

RESSALVA

Atendendo solicitação do(a)
autor(a), o texto completo desta tese
será disponibilizado somente a partir
de 31/07/2025.



UNIVERSIDADE ESTADUAL PAULISTA
"JÚLIO DE MESQUITA FILHO"
Campus de Araçatuba

Fernanda de Souza e Silva Ramos

**EFFECT OF DIFFERENT TREATMENTS ON DENTIN
HYPERSENSITIVITY: EVALUATION OF CYTOTOXICITY
AND RANDOMIZED CLINICAL STUDY**

ARAÇATUBA – SP
2023

Fernanda de Souza e Silva Ramos

**EFFECT OF DIFFERENT TREATMENTS ON DENTIN
HYPERSENSITIVITY: EVALUATION OF CYTOTOXICITY
AND RANDOMIZED CLINICAL STUDY**

Tese apresentada à Faculdade de Odontologia de Araçatuba da Universidade Estadual Paulista (Unesp),, como parte integrante dos requisitos para obtenção do título de Doutora, pelo Programa de Pós-Graduação em Odontologia, área de Concentração em Dentística.

Orientadora: Profa. Dra. Ticiane Cestari Fagundes

Catálogo na Publicação (CIP)

Diretoria Técnica de Biblioteca e Documentação – FOA / UNESP

R175e Ramos, Fernanda de Souza e Silva.
Effect of different treatments on dentin hypersensitivity :
evaluation of cytotoxicity and randomized clinical study /
Fernanda de Souza e Silva Ramos. - Araçatuba, 2023
84 f. : il. ; tab.

Tese (Doutorado) – Universidade Estadual Paulista,
Faculdade de Odontologia de Araçatuba
Orientadora: Profa. Ticiane Cestari Fagundes

1. Cell biology 2. Clinical trial 3. Dentin desensitizing
agents 4. Tooth abrasion 5. Tooth erosion 6. Dentin
sensitivity 7. I. T.

Black D2
CDD 617.6

Claudio Hideo Matsumoto – CRB-8/5550

Dedicat6ria

A Deus

Dedico este trabalho a Deus, pois ele tornou isso possível. Ele me deu força nas tormentas em que passei e não me dá fardo maior do que eu consiga carregar. Mesmo logo no início deste curso de doutorado, quando fomos assolados pela pandemia ele não me deixou desanimar. Ele ouviu meus apelos e orações e me guiou durante todo o caminho.

Aos meus pais

Por serem meu exemplo, minha fortaleza, por sempre me apoiarem em todas as tribulações que passamos. Mesmo estando longe, são presentes em minha vida diária, com os valores que me passaram e o amor que dedicam a mim. Alcançar esta conquista foi um feito nosso.

Ao meu irmão

Por ser meu parceiro, melhor amigo. Com quem posso conversar sobre tudo, seu jeito leve de levar a vida, me passava a tranquilidade necessária nos momentos de estresse. Por todas as vezes que, em meio as suas férias, vinha me visitar e me “buscar” para que eu pudesse descansar um pouco. Por todo o apoio que me deu durante as tribulações da pandemia.

Aos meus avós

Por serem um refúgio em toda a minha vida, por sempre torcerem por mim, mesmo quando a saúde não permite que façam mais. Agradeço por todo o apoio que me deram por toda a minha vida.

A minha avó Rosa Message Ramos

Dedico essa tese em memória à senhora, que acabou de nos deixar, após muito lutar. A senhora que sempre me apoiou em minhas escolhas, mas que infelizmente não me viu receber este título. Dedico ele a senhora, seu apoio em toda a minha vida foi o que me trouxe até aqui.

Agradecimentos
Especiais

AGRADECIMENTOS ESPECIAIS

A minha orientadora

Ticiane Cestari Fagundes

Por nos manter ativos mesmo durante as dificuldades da pandemia, por sempre acreditar em meu potencial. Por ser compreensiva com os desafios que se seguiram. Por insistir quando eu já havia desistido, o que me proporcionou conseguir uma bolsa FAPESP, mesmo chegando ao fim da minha jornada do doutorado. Pela paciência e seu olhar para detalhes, pelo incentivo e objetividade. Muito obrigada!

A minha amiga

Lara Maria Bueno Esteves

Por ser um anjo que me apareceu em Araçatuba. Aquela que passou as dificuldades junto a mim, sempre apoiando uma a outra. Muito obrigada pela paciência e força que me proporcionou. Um caminho de sucesso a aguarda, levarei você para a vida.

A minha amiga

Isabela Caroline de Sousa Ervolino

Por ser uma presença constante na minha vida a mais de 10 anos. Por tudo em que me ajudou, pela amizade. Por sempre vir e me tirar um pouquinho da rotina. Pela sua alegria constante, o sucesso já está acontecendo na sua vida, e só tende a crescer ainda mais.

A minha amiga

Ariane Rodrigues Barion

Por me abrir o caminho para vir para Araçatuba. Por me receber em sua casa na época em que tudo era apenas um sonho. Por ter pais maravilhosos que me receberam de braços abertos. Muito obrigada minha cara veterana da UFMS.

Aos meus amigos

Érika Mayumi Omoto, que tenho o prazer de acompanhar desde a iniciação científica, agora finalizando o mestrado, que você cresça cada vez mais futura doutoranda da professora Ticiane.

Karen Milaré Seicento Aidar, pela sua energia positiva, disposição. É a mais recente do mestrado, mas uma parceira, que me arrasta para a academia para ao menos mantermos a forma, neste departamento dos lanches e bolos.

Mariana Queiroz, pela convivência e parceria, apesar de obter um título em prótese, o coração será sempre da Dentística.

Caio César Pavani, agora professor do departamento, me honrou com sua presença em minha banca de qualificação, será sempre meu amigo de pós-graduação.

Aos meus colegas e amigos da Pós-graduação

Por sempre compartilhamos todos os momentos de alegria e dificuldades em nosso humilde departamento. Desejo a todos muitos sucessos nesta jornada.

As minhas alunas de iniciação científica

Larissa Albertinazzi e Vitória Marega Marchetti, pela paciência e disposição para desenvolver as pesquisas. Ambas possuem um futuro brilhante, pois possuem o comprometimento e a garra necessários para desenvolver e passar pelas dificuldades. Obrigada pela parceria e amizade que desenvolvemos.

Agradecimientos

AGRADECIMENTOS

À Faculdade de Odontologia do Campus de Araçatuba - UNESP, ao diretor Prof. Dr. Glauco Issamu Miyahara e ao vice-diretor Prof. Dr. Alberto Carlos Botazzo Delbem.

A Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) pelo Auxílio à Pesquisa (Processo nº 2020/07625-0) e pela Bolsa (Processo nº 2020-07443-9) que propiciaram o desenvolvimento deste trabalho.

Ao coordenador do curso de Pós-graduação em odontologia Prof. Wirley Gonçalves Assunção, pela disponibilidade e empenho para que o programa de pós-graduação seja de excelência.

Aos professores do curso de pós-graduação por todo o conhecimento que nos proporcionaram.

A Professora Cristiane Duque por abrir as portas do laboratório de Citologia e nos apoiar para o desenvolvimento deste trabalho.

A Professora Leticia Helena Theodoro por nos propiciar o contato com a Universidade de Toronto, o que nos proporcionou uma bela parceria.

Ao Professor Bernhard Ganss, da Universidade de Toronto, pela parceria e o fornecimento do material Amelotina.

Aos Professores Alberto Carlos Botazzo Delbem e Juliano Pelim Pessam, pela parceria em relação ao material trimetafosfato de sódio.

A Marina Trevelin Souza da Universidade Federal de São Carlos, que nos proporcionou o material Biosilicato.

Aos colegas e amigos do laboratório de Citologia, por sempre me receberem de braços abertos e por terem a paciência de me ensinar quando necessário, em especial a Vanessa Rodrigues dos Santos por me acompanhar nos estudos de citologia.

Aos professores da disciplina de Dentística, Prof. Dr. André Luiz Fraga Briso, Prof. Dr. Renato Herman Sundfeld, Prof. Dr. Ricardo Coelho Okida, Prof. Dr. Sílvio José Mauro, Profa. Dra. Ticiane Cestari Fagundes e mais recentemente

Prof. Anderson Catelan e Prof. Caio César Pavani. O acompanhamento das disciplinas na graduação nos proporcionou um experiência muito importante para o nosso desenvolvimento acadêmico.

Aos funcionários do departamento de Odontologia Restauradora, Carlos Suetake e Jorge Trevelim, pela paciência e disposição em sempre nos auxiliarem quando precisamos.

A Universidade Federal do Mato Grosso do Sul, faculdade de que sou egressa, mas que me abriu as portas para me receber como professora substituta, em especial a Profa. Margareth Coutinho, minha orientadora do ICC a quem eu devo o fato de ter escolhido esse caminho na pós-graduação. Muito Obrigada!

Epígrafe

A vida não é fácil para nenhum de nós, mas isso não importa. O que importa é preservar e, acima de tudo, ter confiança de si mesmo. É preciso sentir confiança para fazer algo e alcançar os objetivos, custe o que custar.

Dra. Marie Curie

Resumo Geral

Ramos FSS. Efeito de diferentes tratamentos na hipersensibilidade dentinária: avaliação da citotoxicidade e estudo clínico randomizado [tese]. Araçatuba: Universidade Estadual Paulista (Unesp), Faculdade de Odontologia; 2023.

RESUMO GERAL

Objetivos: O objetivo deste estudo foi investigar os efeitos de diferentes categorias de tratamentos para hipersensibilidade dentinária em relação ao desgaste e citotoxicidade usando os seguintes protocolos: verniz placebo (PLA), verniz fluoretado (FLU), verniz de fluoreto de sódio (NaF) + Trimetafosfato de sódio (TMP), verniz adesivo universal (SBU), verniz S-PRG (SPRG), biosilicato (BIOS) e solução de amelotina (AMTN). Adicionalmente, FLU, SBU, SPRG e BIOS tiveram sua longevidade clínica avaliada. *Metodologia:* Setenta blocos de dentina radicular bovina foram seccionados. Metade da superfície de cada espécime não foi tratada (controle) e a outra metade foi imersa em EDTA e tratada com os materiais dessensibilizantes. Após a aplicação, os corpos de prova foram submetidos a um desafio erosivo-abrasivo e o desgaste foi analisado por perfilômetro óptico. Diluições seriadas de extratos obtidos a partir do meio de cultura contendo discos impregnados com esses dessensibilizantes foram aplicadas em culturas de fibroblastos e células odontoblásticas. A citotoxicidade e a produção de proteína total (PT) por ensaios colorimétricos foram determinadas após 24h. Em relação ao ensaio clínico, 192 exposições radiculares não cavitadas foram analisadas usando escala visual analógica (VAS) e visual computadorizada (CoVAS), antes dos tratamentos (*baseline*) e após 7, 15, 30 dias, 6 e 12 meses. Os dados foram analisados usando Kruskal-Wallis, Dunn's para desgaste, One-way ANOVA, Tukey e modelo de regressão linear com efeitos fixos e pós-teste usando contrastes ortogonais ($p \leq 0.05$). *Resultados:* O SBU foi o único material que não apresentou desgaste. O menor desgaste foi observado para AMTN, sendo estatisticamente semelhante ao TMP. A viabilidade celular foi significativamente reduzida para PLA, FLU, TMP e SBU em a fibroblastos e TMP e SBU em células semelhantes a odontoblastos considerando o extrato não diluído. PT mostraram níveis variados de concentrações de proteína sem diferença entre os grupos para fibroblastos. No estudo clínico, todos os dessensibilizantes foram eficazes na redução da HD, em comparação com os dados iniciais para ambas as escalas. Na escala VAS, observou-se redução significativa de HD a partir de 7 dias para BIOS e SBU, e a partir de 15 dias para FLU e SPRG. Para a escala CoVAS, todos os dessensibilizantes foram capazes de reduzir significativamente a HD após 7 dias, exceto o SPRG, que apresentou essa redução após 15 dias. Nenhum dessensibilizante retornou ao nível de sensibilidade inicial após 12 meses para ambas as escalas. Não foram encontradas diferenças

estatísticas entre os dessensibilizantes para todos os momentos de avaliação, para ambas as escalas. *Conclusão:* O adesivo universal protegeu a superfície dentinária após o desafio erosivo-abrasivo. Extratos não diluídos de adesivos universais e vernizes fluoretados apresentam citotoxicidade, principalmente para fibroblastos. Todos os tratamentos em consultório foram eficazes na redução da HD ao longo de 12 meses, com níveis de dor semelhantes.

Palavras-chave: Abrasão Dentária. Biologia Celular. Dessensibilizantes Dentinários. Ensaio Clínico. Ensaio Clínicos Randomizados. Erosão Dentária. Sensibilidade da Dentina.

General Abstract

Ramos FSS. Effect of different treatments on dentin hypersensitivity: evaluation of cytotoxicity and randomized clinical study [tese]. Araçatuba: Universidade Estadual Paulista (Unesp), Faculdade de Odontologia; 2023.

GENERAL ABSTRACT

Objectives: The aim of this study was to investigate the effects of different categories of treatments for dentin hypersensitivity in relation to wear and cytotoxicity using the following protocols: placebo varnish (PLA), fluoride varnish (FLU), sodium fluoride varnish (NaF) + sodium trimetaphosphate (TMP), universal adhesive (SBU), S-PRG varnish (SPRG), biosilicate (BIOS) and amelotin solution (AMTN). Additionally, FLU, SBU, SPRG and BIOS had their clinical longevity evaluated. *Methods:* Seventy bovine root dentin blocks were sectioned. Half of the surface of each specimen was untreated (control) and the other half was immersed in EDTA and treated with the desensitizing materials. After application, the specimens underwent an erosive-abrasive challenge and the wear was analyzed by optical profilometer. Serial dilutions of extracts obtained from the culture medium containing discs impregnated with those desensitizers were applied on fibroblasts and odontoblasts-like cells cultures. Cytotoxicity and production of total protein (TP) by colorimetric assays were determined after 24h. Regarding clinical trial, 192 non-cavitated root exposures were analyzed using visual analogue (VAS) and computerized visual scales (CoVAS), before treatments (baseline) and after 7, 15, 30 days, 6 and 12 months. Data were analyzed using Kruskal-Wallis, Dunn's for wear, One-way ANOVA, Tukey, and linear regression model with fixed effects and post-test using orthogonal contrasts for clinical ($p \leq 0.05$). *Results:* SBU was the only material that did not show wear. The lowest wear was observed for AMTN, being statistically similar to TMP. Cell viability was significantly reduced for PLA, FLU, TMP and SBU in fibroblasts-like cell and TMP and SBU in odontoblast-like cell considering undiluted extract. TP showed varied levels of protein concentrations with no difference between groups at 24h for fibroblasts-cell. For clinical study, all desensitizers were effective in reducing DH, compared with baseline data for both scales. On the VAS scale, a significant reduction in DH was observed after 7 days for BIOS and SBU, and after 15 days for FLU and SPRG. For the CoVAS scale, all desensitizers were able to significantly reduce DH after 7 days, except for SPRG, which showed this reduction after 15 days. No desensitizer returned to initial sensitivity level after 12-months for both scales. No statistical differences were found among desensitizers for all times of evaluation, for both scales. *Conclusion:* Universal adhesive protected the wear of DH after challenge. Undiluted extracts of universal adhesives and fluoride varnishes show cytotoxicity,

mainly for fibroblasts. All in-office treatments were effective for reducing DH over 12 months, with similarity levels of pain.

Keywords: Cell Biology. Clinical Trial. Desensitizing Agents. Dental Abrasion. Dental Erosion. Dentin Sensitivity. Randomized Clinical Trial.

Listas e Sumário

LISTA DE FIGURAS

Capítulo 1

Figure 1 Study design illustration. Dentin wear surface were assessed using an optical profilometer. 51

Figure 2 Representative image of the 3-D plot of surface loss (a) and surface preservation (b) after erosive-abrasive challenge. 51

Figure 3 Percentage of NIH/3T3 cell viability (mean+standard deviation) after treatments with different materials. Different uppercase letters show statistical difference among the groups, considering each extract dilution separately (100% - undiluted extract, 50% diluted, 25% diluted, 12.5% diluted in DMEM). 52

Figure 4 Percentage of MDPC-23 cell viability (mean+standard deviation) after treatments with different materials. Different uppercase letters show statistical difference among the groups, considering each extract dilution separately (100% - undiluted extract, 50% diluted, 25% diluted, 12.5% diluted in DMEM). 52

Figure 5 Total protein concentrations (ug/mL) obtained by NIH/3T3 after treatments with different materials. Different uppercase letters show statistical difference among the groups, considering each extract dilution separately (100% - undiluted extract, 50% diluted, 25% diluted, 12.5% diluted in DMEM). Values are expressed in means/standard deviations. 53

Figure 6 Total protein concentrations (ug/mL) obtained by MDPC-23 after treatments with different materials. Different uppercase letters show statistical difference among the groups, considering each extract dilution separately (100% - undiluted extract, 50% diluted, 25% diluted, 12.5% diluted in DMEM). Values are expressed in means/standard deviations. 53

Capítulo 2

Figure 1 Consort flowchart. Np: patient number, Nd: number of teeth 59

Figure 2 Curves with peaks showing the moment of the highest intensity of sensitivity by group and time of evaluation. 67

LISTA DE TABELAS

Capítulo 1

- Table 1** Characteristics and mode of application of in-office desensitizing materials used in this study. 49
- Table 2** Data referring to optical profilometry (μm ; Median 25%/75%) of the different in-office desensitizers after the erosive-abrasive challenge. 50

Capítulo 2

- Table 1** Inclusion and exclusion criteria 60
- Table 2** Characteristics and mode of application of in-office desensitizing materials used in this study 62
- Table 3** Descriptive results from characteristics of patients and teeth, described as mean (\pm standard deviation) or number (percentage %) per group 64
- Table 4** Descriptive results of harmful habits and oral treatments/instructions, described as number (percentage %) per group 65
- Table 5** Mean (\pm standart of deviation) of times analyzed and presented by different desensitizing materials according to the VAS scale 66
- Table 6** Mean (\pm standart of deviation) of times analyzed and presented by different desensitizing materials according to the CoVAS scale 66

LISTA DE ABREVIATURAS, SÍMBOLOS E SIGLAS

%	percentage
μM	Micromole
Al_3^+	Aluminum
AMTN	Amelotin
ANOVA	Analysis of variance
BIOS	Biosilicate
BO_3^{3-}	Borate
C	control
$\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$	calcium nitrate tetrahydrate
CaCl_2	Calcium chloride
CaF_2	Calcium fluoride
cm	Centimeters
CO_2	Carbon dioxide
CONSORT	Consolidated Standards of Reporting Trials
CoVAS	Computerized visual scale
DH	Dentin hypersensitivity
DMEM	Dulbecco's Modified Eagle's Medium
DMFT	Missing and filled permanent teeth
EDTA	ethylenediaminetetraacetic acid
ETW	Erosive tooth wear
F	Fluor
F^-	Fluoride
FLU	Fluoride varnish
GBI	Gum bleeding index
h	Hour
H_2O	Water
HCl	Hydrogen chloride

HTC	hypersensitive (EDTA immersion), treated (with desensitizing agents), challenged (erosive-abrasive cycles)
KCl	Potassium chloride
KH ₂ PO ₄	Potassium dihydrogen phosphate
M	Mol
MDP	Methacryloyloxydecyl dihydrogen phosphate
MDPC-23	Odontoblast-like cell
min	Minutes
min	Minutes
ml	Milliliters
mm	Millimeter
mmol/L	millimol per liter
mW/cm ²	milliwatts per square centimeter
Na ⁺	Sodium
NaCl	Sodium chloride
NaF	Sodium fluoride
NaH ₂ PO ₄ ·2H ₂ O	monobasic sodium phosphate
NCLC	Non-carious cervical lesions
NIH/3T3	ATCC CRL-1658 = Fibroblast-like cell
nm	Nanometer
pH	hydrogen potential
PLA	Placebo varnish
REBEC	Brazilian Registry of Clinical Trials
s	Seconds
SBU	Universal adhesive
SiO ₃ ²⁻	Silicate
SPRG	S-PRG varnish
Sr ₂ ⁺	Strontium
TEGDMA	Triethylene glycol dimethacrylate
TMP	Sodium trimetaphosphate
TP	Total protein
UI/mL	International unit per milliliter
VAS	Visual analogue scale
VPI	Visible plaque index

w/w	weight/weight
X	Times
$\mu\text{g/mL}$	Micrograms per milliliter
μL	Microliters
μm	Micrometers

SUMÁRIO

1 GENERAL INTRODUCTION	26
2 CAPÍTULO 1 - Analysis of dentin wear and biological properties promoted by innovative and experimental in-office desensitizing materials	29
2.1 Abstract.....	30
2.2 Introduction	30
2.3 Material and methods	32
2.4 Results	37
2.5 Discussion.....	38
2.6 Conclusions	42
2.7 References	42
3 CAPÍTULO 2 - Longevity of different in-office treatments for dentin hypersensitivity: a 12-month randomized and parallel clinical trial	55
3.1 Abstract.....	56
3.2 Introduction	56
3.3 Material and methods	58
3.4 Results	63
3.5 Discussion.....	67
3.6 Conclusions	70
3.7 References	70
ANEXOS	75

*General
Introduction*

1 GENERAL INTRODUCTION

Dentin hypersensitivity (DH) is defined as short-term pain caused by thermal, tactile, chemical or osmotic stimuli (QUE *et al.*, 2013; FAVARO ZEOLA; SOARES; CUNHA-CRUZ, 2019; FELIX; OUANOUNOU, 2019). Among the mechanisms that explain DH, the hydrodynamic theory assumes that external stimuli move the fluid inside the dentinal tubules, causing contraction and distension of odontoblastic processes, stimulating the nerve fibers of the dentin-pulp interface (CHUNG; JUNG; OH, 2013). This condition is closely related to root exposure, with or without non-cariou cervical lesions (NCLC) and the erosion is probably the major predictor of dentin hypersensitivity (ALCANTARA *et al.*, 2018).

The proposed treatments include surgical procedure for root coverage, adhesive restorations in cases of cavitation or desensitizing treatments (PEUMANS; POLITANO; VAN MEERBEEK, 2020). Desensitizing products act by obliterating dentinal tubules or reducing nervous excitability; however, DH reduction may have short-term effectiveness (OZEN *et al.*, 2009; YILMAZ; KURTULMUS-YILMAZ; CENGIZ, 2011). Currently, three product categories have been tested in for the treatment of DH: fluoride varnishes, products with photocuring agents, and experimental solutions of bioactive products.

The high fluoride concentration in the varnishes makes them one of the materials of choice for DH; however, due to limitations regarding the duration of its effects, studies have indicated that the addition of calcium salts and/or organic or inorganic phosphates can optimize the action on the dental tissue (DANELON *et al.*, 2020; FAVRETTO *et al.*, 2018). Among them, sodium trimetaphosphate (TMP) has demonstrated remineralizing action on the dental tissue when associated with fluorides through adsorption to the dentin surface, promoting obliteration of the dentinal tubules, protection of the collagen matrix and deposition of calcium phosphate-apatite (DANELON *et al.*, 2020; FAVRETTO *et al.*, 2018).

Currently, particles in powder form have been developed for bioactive purposes. Among them, biosilicates have been introduced with the objective of promoting the remineralization of hard tissues by the precipitation of calcium phosphate (PINTADO-PALOMINO; TIRAPELLI, 2015; RENNO *et al.*, 2013; TIRAPELLI *et al.*, 2011). Such properties give biosilicate a potential obliterating effect on dentinal tubules, in addition to remineralization and preventing demineralization in dentin. (PINTADO-PALOMINO; TIRAPELLI, 2015; TIRAPELLI *et al.*, 2010, 2011). Scientific advances have also led to the discovery of an enamel matrix protein secreted by ameloblasts, knowledge as amelotin (AMTN). This protein influences the

biomineralization of dental structure, promoting the precipitation of calcium phosphate, formation of hydroxyapatite and collagen matrix (ABBARIN *et al.*, 2015; IKEDA *et al.*, 2018); however, this action and results in the dentin was weakly investigated.

Considering the photocuring products, universal adhesive systems have been used as an option for promoting a desensitizing effect by sealing the dentinal tubules and forming a hybrid layer (ASKARI; YAZDANI, 2019; RAVISHANKAR *et al.*, 2018), presenting an 80% reduction in sensitivity after three months of application (ASKARI; YAZDANI, 2019).

Recently, a product was launched on the dental market that combines all the mentioned compositions, being composed of a fluoride varnish photocured with pre-reacted surface glass particles. This bioactive technology allows the multifunctional glass particles to be trapped in the polyacid matrix, releasing fluoride, strontium, borate, aluminum, silicate and sodium ions. Thus, there is the neutralization of acids from food and remineralization of tissues, associating with obliteration by means of photoactivated monomers (RAVISHANKAR *et al.*, 2018).

Therefore, it is opportune to develop a study that evaluate in vitro and in vivo effect of different treatments on DH.

3.6 Conclusions

Considering the experimental design and the findings, this randomized clinical trial demonstrated that some characteristics related to root exposure and tooth may influence the initial intensity of DH. All in-office treatments evaluated were effective in reducing DH over 12 months, with similarity levels of pain among desensitizers. No difference was found between the different desensitizing protocols evaluated.

Conflict of Interest: The authors declare that they have no conflict of interest.

Funding: This research was supported by the São Paulo Research Foundation—FAPESP [research grant number 2020/07625-0] and the scholarship [scholarship grant number 2020/07443-9]

3.7 References

1. Marto CM, Paula AB, Nunes T, Pimenta M, Abrantes AM, Pires AS, Laranjo M, Coelho A, Donato H, Botelho MF, Ferreira MM, Carrilho E (2019) Evaluation of the efficacy of dentin hypersensitivity treatments: a systematic review and follow-up analysis. *J Oral Rehabil* 46:952-990. <https://doi.org/10.1111/joor.12842>
2. Zeola FL, Soares PV, Cunha-Cruz J (2019) Prevalence of dentin hypersensitivity: systematic review and meta-analysis. *J Dent* 81:1-6. <https://doi.org/10.1016/j.jdent.2018.12.015>

3. Felix J, Ouanounou A (2019) Dentin hypersensitivity: Etiology, diagnosis, and management. *Compend Contin Educ Dent* 40:653-657
4. Freitas SAA, Oliveira NMA, de Geus JL, Souza SFC, Pereira AFV, Bauer J (2021) Bioactive toothpastes in dentin hypersensitivity treatment: A systematic review. *Saudi Dent J*. 33:395-403. <https://doi.org/10.1016/j.sdentj.2021.04.004>
5. Peumans M, Politano G, Van Meerbeek B (2020) Treatment of noncarious cervical lesions: When, why and how. *Int J Esthet Dent* 15:16-42
6. Alencar CM, Leite KLF, Ortiz MIG, Magno MB, Rocha GM, Silva CM, Maia LC (2019) Morphological and chemical effects of in-office and at-home desensitising agents containing sodium fluoride on eroded root dentin. *Arch Oral Biol* 110: 104619. <https://doi.org/10.1016/j.archoralbio.2019.104619>
7. Kim HN, Kim JB, Jeong SH (2018) Remineralization effects when using different methods to apply fluoride varnish in vitro. *J Dent Sci* 13:360-366. <https://doi.org/10.1016/j.jds.2018.07.004>
8. Pichaiakrit W, Thamrongananskul N, Siralertmukul K, Swasdison S (2019) Fluoride varnish containing chitosan demonstrated sustained fluoride release. *Dent Mater J* 38:1036-1042. <https://doi.org/10.4012/dmj.2018-112>
9. Tirapelli C, Panzeri H, Soares RG, Peitl O, Zanotto ED (2010) A novel bioactive glass-ceramic for treating dentin hypersensitivity. *Braz Oral Res* 24:381-387. <https://doi.org/10.1590/s1806-83242010000400002>
10. Tirapelli C, Panzeri H, Lara EH, Soares RG, Peitl O, Zanotto ED (2011) The effect of a novel crystallized bioactive glass-ceramic powder on dentine hypersensitivity: a long-term clinical study. *J Oral Rehabil* 38:253-262. <https://doi.org/10.1111/j.1365-2842.2010.02157.x>
11. Patil SA, Naik BD, Suma R (2015) Evaluation of three different agents for in-office treatment of dentinal hypersensitivity: a controlled clinical study. *Indian J Dent Res* 26:38-42. <https://doi.org/10.4103/0970-9290.156796>
12. Askari M, Yazdani R (2019) Comparison of two desensitizing agents for decreasing dentin hypersensitivity following periodontal surgeries: A randomized clinical trial. *Quintessence Int* 50:320-329. <https://doi.org/10.3290/j.qi.a42096>

13. Ravishankar P, Viswanath V, Archana D, Keerthi V, Dhanapal S, Lavanya Priya KP (2018) The effect of three desensitizing agents on dentin hypersensitivity: A randomized, split-mouth clinical trial. *Indian J Dent Res* 29:51-55. https://doi.org/10.4103/ijdr.IJDR_458_17
14. Mosquim V, Caracho RA, Zabeu GS, Condi LDS, Foratori-Junior GA, Borges AFS, Wang L (2022) Resin-based materials to control human dentin permeability under erosive conditions in vitro: a hydraulic conductance, confocal microscopy and FTIR study. *Dent Mater* 38:1669-1678. <https://doi.org/10.1016/j.dental.2022.08.012>
15. Sivaramakrishnan G, Sridharan K (2019) Fluoride varnish versus glutaraldehyde for hypersensitive teeth: a randomized controlled trial, meta-analysis and trial sequential analysis. *Clin Oral Investig* 23:209-220. <https://doi.org/10.1007/s00784-018-2428-8>
16. Moura GF, Zeola LF, Silva MB, Sousa SC, Guedes FR, Soares PV (2019) Four-session protocol effectiveness in reducing cervical dentin hypersensitivity: a 24-week randomized clinical trial. *Photobiomodul Photomed Laser Surg* 2019 37:117-123. <https://doi.org/10.1089/photob.2018.4477>
17. Sgreccia PC, Barbosa RES, Damé-Teixeira N, Garcia FCP (2020) Low-power laser and potassium oxalate gel in the treatment of cervical dentin hypersensitivity – a randomized clinical trial. *Clin Oral Investig* 24:4463-4473. <https://doi.org/10.1007/s00784-020-03311-7> 2020.
18. Rahal V, Gallinari MO, Barbosa JS, Martins-Junior RL, dos Santos PH, Cintra LTA, Briso ALF (2018) Influence of skin cold sensation threshold in the occurrence of dental sensitivity during dental bleaching: a placebo controlled clinical trial. *J Appl Oral Sci* 18:e20170043. <https://doi.org/10.1590/1678-7757-2017-0043>
19. Ritter AV, Dias WL, Miguez P, Caplan DJ, Swift EJ Jr (2006) Treating cervical dentin hypersensitivity with fluoride varnish: a randomized clinical study. *J Am Dent Assoc* 137:1013-1020. <https://doi.org/10.14219/jada.archive.2006.0324>
20. de Castro Oliveira L, Marchetti VM, de Souza E Silva Ramos F, Delbem ACB, Souza MT, Ganss B, Theodoro LH, Fagundes TC (2022) In vitro dentin permeability and tubule occlusion of experimental in-office desensitizing materials. *Clin Oral Investig* 27:1265-1276. <https://doi.org/10.1007/s00784-022-04760-y>
21. West NX, Lussi A, Seong J, Hellwig E (2013) Dentin hypersensitivity: pain mechanisms and aetiology of exposed cervical dentin. *Clin Oral Investig* 17:9-19. <https://doi.org/10.1007/s00784-012-0887>

22. Shinohara MS, Carvalho PRM, Neves Marcon L, Gonçalves DFM, Ramos FSS, Fagundes TC (2020) Randomized clinical trial of different adhesion strategies in noncarious cervical lesion restorations: 1-year follow-up. *Quintessence Int* 51:352-363. <https://doi.org/10.3290/j.qi.a44367>
23. Menezes-Silva R, Velasco SRM, Bastos RS, Molina G, Honório HM, Frencken JE, Navarro, MFL (2019) Randomized clinical trial of class II restoration in permanent teeth comparing ART with composite resin after 12 months. *Clin Oral Investig* 23:3623-3635. <https://doi.org/10.1007/s00784-018-2787-1>
24. Briso ALF, Rahal V, Azevedo FA, Gallinari MO, Gonçalves RS, Frascino SMB, Santos PHD, Cintra LTA (2018) Neurosensory analysis of tooth sensitivity during at-home dental bleaching: a randomized clinical trial. *J Appl Oral Sci* 26:e20170284. <https://doi.org/10.1590/1678-7757-2017-0043>
25. Shiiya T, Kataoka A, Tomiyama K, Fujino F, Mukai Y (2021) Anti-demineralization characteristics of surface pre-reacted glass-ionomer (S-PRG) filler-containing varnishes. *Dent Mater J* 40:416-421. <https://doi.org/10.4012/dmj.2019-396>
26. Wang L, Magalhães AC, Francisconi-Dos-Rios LF, Calabria MP, Araújo D, Buzalaf M, Lauris J, Pereira JC (2016) Treatment of dentin hypersensitivity using nano-hydroxyapatite pastes: a randomized three-month clinical trial. *Oper Dent* 41:93-101. <https://doi.org/10.2341/15-145-C>
27. Yilmaz HG, Kurtulmus-Yilmaz S, Cengiz E (2011) Long-term effect of diode laser irradiation compared to sodium fluoride varnish in the treatment of dentine hypersensitivity in periodontal maintenance patients: A randomized controlled clinical study. *Photomed Laser Surg* 29:721-725. <https://doi.org/10.1089/pho.2010.2974>
28. Forouzande M, Rezaei-Soufi L, Yarmohammadi E, Ganje-Khosravi M, Fekrazad R, Farhadian M, Farmany A. Effect of sodium fluoride varnish, Gluma, and Er,Cr:YSGG laser in dentin hypersensitivity treatment: a 6-month clinical trial. *Lasers Med Sci*. 2022 Sep;37(7):2989-2997. doi: 10.1007/s10103-022-03583-3
29. Liu XX, Tenenbaum HC, Wilder RS, Quock R, Hewlett ER, Ren YF (2020) Pathogenesis, diagnosis and management of dentin hypersensitivity: an evidence-based overview for dental practitioners. *BMC Oral Health* 20:220. <https://doi.org/10.1186/s12903-020-01199-z>

30. Sgreccia PC, Damé-Teixeira N, Barbosa RES, Araújo PF, Zanatta RF, Garcia FCP (2022) Assessment of the Oral Health Impact Profile (OHIP-14) improvement of different treatments for dentin hypersensitivity in noncarious cervical lesions-a randomized clinical study. *Clin Oral Investig* 26:6583-6591. <https://doi.org/10.1007/s00784-022-04610-x>
31. Teixeira DNR, Zeola LF, Machado AC, Gomes RR, Souza PG, Mendes DC, Soares PV (2018) Relationship between noncarious cervical lesions, cervical dentin hypersensitivity, gingival recession, and associated risk factors: a cross-sectional study. *J Dent* 76:93-97. <https://doi.org/10.1016/j.jdent.2018.06.017>
32. 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. *J Oral Rehabil* 43:960–966. <https://doi.org/10.1111/joor.12445>
33. Zuza A, Racic M, Ivkovic N, Krunic J, Stojanovic N, Bozovic D, Bankovic-Lazarevic D, Vujaskovic M (2019) Prevalence of non-carious cervical lesions among the general population of the Republic of Srpska, Bosnia and Herzegovina. *Int Dent J* 69:281-288. <https://doi.org/10.1111/idj.12462>
34. Hass V, Cardenas A, Siqueira F, Pacheco R, Zago P, Silva D, Loguercio A (2019) Bonding performance of universal adhesive systems applied in etch-and-rinse and self-etch strategies on natural dentin caries. *Oper Dent* 44:510-520. <https://doi.org/10.2341/17-252-1>
35. Fujimoto Y, Iwasa M, Murayama R, Miyazaki M, Nagafuji A, Nakatsuka T (2010) Detection of ions released from S-PRG fillers and their modulation effect. *Dent Mater J* 29:392-397. <https://doi.org/10.4012/dmj.2010-015>
36. Younus MZ, Ahmed MA, Syed AUY, Baloch JM, Ali M, Sheikh A (2021) Comparison between effectiveness of dentine desensitizer and one bottle self-etch adhesive on dentine hypersensitivity. *Technol Health Care* 29:1153-1159. <https://doi.org/10.3233/THC-202636>

ANEXOS

ANEXO A – General Introduction References

Abbarin N, San Miguel S, Holcroft J, Iwasaki K, Ganss B. The enamel protein amelotin is a promoter of hydroxyapatite mineralization. *J Bone Miner Res.* 2015 May;30(5):775-85.

Alcântara PM, Barroso NFF, Botelho AM, Douglas-de-Oliveira DW, Gonçalves PF, Flecha OD. Associated factors to cervical dentin hypersensitivity in adults: a transversal study. *BMC Oral Health.* 2018 Sep 3;18(1):155-61.

Askari M, Yazdani R. Comparison of two desensitizing agents for decreasing dentin hypersensitivity following periodontal surgeries: a randomized clinical trial. *Quintessence Int.* 2019;50(4):320-9.

Chung G, Jung SJ, Oh SB. Cellular and molecular mechanisms of dental nociception. *J Dent Res.* 2013 Nov;92(11):948-55.

Danelon M, Pessan JP, Prado KM, Ramos JP, Emerenciano NG, Moretto MJ, Martinhon CCR, Delbem ACB. Protective effect of fluoride varnish containing trimetaphosphate against dentin erosion and erosion/abrasion: an in vitro study. *Caries Res.* 2020;54(3):292-6.

Favaro Zeola L, Soares PV, Cunha-Cruz J. Prevalence of dentin hypersensitivity: Systematic review and meta-analysis. *J Dent.* 2019 Feb;81:1-6.

Favretto CO, Delbem ACB, Moraes JCS, Camargo ER, de Toledo PTA, Pedrini D. Dentinal tubule obliteration using toothpastes containing sodium trimetaphosphate microparticles or nanoparticles. *Clin Oral Investig.* 2018 Dec;22(9):3021-9.

Felix J, Ouanounou A. Dentin hypersensitivity: etiology, diagnosis, and management. *Compend Contin Educ Dent.* 2019;40(10):653-7.

Ikeda Y, Neshatian M, Holcroft J, Ganss B. The enamel protein ODAM promotes mineralization in a collagen matrix. *Connect Tissue Res.* 2018 Dec;59(sup1):62-6.

Ozen T, Orhan K, Avsever H, Tunca YM, Ulker AE, Akyol M. Dentin hypersensitivity: a randomized clinical comparison of three different agents in a short-term treatment period. *Oper Dent.* 2009;34(4):392-8.

Peumans M, Politano G, Van Meerbeek B. Treatment of noncarious cervical lesions: when, why, and how. *Int J Esthet Dent.* 2020;15(1):16-42.

- Pintado-Palomino K, Tirapelli C. The effect of home-use and in-office bleaching treatments combined with experimental desensitizing agents on enamel and dentin. *Eur J Dent.* 2015;9(1):66-73.
- Que K, Guo B, Jia Z, Chen Z, Yang J, Gao P. A cross-sectional study: non-carious cervical lesions, cervical dentine hypersensitivity and related risk factors. *J Oral Rehabil.* 2013 Jan;40(1):24-32.
- Ravishankar P, Viswanath V, Archana D, Keerthi V, Dhanapal S, Lavanya Priya KP. The effect of three desensitizing agents on dentin hypersensitivity: A randomized, split-mouth clinical trial. *Indian J Dent Res.* 2018;29(1):51-5.
- Renno AC, Bossini PS, Crovace MC, Rodrigues AC, Zanotto ED, Parizotto NA. Characterization and in vivo biological performance of biosilicate. *Biomed Res Int.* 2013;2013:141427.
- Tirapelli C, Panzeri H, Lara EH, Soares RG, Peitl O, Zanotto ED. The effect of a novel crystallised bioactive glass-ceramic powder on dentine hypersensitivity: a long-term clinical study. *J Oral Rehabil.* 2011 Apr;38(4):253-62.
- Tirapelli C, Panzeri H, Soares RG, Peitl O, Zanotto ED. A novel bioactive glass-ceramic for treating dentin hypersensitivity. *Braz Oral Res.* 2010;24(4):381-7.
- Yilmaz HG, Kurtulmus-Yilmaz S, Cengiz E. Long-term effect of diode laser irradiation compared to sodium fluoride varnish in the treatment of dentine hypersensitivity in periodontal maintenance patients: a randomized controlled clinical study. *Photomed Laser Surg.* 2011 Nov;29(11):721-5.