFT*     | Median        |                |               |               |         |
|           | <9            | 32 (45.7)      | 18 (50)       | 14 (41.2)     | >0.459  |
|           | ≥9            | 38 (54.3)      | 18 (50)       | 20 (58.8)     |         |
| DMFS*     | Median        |                |               |               |         |
|           | <13.5         | 35 (50)        | 19 (52.8)     | 16 (47.1)     | >0.632  |
|           | ≥13.5         | 35 (50)        | 17 (47.2)     | 18 (52.8)     |         |
| NUMBER OF| SURFACES*;    |                |               |               |         |
|           | 1              | 31 (44.3)      | 18 (50)       | 13 (38.2)     | >0.322  |
|           | ≥2             | 39 (55.7)      | 18 (50)       | 21 (61.8)     |         |
| GROUP OF TEETH | Premolar | 18 (25.7)      | 8 (22.2)      | 10 (29.4)     | >0.492  |
|           | Molar         | 52 (74.3)      | 28 (77.8)     | 24 (70.6)     |         |
| PRESENCE OF| ANTAGONIST¹   | yes            | 61 (87.1)     | 30 (83.3)     | 31 (91.2)| >0.459  |
|           | no             | 9 (12.9)       | 6 (16.7)      | 3 (8.8)       |         |
| DFMT-T°   | Median        |                |               |               |         |
|           | <9            | 32 (45.7)      | 18 (50)       | 14 (41.2)     | >0.459  |
|           | ≥9            | 38 (54.3)      | 18 (50)       | 20 (58.8)     |         |

Table baseline variables of the study, qui-square test P < 0.05. °VPI: Visible plaque index; GBI: gingival bleeding index. DFM-T: decay, missing, filled teeth, DFMT-S: decay, missing, filled surfaces; number of surfaces restored/tooth.

**Figure 1:** Flowchart of the study.
Discussion

To the best of our knowledge, this is the first randomized clinical trial that compares the use of an indirect pulp protection with calcium hydroxide liner (Dycal®) or universal adhesive system (Universal Single bond®) in permanent teeth after selective carious tissue removal to soft dentine. The six months follow-up results are important because studies on the evaluation of posterior tooth restorations longevity report that, it is in the first year of follow-up, failures occur due to endodontic reasons commonly17.

The main goal of SRSD is to avoid pulp injuries mainly due to its exposure during carious tissue removal5,18, because pulp exposure decreases the pulp survival. In five years of clinical follow-up, Bjørndal et al.7 reported only 9% of success in conventional pulp-capping procedures (direct pulp capping or partial pulpotomy). Although SRSD increases pulp viability, after SRSD, the majority of failures were found to be of pulpal origin19. The careful preoperative diagnosis of the pulp is the key to success in conservative treatment. In our study, pulp health diagnosis was verified with clinical (percussion and cold test) and radiographic exams as inclusion criteria in the research. The absence of pain usually does not exclude the presence of some inflammation. However, irrespective of the degree of inflammation, the majority of patients may respond to a percussion test, even though the teeth have minimal or no pulp inflammation20 and the presence of caries in vital teeth resulted in a more accurate response to cold testing when compared to electric pulp test21.

In a previously randomized clinical trial, the clinical success of SRSD, with indirect pulp protection with glass ionomer cement, was 99% for the first 18 months, 96% after 3 years, and 80% for the 5-year follow-up respectively22,23,4. The present study shows similar results (96.4% overall treatments – Kaplan Meier survival test), with indirect pulp protection with either Calcium hydroxide cement or universal adhesive.
Previous studies in permanent teeth have shown decrease in microbial load and dentine reorganization after cavity sealing independently of the indirect pulp protection material. However, there are few randomized trials evaluating the long-term indirect pulp protection after SRSD in permanent teeth. In these studies, the cavities are reopened after a short period to allow the microbiological and qualitative analysis of the morphological aspects in residual carious dentin. Randomized clinical trials with primary teeth show a successful outcome in longitudinal follow-ups when teeth received pulp protection with CH, only the adhesive system or gutta percha/wax. Schwendicke, in a systematic review, comparing indirect pulp protection material after SRSD in primary teeth did not observe superiority of calcium hydroxide (CH) cement.

The hybrid layer in affected and infected dentin in deep caries is less thick and more porous than in sound dentin. The higher porosity of the intertubular dentin occurs due to the mineral loss of caries process. One of the reasons for using self-etch adhesive systems would be minimized the adhesive monomers diffusion, also minimizing pulp reactions. On the other hand, resistant mineral acid deposition occludes dentin tubules. A comparison of three different adhesive strategies (one-step-self-etch, two-step-self-etch and two-step etch-and-rinse) resulted in lower bond strength to caries-affected dentin than to normal dentin for all adhesives. Clinically, this may not be a problem, since such lesions are normally surrounded by normal dentin or enamel. A previous 5-year follow-up did not show any loss of restoration in this period. In agreement, we choose a universal adhesive system that permit to use as self-etch (one-step). In the present study, there was no loss of restoration in 6 months follow-up.

Possible limitations of this study were that 6 months was a relatively short follow-up period to evaluate the long-lasting treatment success. However, previous study showed that the majority of failures happen during this period. Another limitation is the lack of masking of operators because they knew if liner material had to be applied, but this limitation is inherent to the study design.

**Conclusion**

The present study shows that in short-term (6 months follow-up) there was no difference in the maintenance of pulp vitality by using indirect pulp protection with calcium hydroxide liner or universal adhesive after SRSD followed by composite restoration and leads to the conditional acceptance of the null hypothesis.

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