Bárbara Suelen Moccelini

NECROSE PULPAR E ALTERAÇÃO DE COR DA COROA EM DENTES DECÍDUOS TRAUMATIZADOS: UMA REVISÃO SISTEMÁTICA E META-ANÁLISE

Dissertação submetida ao Programa de Pós-Graduação da Universidade Federal de Santa para a obtenção do Grau de Mestre em Odontologia

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RESUMO

Objetivo: Verificar se existe associação entre a necrose pulpar e a alteração de cor da coroa em dentes decíduos traumatizados através de uma revisão sistemática e meta-análise. Metodologia: Fez-se uma busca eletrônica nas bases de dados: *PubMed, LILACS, Scopus, Web of Science* e literatura cinzenta: *OpenGrey*, *Proquest*, Banco de teses e dissertações da CAPES e *Google Scholar*. Foram incluídos estudos observacionais em dentes decíduos traumatizados (P) com (E) e sem necrose pulpar (C) associados a alteração de cor da coroa (O). Foi realizada uma avaliação metodológica da qualidade dos estudos selecionados. A prevalência de alteração de cor da coroa e o número total de dentes com e sem necrose pulpar foram acessados. Foram utilizados modelos de efeitos aleatórios e a heterogeneidade foi testada usando o índice I^2 ($p \leq 0,05$). Resultados: Oito estudos com baixo risco de viés foram incluídos na análise. Um total de 1,494 dentes decíduos traumatizados fizeram parte da meta-análise conjunta. Destes, 1,414 foram avaliados no primeiro subgrupo (diagnóstico da necrose pulpar através de análise clínica e radiográfica), a análise demonstrou associação positiva (p = 0,0005/ OR 8,37 [2,51, 27,90], I^2=87%). Em relação a 80 dentes avaliados no segundo subgrupo (diagnóstico de necrose pulpar através do acesso endodôntico), a análise demonstrou ausência de associação (p = 0,36/ OR 2,46 [0,36, 16,94], I^2=54%). A meta-análise agrupada mostrou associação positiva (p = 0,0003/ OR 5,93 [2,24, 15,72], I^2=83%). Conclusão: Existe uma associação significativa entre a necrose de pulpar diagnosticada através de análise clínica e radiográfica e a alteração de cor da coroa. Os resultados devem ser considerados com cautela uma vez que o diagnóstico de necrose de polpa foi realizado por critérios limitados.

Palavras-chave: Trauma dental, Dente decíduo, Necrose pulpar, Alteração de cor da coroa.

ABSTRACT

Objetive: The study verified if there is an association of pulp necrosis and crown discolouration in traumatized primary teeth through a systematic review and meta-analysis. Methods: A systematic literature search was conducted in PubMed/Medline, Lilacs/BBO, Scopus, Web of Science, Cochrane Library databases, and also in the grey literature. The PECO strategy was used to identify studies in traumatized primary teeth (P) with (E) or without (C) pulpal necrosis and its association with crown discoloration (O). A methodological quality assessment appraisal was conducted. The total number of teeth with and without pulp necrosis and the prevalence of crown discolouration were accessed. Random-effects models were employed, and heterogeneity was tested using the I^2 index ($p \leq 0.05$). Results*:* Eight studies with low risk of bias, were included in the analysis. A total of 1.494 traumatized primary teeth participated in the pooled meta-analysis. Of these, 1.414 were evaluated in the first subgroup (diagnosis of pulp necrosis through clinical and radiographic analysis) and the analysis demonstrated a positive association (p=0.0005/ OR 8.37 [2.51, 27.90], I^2=87%). Regarding 80 teeth in the second subgroup (diagnosis of pulp necrosis through endodontic access), the analysis demonstrated an absence association (p=0.36/ OR 2.46 [0.36, 16.94], I^2=54%) The pooled meta-analysis showed a positive association (p=0.0003/ OR 5.93 [2.24, 15.72], I^2=83%). Conclusion: There is a significant association between pulp necrosis diagnosed through clinical and radiographic analysis and crown discolouration. The results should be considered with caution once the diagnosis of pulp necrosis was performed by limited criteria.

Keywords: Dental trauma, Primary teeth, Pulp necrosis, Crown discoloration

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LISTA DE ABREVIATURAS E SIGLAS

BBO – Bridge Base Online
LILACS – Centro Latino-Americano e do Caribe de Informação em Ciências da Saúde
MeSH – *Medical Subject Headings*
PRISMA – *Preferred Reporting Items for Systematic Reviews and Meta-Analysis*
PROSPERO – *International Prospective Register of Systematic Reviews*
TDI – *Traumatic Dental Injuries*
UFSC – Universidade Federal de Santa Catarina
UNIEDU – Programa de Bolsas Universitárias de Santa Catarina

SUMÁRIO

1. CONTEXTUALIZAÇÃO

A interação da criança com o mundo a sua volta permite a ela o desenvolvimento das habilidades cognitivas e motoras. A aquisição de habilidades e o aprimoramento motor na infância podem desencadear diversas situações negativas, como exemplo, os traumas (BUSHNELL, 1993). Neste âmbito, traumas em tecidos dentais são frequentes em crianças e podem causar consequências físicas e emocionais (KRAMER; FELDENS, 2013). Traumas mais graves do tipo avulsão dental e a alteração de cor da coroa estão relacionados a um impacto negativo na qualidade de vida das crianças e suas famílias (VIEGAS et al., 2014).

Devido a sua gravidade e prevalência alta, o traumatismo dental é considerado um problema de saúde pública (ALDRIGUI et al., 2011). Pesquisas epidemiológicas realizadas somente com avaliação clínica relatam uma prevalência do traumatismo dental em pré-escolares entre 13,3% a 62,1% (VIEGAS et al., 2010; BONINI et al., 2012; CORRÊA-FARIA et al., 2015; KRAMER et al., 2015). Em um estudo onde o diagnóstico do traumatismo dental foi realizado a partir de uma avaliação clínica e radiográfica a prevalência foi de 63,0% (HOLAN; YODKO, 2017). Em tecido dental, as lesões de fratura de esmalte são as mais prevalentes (VIEGAS et al., 2010; NORTON; O'CONNELL, 2012; ELKARMI, 2015), já nos tecidos de suporte, as subluxações são mais frequentes (TANNURE et al., 2012; QASSEM et al., 2015).

Em relação a faixa etária de maior ocorrência, alguns estudos referem aos 4-5 anos de idade (PIOVESAN et al., 2012; KRAMER et al., 2015), outros em crianças menores 1-3 anos (COLAK et al., 2009; JESUS et al., 2010). Em idades menores são mais frequentes os traumas do tipo luxação (CARDOSO; DE CARVALHO ROCHA, 2010). Embora, artigos afirmem que não há diferença significativa entre os sexos (NORTON; O'CONNELL, 2012; FELDENS et al., 2014; ELKARMI et al., 2015; KRAMER et al., 2015), estudos encontraram maior ocorrência no sexo masculino (GONDIM; MOREIRA NETO, 2005; ALDRIGUI et al., 2013). De comum acordo, a literatura refere que os dentes mais afetados são os incisivos centrais superiores (VIEGAS et al., 2010; (NORTON; O'CONNELL, 2012 CORRÊA-FARIA et al., 2015; KRAMER et al., 2015).

A principal etiologia do traumatismo dental em dentes decíduos são as quedas de modo geral, sendo as da própria altura mais frequentes em idades menores (KENWOOD; SEOW, 1989; FRIED et al., 1996 CARDOSO; DE CARVALHO ROCHA, 2002). As maloclusões em dentes anteriores do tipo overjet acentuado e mordida aberta anterior, assim

como, o selamento labial inadequado estão associadas a uma maior ocorrência de trauma em pré-escolares (NORTON; O'CONNELL, 2012; PIOVESAN et al., 2012; CORRÊA-FARIA et al., 2015; KRAMER et al., 2015).

Segundo o guia americano de traumatismo dental (MALMGREN et al., 2013), na primeira infância o traumatismo dental determina uma maior procura pelo atendimento de emergência odontológica, representando um grande desafio para clínicos e especialistas. No entanto, Aldrigui et al. (2013), relatam que 57% dos participantes do estudo foram atendidos 30 dias após o trauma e somente 10% em caráter de urgência. Ademais, o traumatismo dental muitas vezes é subdiagosticado. Tal fato é justificado pela elevada ocorrência das lesões do tipo subluxação e luxações leves que acometem principalmente tecidos ocultos dos dentes (HOLAN; YODKO, 2017) e pequenas lesões que envolvem somente fratura de esmalte. Tais lesões, podem apresentar sinais clínicos visíveis (pequenos sangramentos, leves deslocamentos, mobilidade leve e perda da estrutura), porém, passageiros, que se curam sem maiores complicações aparentes (SKAARE; JACOBSEN, 2005) ou muitas vezes são imperceptíveis aos olhos leigos dos pais, assim como, de profissionais, quando não há uma avaliação criteriosa, ou exame radiográfico complementar (HOLAN; YODKO, 2017).

O sucesso do tratamento e a manutenção do dente decíduo traumatizado, estão vinculados ao acompanhamento periódico e ao diagnóstico de sinais clínicos e radiográficos de alterações decorrentes do trauma, principalmente a infecção pulpar (DE CARVALHO ROCHA; CARDOSO, 2004; TANNURE et al., 2012). A hiperemia pulpar, muitas vezes sobrevém ao trauma, sendo que o aumento e as mudanças do fluxo sanguíneo na polpa dental podem ser suficientes para iniciar alterações degenerativas e necrose pulpar (KRAMER; FELDENS, 2013). Outro fator, é a contaminação bacteriana (BORUM; ANDREASEN, 1998) que ocorre por infecção do ligamento periodontal, tendo como via, o sulco gengival (ANDREASEN; ANDREASEN, 2001) e por contaminação através dos túbulos dentinários em traumas que envolvem a perda de esmalte e dentina (KRAMER; FELDENS, 2013).

O diagnóstico da necrose pulpar após o trauma em dentes decíduos é apontado como um grande desafio, uma vez que não são utilizados testes de vitalidade como na dentição permanente (BORUM; ANDREASEN, 1998; CARDOSO; DE CARVALHO ROCHA, 2004). Além disso, radiograficamente, pode haver sobreposição de imagens entre ápice do dente decíduo e o saco pericoronário do germe do dente permanente sucessor (BORUM; ANDREASEN, 1998; HOLAN, 2006).

Pode haver, também, dúvida em relação a reabsorção fisiológica da raiz do dente decíduo e a reabsorção patológica (HOLAN, 2004).

A severidade do trauma, o grau de mobilidade e deslocamento dentário após o trauma e a idade da criança no momento do trauma, são fatores associados a necrose pulpar no estudo de Borum e Andreasen, 1998. Em seu estudo Aldrigui et al. 2013 encontraram associação positiva entre a necrose pulpar e o deslocamento dental após o trauma, a fratura com exposição pulpar, o auto-ralato de dor, alteração de cor e a reabsorção inflamatória interna e a perda óssea. Embora o estudo de Aldrigui et al. 2013 aponte que o auto-relato de dor durante o acompanhamento do dente decíduo traumatizado seja considerado um fator de risco para a necrose pulpar, por não ser confiável na dentição decídua, os testes pulpares e elétricos não são indicados para o diagnóstico da necrose pulpar (BORUM; ANDREASEN, 1998; DE CARVALHO ROCHA; CARDOSO, 2004). Deste modo, para se estabelecer o diagnóstico de vitalidade ou não da polpa dental em dentes decíduos, estudos sugerem como mais confiável, os sinais clínicos de fístula e/ou abcesso. Adicional a estes sinais, também são considerados os radiográficos de lesão periapical e reabsorção radicular inflamatória externa (KENWOOD; SEOW, 1989; ALDRIGUI et al. 2013). Alguns estudos consideram a soma de sinais clínicos e/ou radiográficos como fatores indicativos/complementares ao diagnóstico de necrose pulpar durante o acompanhamento dos dentes decíduos traumatizados, alteração nos tecidos moles, sensibilidade a precursão e a palpação (HOLAN; FUKS, 1996; DIAB; ELBADRAWY, 2000), alteração de cor da coroa escura (WILSON, 1995), mobilidade prolongada e paralisação da formação radicular (BORUM; ANDREASEN, 1998). No entanto, somente ao fazer o acesso endodôntico do dente decíduo, o clínico irá tomar conhecimento da verdadeira condição pulpar (HOLAN, 1996; EVANS et al., 1999; HORI et al., 2011).

A alteração de cor da coroa é uma consequência comum após o trauma em dentes decíduos (KENWOOD; SEOW, 1989; BORUM; ANDREASEN, 1998; CARDOSO; DE CARVALHO ROCHA, 2002; DE CARVALHO ROCHA; CARDOSO, 2004), podendo ser o único sinal/sequela evidente do traumatismo dental (HOLAN, 2004; HOLAN; YODKO, 2017). Muitos pais buscam atendimento odontológico mediante o aparecimento da alteração de cor, não somente por preocupação, mas também por motivo estético (SOARES; CARDOSO; BOLAN, 2015). Neste sentido, o estudo de Viegas et al., 2014 verificou que a alteração de cor está associada ao impacto negativo na qualidade de vida das crianças, assim como, dos pais/cuidadores.

Embora, estudos tenham encontrado associação positiva entre a alteração de cor da coroa e a necrose pulpar (CARDOSO; DE CARVALHO ROCHA, 2010; ALDRIGUI et al. 2013; QASSEM et al., 2015), a alteração de cor não está claramente descrita como sendo indicador clínico de necrose pulpar. Essa ausência de informação deixa o clínico inseguro frente a casos onde se tem o relato do trauma e a alteração da cor da coroa do dente sem outro achado clínico ou radiográfico. Neste sentido, o clínico fica em dúvida se o dente deve ser tratado ou não.

Holan (1996), avaliou a condição da polpa dental a partir do acesso endodôntico de 50 dentes com alteração de cor escura, 37 dentes apresentaram necrose pulpar, 10 necrose parcial e somente 1 dente vitalidade pulpar. O autor conclui, que a alteração de cor em incisivos decíduos pode ser interpretada como sinal de degeneração pulpar. Cardoso e de Carvalho Rocha (2010), encontraram associação significativa entre a alteração de cor e o diagnóstico de necrose pulpar através do status da polpa dental durante o acesso endodôntico, entretanto, quase metade dos dentes (42,8%) sem alteração de cor da coroa estavam necrosados.

O conceito mais adotado pela literatura atual para dentes decíduos traumatizados com alteração de cor da coroa é: somente após o aparecimento de sinais clínicos de fístula/abcesso ou radiográficos de lesão periapical e reabsorção radicular patológica, pode-se indicar tratamento endodôntico devido a perda da vitalidade dental (CARDOSO; DE CARVALHO ROCHA, 2010; ALDRIGUI et al., 2013). No entanto, com o avanço do processo infeccioso e o diagnóstico tardio da necrose pulpar, aumenta-se a possibilidade de danos extensivos ao dente, o que pode levar a uma inviabilização do tratamento endodôntico, com aumento da exodontia precoce (ALDRIGUI et al., 2013). Ademais, além das sequelas no dente decíduo, o dente sucessor permanente também pode ser afetado (HOLAN, 2006).

Não há na literatura atual, uma resposta sedimentada em relação a questão: Existe associação entre a necrose pulpar e a alteração de cor em dentes decíduos traumatizados? Princípios científicos sólidos, mais precisos, com evidencias clínicas sintetizadas, auxiliam o conhecimento e a prática clínica (ATALLAH, 1997). Neste âmbito, a partir de uma revisão sistemática e a meta-análise, busca-se incluir uma estimativa mais precisa em relação aos resultados encontrados em pesquisas anteriores. Tais pesquisas são ferramentas importantes para preencher lacunas existentes na literatura, pois, auxiliam na tomada de decisão clínica a partir da integração de resultados de estudos independentes (HAIDICH, 2010). Deste modo, o objetivo do presente estudo foi verificar através de

uma revisão sistemática e meta-análise da literatura, a associação entre a necrose pulpar e a alteração de cor em dentes decíduos traumatizados.

2. OBJETIVOS

2.1 Objetivo geral

Objetiva-se, por meio de uma revisão sistemática da literatura verificar se existe associação entre a necrose pulpar e a alteração de cor em dentes decíduos traumatizados.

2.2 Objetivos específicos

- Verificar a associação entre o diagnóstico da necrose pulpar e a alteração de cor da coroa através de avaliação clínica e radiográfica.

- Verificar a associação entre o diagnóstico da necrose pulpar e a alteração de cor da coroa através da inspeção visual durante o acesso endodôntico.

3. METODOLOGIA

Esta revisão sistemática e meta-análise seguiu as orientações preconizadas pelo *Preferred Reporting Items for Systematic Reviews and Meta-Analysis* (PRISMA) (MOHER et al., 2015) (ANEXO 1), e as diretrizes de Maia e Antonio (MAIA; ANTONIO, 2012). O protocolo desenvolvido foi registrado no banco de dados *International Prospective Register of Systematic Reviews* (PROSPERO) sob o número CDR 42016044077 (ANEXO 2).

3.1 *Busca na literatura*

Uma pesquisa eletrônica foi realizada em no mês de maio de 2017 nas seguintes bases de dados eletrônicas: *PubMed/Medline, LILACS/ BBO, Scopus, Web of Science, Cochrane Library* e nas bases de dados da literatura cinzenta: *ProQuest, Open Grey,* Banco de Teses e Dissertações da CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior), *Google Scholar*. Foram utilizados os seguintes *MeSH terms*: 'tooth, deciduous', 'tooth injuries', 'dental pulp necrosis', 'dental pulp', 'crowns' and 'color'. Além disso, foram incluídos *MeSH synonyms*, termos relacionados e termos livres. Os termos foram combinados com os operadores booleanos *"AND"* e "*OR"*. Não foram aplicadas restrições de idioma ou data. A seleção dos estudos foi feita de forma independente por dois pesquisadores que aplicaram os critérios de inclusão e exclusão a partir títulos e resumos encontrados nesta revisão. Foi realizada também, uma pesquisa manual nas referências dos estudos incluídos. Foram feitos contatos com *experts* para identificar estudos não publicados ou em curso relacionados ao tema deste estudo.

3.2 *Critérios de elegibilidade*

Os critérios de inclusão para esta revisão estão de acordo com o acrônimo (PICOS-PECOS) Paciente/Problema; Intervenção/Exposição; Comparação e Desfecho. Foram incluídos estudos observacionais em dentes decíduos traumatizados (P) com (E) e sem necrose pulpar (C) e associados a alteração de cor da coroa (O). Foram utilizados os seguintes critérios de exclusão: artigos de revisão, resumos de conferências, cartas, estudos in vitro, relato de caso, estudos com menos de um mês de acompanhamento, estudos que incluíram amostra com neoplasias malignas, desnutrição e doenças crônicas, estudos onde a alteração de cor da coroa foi identificada após o tratamento endodôntico, superposição

amostral e estudos em que não apresentavam grupo controle (dentes traumatizados sem alteração de cor da coroa) (APÊNDICE A).

Todas as referências identificadas nos bancos de dados eletrônicos foram digitalizadas por título e resumo e os estudos duplicados foram removidos. Os critérios de elegibilidade foram utilizados para selecionar os estudos por título e resumo dos bancos de dados. Quando o título e o resumo não forneceram informações suficientes, o artigo completo foi examinado. Os textos completos só foram descartados em casos de consenso mútuo entre os revisores (BSM) e (NAA). Em caso de desacordo, um terceiro revisor (MC) foi consultado para uma decisão final sobre a inclusão ou não do estudo.

3.3 *Lista dos Dados*

Dois pesquisadores (BSM) e (NAA) de forma independente extraíram as informações necessária dos artigos selecionados. Foram extraídos os seguintes dados: características do estudo (autores, ano de publicação, país, desenho do estudo, número de participantes incluídos no estudo, idade dos participantes em anos), características da população (número de dentes decíduos traumatizados), características da exposição (número de dentes com necrose pulpar), características da comparação (número de dentes sem necrose pulpar), características do desfecho (número de dentes com alteração de cor da coroa). Os desentendimentos entre os autores foram resolvidos através de consenso mútuo ou discussão em conjunto com o terceiro revisor (MC). Foi feito o contato com os autores dos artigos selecionados quando os dados relevantes não foram relatados ou para informações adicionais.

3.4 *Avaliação da qualidade e Risco de viés*

A avaliação da qualidade metodológica e o risco de viés dos estudos foram verificados através da lista de diretrizes descritas por Fowkes e Fulton (FOWKES; FULTON, 1991). Esta lista de avaliação da qualidade permite a classificação de estudos transversais, de coorte, ensaios clínicos e estudos de caso-controle. Contém também, perguntas sobre o desenho do estudo, amostra, grupo controle, qualidade da avaliação e resultados, integridade e distorção das influências. Ao aplicar os critérios de avaliação do guia, foi tomada uma decisão sobre a qualidade metodológica utilizada nos estudos, se satisfatória ou não, para produzir informações úteis. Foi realizado o registro de atribuição de “maior” (++) ou “menor” (+) problema e "nenhum problema" foi

atribuído (0). Foi registrado “NA”, para itens onde a pergunta da lista de verificação não era aplicável.

Os autores elaboraram uma padronização da avaliação para cada questão da lista de verificação. Em relação a amostra, foram aplicadas as seguintes considerações: *“*Procedência da amostra*”* i) quando não informada (++); ii) informações parciais (+); iii) quando bem descritas (0). *“*Método de amostragem*”* (em artigos que objetivaram verificar a relação entre o diagnóstico de necrose e a alteração de cor da coroa) i) foi realizado o cálculo amostral (0); ii) descrição deficiente da amostra (+); iii) não fez o cálculo amostral (++); iiii) utilizou-se ‘NA’ para dados secundários. "Tamanho da amostra" i) foi realizado o cálculo amostral para verificação do tamanho ideal da amostra (0), para estudos sem o cálculo da amostra, 145 dentes foram considerados como o tamanho ideal da amostra de acordo com Qassem et al., 2015, ii) amostra > 145 (+); iii) amostra <145 (++).

Para os *“*Critérios de Inclusão/Exclusão*”* i) descreveu os critérios de inclusão e exclusão (0); ii) descreveu somente critérios de inclusão ou de exclusão (+); iii) não informa quais critérios inclusão/exclusão foram utilizados na pesquisa (++). Para verificar o *“*Controle de qualidade*”* utilizou-se (++) em estudos que não foram realizados com treinamento e calibração dos examinadores, (+) caso realizado somente com treinamento ou com a calibração e (0) foi realizado o treinamento e a calibração. Para “Fatores de confundimento*”* foram considerados os seguintes critérios: (++) quando a pesquisa não fez menção ao fator considerado (cárie), (+) quando utilizou somente na discussão e (0) quando usado como fator de exclusão e de confundimento da análise estatística ou na discussão do artigo.

Após a avaliação detalhada dos métodos e resultados, os estudos foram analisados quanto à possibilidade de distorção das influências. Por fim, para resumir a avaliação crítica e determinar o valor do estudo, três perguntas sobre cada categoria “Viés*”, “*Confundimento*”* e *“*Chance” foram respondidas. Se essas três perguntas resumidas foram respondidas com “Não”, então o estudo apresenta maior propensão a apresentar baixo risco de viés.

3.5 Medidas de sumarização e Meta - análise

Em relação ao número de dentes decíduos traumatizados, os critérios utilizados foram: associação ou relação da presença/ausência de necrose pulpar e a alteração de cor coroa. Para o diagnóstico de necrose pulpar, considerou-se: diagnóstico clínico (presença de abscesso e/ou

fístula), para o diagnóstico radiográfico (lesão periapical, reabsorção radicular patológica externa) e quanto ao status da polpa através de inspeção visual durante o acesso endodôntico (vital ou necrótica).

Os dados extraídos foram analisados usando o software *RevMan (Review Manager v. 5.3, The Cochrane Collaboration, Copenhagen, Dinamarca*) foi avaliada a relação entre a necrose pulpar e a alteração de cor da coroa em dentes decíduos traumatizados. Uma análise de subgrupos foi realizada, com um subconjunto de estudos que realizam o diagnóstico de necrose pulpar através da avaliação clínica e radiográfica e outro subconjunto de estudos que realizaram o diagnóstico de necrose de pulpar através do acesso endodôntico dos dentes traumatizados. A prevalência da alteração de cor da coroa (eventos) e o número total de dentes com e sem necrose de pulpar foram utilizados para calcular a relação da razão de chance com um intervalo de confiança de 95% (IC). Foram utilizados modelos de efeitos aleatórios e a heterogeneidade foi testada usando o índice I^2 (HIGGINS; GREEN, 2011). Se alguma informação necessária para a meta-análise estava ausente em qualquer um dos estudos selecionados, os autores foram contatados para fornecer os dados faltantes. As análises de sensibilidade foram realizadas para estimar e verificar a influência dos estudos, individualmente ou agrupados, nos resultados agrupados.

4. ARTIGO

Title: Pulp necrosis and crown discoloration: a systematic review and meta-analysis

Artigo a ser submetido à revista:

International Journal of Paediatric Dentistry (ANEXO 3)

International Journal of Paediatric Dentistry:

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Pulp necrosis and crown discoloration.

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Summary

Objetive: The study verified if there is an association of pulp necrosis and crown discolouration in traumatized primary teeth through a systematic review and meta-analysis.

Methods: A systematic literature search was conducted in PubMed/Medline, Lilacs/BBO, Scopus, Web of Science, Cochrane Library databases, and also in the grey literature. The PECO strategy was used to identify studies in traumatized primary teeth (P) with (E) or without (C) pulpal necrosis and its association with crown discoloration (O). A methodological quality assessment appraisal was conducted. The total number of teeth with and without pulp necrosis and the prevalence of crown discolouration were accessed. Random-effects models were employed, and heterogeneity was tested using the I^2 index ($p \leq 0.05$). *Results:* Eight studies with low risk of bias, were included in the analysis. A total of 1.494 traumatized primary teeth participated in the pooled meta-analysis. Of these, 1.414 were evaluated in the first subgroup (diagnosis of pulp necrosis through clinical and radiographic analysis) and the analysis demonstrated a positive association (p=0.0005/ OR 8.37 [2.51, 27.90], I^2=87%). Regarding 80 teeth in the second subgroup (diagnosis of pulp necrosis through endodontic access), the analysis demonstrated an absence association (p=0.36/ OR 2.46 [0.36, 16.94], I^2=54%) The pooled meta-analysis showed a positive association (p=0.0003/ OR 5.93 [2.24, 15.72], I^2=83%).

Conclusion: There is a positive association between pulp necrosis diagnosed through clinical and radiographic analysis and crown discolouration. The results should be considered with caution once the diagnosis of pulp necrosis was performed by limited criteria.

Introduction

There is a high prevalence of traumatic dental injury (TDI) in the primary teeth[1–3,] and the complications due TDI are observed immediately after the trauma or in the long term.[4] Pulp necrosis in post-trauma is a frequent sequela, affecting 22.3% to 24.0% of TDI in primary teeth.[5,6] The anoxia of pulp tissue[7] and bacterial contamination6 are the main causes of pulp vitality loss.

Diagnosis of pulp necrosis poses a challenge for paediatric dentistry,[8,9] once pulp vitality tests (thermal and/or electric) and pain reports are contraindicated for the diagnosis of pulp necrosis in children.[10,11] To determine if the pulp is vital or not vital in traumatic primary teeth, studies propose diagnosis based on clinical (fistula/abscess) and radiographic findings (periapical bone rarefaction, inflammatory lesion).[4,5,12,13] However, radiographic examinations can be imprecise because the images may overlap between the root apex of the primary tooth and the germ of the successor permanent tooth. In addition, there is the normal process of physiological resorption.[6,14] For this reason, a definitive diagnosis of the pulp condition is achieved through visual inspection, with presence or absence of bleeding during endodontic access.[9,14-16]

In addition, studies refer the aspect of crown discoloration as an indication of pulp necrosis.[6,14] Dark coronal discoloration in primary teeth can possibly be considered an early sign of pulp degeneration,[14] and some studies have found a positive association between diagnosis of pulpal necrosis and presence of crown discoloration in traumatized primary teeth.[4,5,17] The crown discoloration gives the clinician some suspect of pulpal changes, however, traumatized teeth without crown discoloration may also present such changes,[18] and the absence of symptoms or radiographic changes alone cannot be considered conclusive diagnosis of pulp vitality, because pulpal degeneration can occur without the appearance of symptoms.[10]

Crown discoloration is considered an unfavourable outcome after TDI and also is a sequela frequently found in traumatized primary teeth.[6,17,19,]20 Its clinical indication as diagnosis of pulpal necrosis is not clear in the current literature. The present systematic review and meta-analysis aims to verify if there is an association between presence of crown discoloration and pulp necrosis in traumatized primary teeth.

Materials and methods

This systematic review and meta-analysis was reported according to PRISMA protocol21 and the Maia and Antonio guideline.22 The developed protocol was registered in the PROSPERO database under number CRD42016044077.

Literature search strategy

A systematic search was conducted in the following electronic databases: PubMed/Medline, Lilacs/BBO, Scopus, Web of Science, Cochrane Library and also in the grey literature: ProQuest, Open Grey, CAPES Thesis Bank, Google Scholar (Appendix 1) through May 2017. MeSH terms such as 'tooth, deciduous', 'tooth injuries', 'dental pulp necrosis', 'dental pulp', 'crowns' and 'color' were used. Moreover, included were MeSH synonyms, related terms, and free terms. The terms were combined with the Boolean operators 'AND' and 'OR', respecting each databases rules. No language or date restrictions were applied. The selection of the studies was made independently by two researchers (BSM and NAA) applying the eligibility criteria on the titles and abstracts, as well as in the full text found in this review. There was also a search in the references of the included studies. Contacts were made with experts to identify related unpublished and ongoing studies.

Eligibility Criteria

The inclusion criteria for this review are according to the Population, Exposition, Comparisons, and Outcome (PECO)[23] strategy. The PECO strategy was used to identify observational studies in primary traumatized teeth (P) with (E) or without (C) pulp necrosis and its association with crown discolouration (O). Review articles, conference abstracts, letters, studies in vitro, case report and studies with follow-up of less than one month, studies with the sample included malignancies, malnutrition and chronic diseases, studies where the crown discolouration was identified after endodontic treatment, sample overlap, studies without a control group (traumatized teeth without pulp necrosis) and studies with the pulp necrosis diagnosed by the presence of crown discolouration were excluded from the present review.

The eligibility criteria were used to select the studies by the title and abstract from the databases, gray literature and manual search. When

the title and abstract did not provide sufficient information, the full article was examined. Texts were included after duplicates were removed. Furthermore, after applying eligibility criteria, the study was only discarded in cases of mutual (BSM and NAA) consensus. In cases of disagreement, a third author (MC) was consulted for a final decision on whether or not to include the study.

Data Extraction

Two researchers (BSM and NAA) extracted the required information from the selected articles independently. The following data were extracted: study characteristics (authors, year of publication, country, study design, number of participants included in the study, age of the participants in years), population characteristics (number of traumatized primary teeth), exposition characteristics (number of teeth with pulp necrosis), comparison characteristics (number of teeth without pulp necrosis), outcome characteristics (number of teeth with and without crown discolouration). Disagreements between the authors were resolved by discussing with a third author (MC) or mutual consensus. Authors were contacted for further details when relevant data was not reported or for additional information.

Quality assessment and Risk of bias

The quality assessment and bias control of the studies were applied according to guidelines and critical appraisal described by Fowkes and Fulton.[24] This quality assessment enables the classification of cross-sectional, cohort, controlled trial, and case–control studies. The checklist contains questions on study design, study sample, control group, quality of measurements and outcomes, completeness and distorting influences. When checking the criteria for each question, the importance of failures in relation to their expected effect on the results was scored as "major" (++) or "minor" (+) problem, and "no problem" was assigned as (0). 'NA' was registered, for items where the checklist question was not applicable.

The authors elaborated a standardization of the evaluation for each question of the checklist. In relation to the sample, the following considerations were applied in the items. "Source of Sample" i) when not informed (++) was assigned; ii) partial information (+) was assigned; iii) when well described (0) was assigned. "Sampling Method" (in articles

that aimed to verify the relationship between the diagnosis of pulp necrosis and the crown discolouration) i) the sample calculation was performed (0) was assigned; (ii) poor description of the sample (+) was assigned; iii) did not make the sample calculation (++) was assigned; iiii) 'NA' was assigned for secondary data. “Sample size” i) the sample calculation was performed for ideal sample size (0) was assigned, for studies without the sample calculation and 145 teeth were considered as an ideal sample size according to Qassem et al. 2015,[17] ii) with sample > 145 (+) was assigned, iii) with sample < 145 (++) was assigned. For “Entry Criteria/Exclusions” i) described the inclusion and exclusion criteria (0) was assigned; ii) described only inclusion or exclusion criteria (+) was assigned; iii) does not inform which inclusion/exclusion criteria were used in the search (++) was assigned.

In the item “Quality Control” if the studies did not performe the training or the calibration of the examiners (++) was assigned, if performed only with training or calibration (+) was assigned and if training and calibration were carried out (0) was assigned.

For the item “Confounding Factors” if the research did not mention the considered factor (caries) (++) was assigned, when used only in the discussion (+) was assigned, and if used as an exclusion factor and in the confounding of statistical analysis or article discussion (0) was assigned.

After the detailed evaluation of the methods and results, the studies were analysed regarding the possibility of distortion of influences. Lastly, to summarize the critical evaluation and to determine the value of the study by grading the evidences, three questions about “Bias”, “Confounding” and “Chance” were answered. If these three summary questions were answered with “NO”, then there was a high probability that the study presented methodological soundness (low risk of bias).

Summary measures and Meta-analysis

Only studies classified as “NO” for Summary Questions were included in quantitative analysis. In relation to the number of traumatized primary teeth, the criteria used was the association between the presence or absence of pulp necrosis and crown discolouration. For the diagnosis of pulp necrosis, clinical (presence the abscess and/or fistula) and/or radiographic sigs were used (periapical lesion or pathological root resorption) as well as the pulp status at the time of the endodontic access (vitality or necrosis).

The extracted data were analysed using RevMan software (Review Manager, version 5.3, The Cochrane Collaboration; Copenhagen, Denmark) to assess the relationship between pulp necrosis and crown discolouration in deciduous teeth. An overall analysis was performed. Besides, a subgroup analysis was performed with a subset of studies that performed the diagnosis of pulp necrosis through clinical and radiographic analysis and another subset of studies that perform diagnosis of pulp necrosis through tooth endodontic access. The prevalence of crown discolouration (events) and the total number of teeth with and without pulp necrosis were used to calculate the Odds Ratio with a 95% confidence interval (CI). Random-effects models were employed because the studies were not functionally equivalent in which the objective was to generalize the results from the meta-analysis25 and heterogeneity was tested using the I^2 index. Sensitivity analyses were further conducted to estimate and verify the influence of studies, one by one, or grouped, on the pooled results if the heterogeneity was considerable (75 a 100%).26 If possible, Funnel plot will be generated to demonstrate possible publication bias. If some of the information needed for the meta-analysis was absent from any of the selected studies, the authors were contacted to provide the missing data.

Results

A total of 2.520 titles/abstracts were found and retrieved: 2.519 by a search in the selected databases and 1 from the manual search. The 656 duplicated titles/abstracts were eliminated. After excluding duplicate citation, all titles/abstracts (n=1.864) were analysed according to the study criteria, and 1.836 were excluded. Of the 28 selected studies for full texts evaluation, twenty were excluded for the following reasons: did not evaluate the relationship between pulp necrosis and crown discolouration, sample overlap, with the pulp necrosis diagnosed by the presence of crown discolouration without a control group and one full paper copy not available (searches made in libraries/banks of Universities from Brazil, Europe and America/contact with author/institution were not obtained). Finally, eight[4,5,17,19,27-30] studies accorded to the inclusion criteria were included for qualitative and quantitative assessment (Figure 1).

Data extraction

A summary of the descriptive characteristics of the studies is recorded in Table 1. The age of the children varied from 0 to 7 years, only the article from Schröeder et al.[29] did not present data referring to the age of participants, and both sexes were included in all studies. All included articles used clinical and radiographic examinations for the diagnosis of pulp necrosis. Aldrigui et al.,[5] Cardoso and de Carvalho Rocha[4] and Qassem et al.[17] found a statistically significant association between the diagnosis of pulp necrosis and crown discolouration. The remaining articles presented only descriptive data. The studies of Cardoso and de Carvalho Rocha,[4] Qassem et al.[17] and Tanurre et al.[30] reported data on endodontic access/endodontic treatment, however, Qassem et al.[17] did not verify the pulp condition.

Quality assessment and Risk of Bias

The evaluation and qualification of the methodology and results of the eligible studies are found in Table 2, according to Fowkes and Fulton[24] quality assessment.

As to the sample, Cardoso and de Carvalho Rocha[4] and Kenwood and Seow[19] do not mention the initial sample size, whether it is representative of the population to be studied or not, therefore it was considered a major problem. In relation to the sampling method, Cardoso and de Carvalho Rocha[4] and Aldrigui et al.[5] do not inform how the sample selection was performed (sample calculation), this was considered a major problem. Cardoso and de Carvalho Rocha[4], Tannure et al.,[30] Colak et al.[27] and Kenwood and Seow[19] did not performe the sample calculation and if the sample was < 145 teeth, it was considered a major problem. Aldrigui et al.,[5] Pugliese D.,[28] Schröeder et al.[29] did not performe the sample calculation and if the sample was >145 teeth, it was considered a minor problem.

Kenwood and Seow[19] did not describe the inclusion and exclusion criteria used in the selection of the study sample, and this was considered a major problem, it was considered a minor problem for studies by Pugliese D.[28] and Tannure et al.[30] do not mention the exclusion criteria and the study by Schröeder et al.[29] the criteria for inclusion was not mentioned.

Regarding the of quality of measurements and outcomes, the quality of the controls was considered a major problem for Cardoso and de Carvalho Rocha,[4] Kenwood and Seow,[19] Schröeder et al.[29] and Pugliese D.,[28] in the four studies the researchers did not receive training

for data collection and calibration was not performed. In Aldrigui et al.,[5] the examiner received training but was not calibrated and this was considered as a minor problem. The studies of Kenwood and Seow,19 Pugliese D.,[28] Qassen et al.,[17] Schröeder et al.[29] and Tannure et al.[30] did not mention confounding factors, and this was considered as a major problem.

Considering the grading of the evidence, based on the answers of summary questions about “Bias”, “Confounding” and “Chance” the eight studies were qualified as having methodological soundness and that is low risk of bias (Table 2).

Meta-analysis

The meta-analysis was conducted only with the data available in the studies included in this systematic review. Eight studies with low risk of bias were included in quantitative synthesis.[4,5,17,19,27-30]

Figure 2 shows the forest plot with the included studies indicating significant overall heterogeneity (I^2=83%).

In an attempt to reduce heterogeneity, sensitivity analysis was performed by removing studies one by one.[26] During this stage, the heterogeneity ranged from 76% to 86%. Since there was no significant heterogeneity reduction, a group analysis was performed. The heterogeneity was reduced to "not important" (I^2=5%) and annulled (I^2=0%). Regardless of the value of heterogeneity, the overall effect remained unchanged, showing that the result of this meta-analysis is real. As a result, the authors decided to remain with the analysis including all possible studies and random-effects models were employed. Table 3 summarizes the heterogeneity analysis process.

A total of 1.494 traumatized deciduous teeth participated in this meta-analysis. Of these, 1.414 were evaluated in the first subgroup (diagnosis of pulp necrosis through clinical and radiographic analysis) and 80 teeth were part of the second subgroup (diagnosis of pulp necrosis through endodontic access).

In the first subgroup (diagnosis of pulp necrosis through clinical and radiographic analysis), of the total number of teeth with pulp necrosis (n=317) 79.18% (n=251) presented crown discolouration, while 42.48% (n=466) of the teeth without pulp necrosis (n=1097) presented crown discolouration, showing a positive association between the analyzed parameters (OR 8.37 [2.51, 27.90], p=0.0005, I^2 = 87%). In the second subgroup (diagnosis of pulp necrosis through endodontic access), 71.93%

(n=41) of the teeth with pulp necrosis (n=57) presented crown discolouration, while 43.48% (n=10) of the teeth without pulp necrosis (n=23) presented crown discolouration, demonstrating no association between the analysed parameters (OR 2.46 [0.36, 16.94], p=0.36, I^2 = 54%).

The pooled meta-analysis showed a positive association between crown discolouration and pulp necrosis in primary teeth (OR 5.93 [2.24, 15.72]; p=0.0003).

Discussion

The results of this systematic review and meta-analysis showed a positive association between pulp necrosis and crown discolouration in traumatized primary teeth when included in studies that used radiographic examination for the diagnosis of pulp necrosis. When considering only studies with visual inspection of the pulp, there was no significant association between the studied variables.

Methods of diagnosis of pulp condition are limited. The clinician should collect data from patient information (primary complaint and dental history), clinical examination, radiographic examination, and pulp tests (electrical and thermal for permanent teeth). These data should infer a possible diagnosis of pulp.[31,32] The diagnosis of the pulp condition in traumatized teeth may be more complex since the immediate pulp responses after the trauma indicate damage to the pulp, but not necessarily pulp necrosis.[33] Thus, the positive association between crown discolouration of traumatized primary teeth and pulp necrosis is another clinical indication in the search for an accurate diagnosis of the pulp condition, since pulp necrosis is a common complication in traumatized teeth.[34]

Schröeder et al.[28] and Aldrigui et al.[5] found a high frequency of periapical lesion on radiographic examination in traumatic primary teeth with crown discolouration and, likewise, Cardoso and de Carvalho Rocha[4] found a positive association performing the diagnosis after endodontic access.

Crown discolouration, although a common sign in traumatized primary teeth,[6,19,20] is not clearly described as being a clinical indicator of pulp necrosis. This lack of information leaves the clinician unsafe in cases where, in addition to the history of the trauma, there is a crown discolouration of the tooth without any clinical or radiographic findings. In addition, crown discolouration is noticeable for most parents, who,

therefore, end up seeking a dental service concerned about the discolouration.[35]

In dealing with traumatized teeth, early identification of vitality is very important because the earlier the clinician establishes a diagnosis, the more appropriate the treatment will be and better prognosis.[36, 37, 38] Dental pulp is usually not available for visual or microscopic evaluation.[32] Therefore, other methods of diagnosis of the pulp condition need to be used.[4] The final diagnosis of pulp necrosis includes progressive crown discolouration, percussion response, periapical lesion, or paralysis of root development in cases of permanent teeth.[13] Diagnosis is rarely based on an isolated finding, but rather on a variety of observations made by the clinician.[4,5,12,13] The clinical situation can be complex and proper diagnosis and treatment requires a multi-step diagnostic process.[32] Even if the association between necrosis and crown discolouration is found, it is prudent that other clinical and/or radiographic signs are verified by the clinician before the endodontic intervention. In cases of doubt, endodontic treatment should be postponed until obvious signs of pulp necrosis are identified.[33] The pulp response to dislocations should be observed with the objective of maintaining vital pulp and avoiding inappropriate endodontic interventions.[39]

Factors cited in the literature are related to pulp necrosis of TDI in primary teeth include: degree of displacement and loosening of tooth, age at time of TDI, crown fracture,[6] severity of trauma, fracture with pulp exposure, report of spontaneous pain, yellow, gray and brown discolouration.[5]

In the present meta-analysis, subgroup analysis was opted for, once the studies presented different criteria for the diagnosis of pulp necrosis. In the first subgroup, an analysis was performed with studies that used clinical and/or radiographic analysis to verify pulp necrosis. The studies that considered the diagnosis of pulp necrosis using the radiographic method alone[19,29] or who did not specify in their methodology which teeth the necrosis was diagnosed by radiographic signs or clinical signs,[5,17,27,28,30] should be viewed with caution due to the limitation that radiographic examinations offer.[6] Holan G.[40] describes in his study with traumatized primary teeth that 72% of these, during radiographic follow-up, expansion of the follicle of the successor permanent tooth was identified, and few teeth were associated with pulp necrosis. The author further states that the expansion of the permanent successor follicle proximal to the apex of primary teeth may be erroneously interpreted as a periapical lesion.[40]

In the second subgroup, the meta-analysis evaluated data from studies that verified pulp necrosis through visual inspection during endodontic access.[4,30] This analysis found that pulp necrosis verified during endodontic access was not positively associated with crown discoloraution. In this sense, it is also important to note that in the study by Cardoso and Rocha,[4] an expressive number of traumatized primary teeth was observed, without crown discoloration but with necrotic pulp as well as teeth with crown discolouration that were not indicated for endodontic treatment because they did not present other signs associated with pulp necrosis.

Some limitations should be considered when interpreting the results of this systematic review and meta-analysis. Some studies have only used the radiographic analysis as a diagnosis of pulp necrosis. Although the studies presented a scientific quality acceptable for this meta-analysis, the majority of the studies did not perform the sample calculation. Another relevant factor is that most of the studies did not aim to verify the relationship described in the present meta-analysis (secondary data). In this sense, longitudinal studies with a design elaborated specifically for this purpose are necessary to support the current evidence.

Despite the positive association between pulp necrosis and crown discolouration in traumatized primary teeth, the data reported in this systematic review should be viewed with caution since the diagnosis of pulp necrosis was performed using limited criteria.

What this paper adds:

A more precise estimate of the association between pulp necrosis and crown discolouration in traumatized primary teeth.

Why this paper is important for paediatric dentists:

Crown discolouration should be viewed with caution as pulp necrosis criteria since most of the studies used radiographic examinations to determine the pulpal condition, which have limitations.

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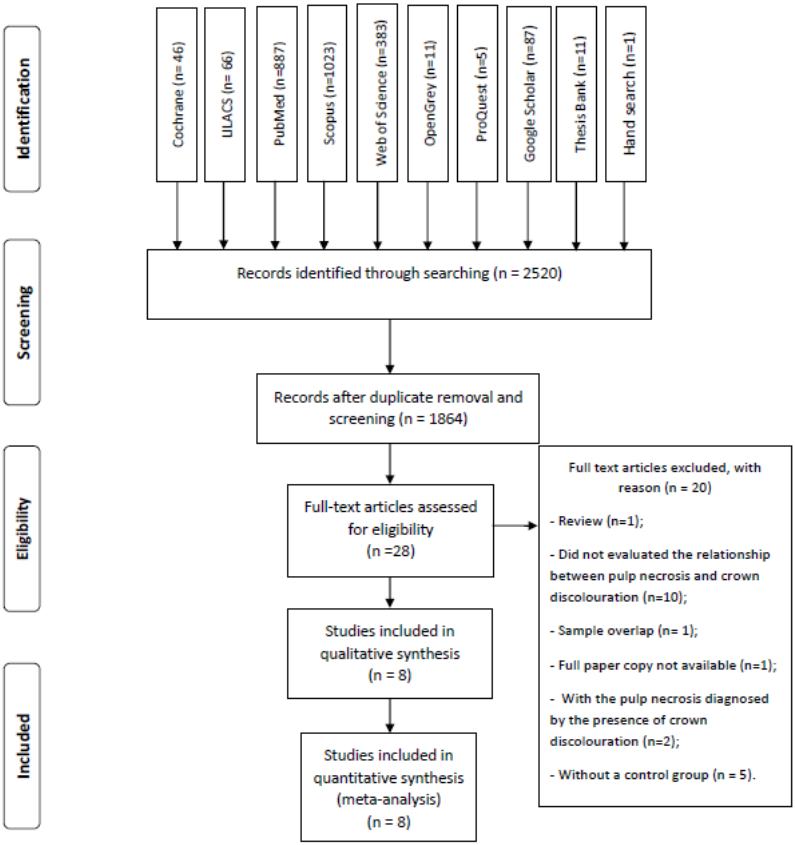

Figure 1. Flowchart diagram of literature search and selection criteria according to PRISMA statement.

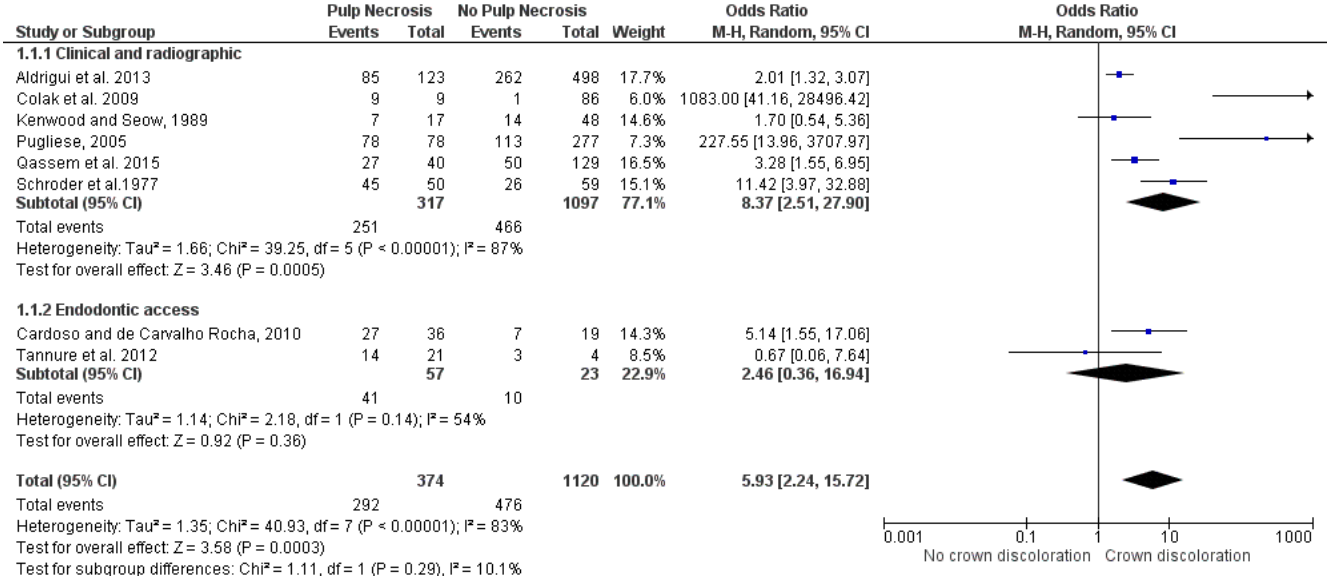

Figure 2. Forest plot with the included studies in meta-analysis.

Table 1. Data extraction of the included studies.

Author year/country	Study sample size (Children)	Source of study	Range of age (years)	Traumatized primary teeth*	Type of exam used for the diagnose of pulp necrosis	Description of teeth	Statistical analysis
Aldrigui et al. 2013/Brazil[5]	521	School of dentistry of the University of São Paulo	0-≥ 5	621	Clinical and/or radiographic	The result showed positive association between occurrence of pulp necrosis and crown discolouration.	Descriptive analysis, Wald test ($p<0.05$), Poisson regression model ($p<0.05$)
Cardoso and de Carvalho 2010/Brazil[4]	47	Trauma Patient Care Program (primary teeth) of the Federal University of Santa Catarina (UFSC, Brazil)	0->1	55	Clinical and/or radiographic and visual inspection	The associations between crown discoloration, clinical alteration, and radiographic alteration were not statistically significant. There was a significant association between crown discoloration and pulp necrosis at the time of endodontic access.	Descriptive analysis, Chi-squared test ($p<0.05$) and Univariate logistic regression ($p<0.05$)
Colak et al. 2009/Serbia[27]	70	Faculty of Dentistry, University of Belgrade, Serbia	0-6	95	Clinical and/or radiographic	Crown discolouration occurred in 10 intruded teeth and pulp necrosis in 9 cases.	Descriptive analysis
Kenwood and Seow 1989/Australia[19]	43	University of Queensland Dental School and Private	2-6	69	Radiographic	21 teeth showed crown discoloration, of these 7 teeth exhibited sigs of pulp necrosis.	Descriptive analysis

		Dental Office					
Pugliese D. 2005/Brazil[28]	247	Baby Clinic of the Araçatuba Dental School, UNESP	0->2	355	Clinical and/or radiographic	78 teeth showed pulp necrosis and crown discolouration.	Descriptive analysis
Qassem et al. 2015/Brazil[17]	128	Centre for the Study and Treatment of Dental Trauma in Primary Dentition (Pelotas, RS, Brazil)	1-7	169	Clinical and/or radiographic	The results showed positive association between pathological root resorption, occurrence of fistula and crown discolouration.	Descriptive analysis, Chi-squared test ($p<0.05$)
Schröeder et al.1977/Sweden[29]	116	School of dentistry, Molmo	-	109	Radiographic	Of the 50 teeth with crown discolouration, 45 presented pulp necrosis.	Descriptive analysis
Tannure et al. 2012/Brazil[30]	17	Dental traumatology Surveillance Center	2-6	25	Clinical and/or Radiographic and visual inspection	14 teeth showed pulp necrosis and crown discolouration.	Descriptive analysis

* Total calculated by author

Table 2. Quality assessment Fowkes e Fulton.[24]

Guideline	Checklist		Aldrigui et al.[5]	Cardoso and Carvalho[4]	Colak et al.[27]	Kenwood and Seow[19]	Pugliese D.[28]	Qassem et al.[17]	Schroeder et al.[29]	Tannure et al.[30]
Study design appropriate to objective?	**Objective**	**Common design**								
	Prevalence	Cross-sectional	NA	NA	NA	NA	NA	NA	NA	NA
	Prognosis	Cohort	NA	NA	NA	NA	NA	NA	NA	NA
	Treatment	Controlled trial	NA	NA	NA	NA	NA	NA	NA	NA
	Cause	Cohort, case–control, cross-sectional	0	0	0	0	0	0	0	0
Study sample representative?	Source of sample		0	++	0	++	0	0	0	0
	Sampling method		++	++	NA	NA	NA	NA	++	NA
	Sample size		+	++	++	++	+	0	+	++
	Entry criteria/exclusions		0	0	0	++	+	0	+	+
	Non-respondents		NA	NA	NA	NA	NA	NA	NA	NA
Control group acceptable?	Definition of controls		0	0	0	0	0	0	0	0
	Source of controls		0	0	0	0	0	0	0	0
	Matching/randomization		NA	NA	NA	NA	NA	NA	NA	NA
	Comparable characteristics		0	0	0	0	0	0	0	0

Quality of measurements and outcomes?	Validity	0	0	0	0	0	0	0	0
	Reproducibility	0	0	0	0	0	0	0	0
	Blindness	NA	NA	NA	NA	N A	NA	NA	NA
	Quality control	+	++	0	++	++	0	++	++
Completeness?	Compliance	NA	NA	NA	NA	NA	NA	NA	NA
	Dropouts	NA	NA	NA	NA	NA	NA	NA	NA
	Deaths	NA	NA	NA	NA	NA	NA	NA	NA
	Missing data	0	0	0	0	0	0	0	0
Distorting influences?	Extraneous treatments	NA	NA	NA	NA	NA	NA	NA	NA
	Contamination	NA	NA	NA	NA	NA	NA	NA	NA
	Changes over time	NA	NA	NA	NA	NA	NA	NA	NA
	Confounding factors	0	0	++	++	++	++	++	++
	Distortion reduced by analysis	0	0	0	0	0	0	0	0
Summary questions	Bias – Are the results erroneously biased in acertain direction?	NO	NO	NO	NO	NO	NO	NO	NO
	Confounding – Are there any serious confounding or other distorting influences?	NO	NO	NO	NO	NO	NO	NO	NO
	Chance – Is it likely that the results occurred by chance?	NO	NO	NO	NO	NO	NO	NO	NO

Table 3. Heterogeneity analysis process.

Included studies	I^{2} [26]	Overall effect
Aldrigui et al.,[5] Cardoso and de Carvalho Rocha,[4] Colak et al.,[27] Kenwood and Seow,[19] Pugliese D.,[28] Qassem et al.,[17] Schröeder et al.,[29] Tannure et al.[30]	83% Considerable heterogeneity	5.93 [2.24, 15.72] (p=0.0003)
Sensitivity analysis one by one	Range from 86% Considerable heterogeneity	Range from p=0.0001 to (p=0.003)
Aldrigui et al.,[5] Cardoso and de Carvalho Rocha,[4] Kenwood and Seow,[19] Qassem et al.,[17] Tannure et al.[30]	5% Heterogeneity not important	2.61 [1.73, 3.94] (p<0.0001)
Aldrigui et al.,[5] Qassem et al.,[17] Kenwood and Seow,[19] Tannure et al.[30]	0% Heterogeneity absent	3.50 [2.01, 6.10] (p<0.0001)

Appendix 1. Search Strategy

PubMed	**#1** primary* [Title/Abstract] OR "tooth, deciduous"[MeSH Terms] OR "primary dentition"[Title/Abstract] OR "primary tooth"[Title/Abstract] OR "primary teeth"[Title/Abstract] OR "deciduous teeth"[Title/Abstract] OR "deciduous tooth"[Title/Abstract] OR "deciduous dentition"[Title/Abstract] OR deciduous[Title/Abstract] OR "milk teeth"[Title/Abstract] OR "milk tooth"[Title/Abstract] OR "baby teeth"[Title/Abstract] OR "baby tooth"[Title/Abstract] OR "infant teeth"[Title/Abstract] OR "primary incisor"[Title/Abstract] OR "primary incisors"[Title/Abstract] OR "tooth injuries"[MeSH Terms] OR "tooth injuries"[Title/Abstract] OR "dental lesions"[Title/Abstract] OR "dental injuries"[Title/Abstract] OR "dental trauma"[Title/Abstract] OR "traumatic injury"[Title/Abstract] OR injuries[Title/Abstract] OR injury[Title/Abstract] OR trauma[Title/Abstract] OR traumatized[Title/Abstract] OR traumatic[Title/Abstract] OR traumatology[Title/Abstract] **#2** "dental pulp necrosis"[MeSH Terms] OR "dental pulp necrosis"[Title/Abstract] OR necrotic[Title/Abstract] OR pulp[Title/Abstract] OR pulps[Title/Abstract] OR pulpal[Title/Abstract] OR necrosis [Title/Abstract] OR necroses[Title/Abstract] **#3** "dental pulp"[MeSH Terms] OR "dental pulp"[Title/Abstract] OR dental[Title/Abstract] OR pulp[Title/Abstract] OR vitality[Title/Abstract] **#4** crowns[MeSH Terms] OR crowns[Title/Abstract] OR crown[Title/Abstract] OR coronal[Title/Abstract] OR discolouration[Title/Abstract] OR discoloration[Title/Abstract] OR discoloured[Title/Abstract] OR discolored[Title/Abstract] OR colour[Title/Abstract] OR color[MeSH Terms] OR color[Title/Abstract] **#1 AND #2 AND #3 AND #4**
LILACS	**#1** MH: primary* OR MH: "tooth, deciduous" OR MH: "primary dentition" OR MH: "primary tooth" OR MH: "deciduous teeth" OR MH: "deciduous tooth" OR MH: "deciduous dentition" OR MH: "deciduous" OR MH: "milk tooth" OR MH: "baby teeth" OR MH: "baby tooth" OR MH: "infant teeth" OR MH: "dente decíduo" OR MH: "dentição primaria" OR MH: "dente de leite" OR MH: "dentes de leite" OR MH: "dente primario" OR MH: "dentes primaries" OR MH: "Diente Primario" OR MH: "dentición primaria" OR MH: "dientes temporales" OR MH: "tooth injuries" OR MH: "dental lesions" OR MH: "dental injuries" OR MH: "dental trauma" OR MH: "traumatic injury" OR MH: injuries OR MH: "traumatismos de los dientes" OR MH: "injúria traumática" OR MH: "lesion traumática" **#2** MH: "dental pulp necrosis" OR MH: necrotic OR MH: pulp OR MH: pulps OR MH: pulpal OR necrosis OR necroses **#3** "dental pulp" OR dental OR pulp OR vitality OR MH: "pulp vitality" OR "vital pulp" OR MH: "vitalidade pulpar" OR MH: "vitalidad pulpar" **#4** crown OR crowns OR coronal OR discolouration" OR discolour OR discolor OR color OR colour OR descoloração **#1 AND #2 AND #3 AND #4**
Scopus	**#1** ((TITLE-ABS-KEY(primary*)) OR (TITLE-ABS-KEY ("tooth, deciduous")) OR (TITLE-ABS-KEY ("primary dentition")) OR (TITLE-ABS-KEY ("primary teeth")) OR (TITLE-ABS-KEY ("deciduous teeth")) OR (TITLE-ABS-KEY ("deciduous tooth")) OR (TITLE-ABS-KEY ("deciduous dentition")) OR (TITLE-ABS-KEY ("Milk Teeth")) OR (TITLE-ABS-KEY ("baby Teeth")) OR (TITLE-ABS-KEY ("primary incisors ")) OR (TITLE-ABS-KEY ("tooth injuries ")) OR (TITLE-ABS-KEY ("dental lesions")) OR (TITLE-ABS-KEY ("dental injuries")) OR (TITLE-ABS-KEY ("dental trauma")) OR (TITLE-ABS-KEY ("traumatic injury")) OR

	(TITLE-ABS-KEY (injuries)) OR (TITLE-ABS-KEY (injury)) OR (TITLE-ABS-KEY ("trauma")) OR (TITLE-ABS-KEY (" traumatized")) OR (TITLE-ABS-KEY ("traumatic")) OR (TITLE-ABS-KEY (" traumatology "))) **#2** (TITLE-ABS-KEY ("dental pulp necrosis")) OR (TITLE-ABS-KEY ("pulp necrosis")) OR (TITLE-ABS-KEY (necrotic)) OR (TITLE-ABS-KEY (pulp)) OR (TITLE-ABS-KEY ("pulps ")) OR (TITLE-ABS-KEY (" pulpal ")) OR (TITLE-ABS-KEY (necrosis)) OR (TITLE-ABS-KEY (necroses)) **#3** (TITLE-ABS-KEY ("dental pulp")) OR (TITLE-ABS-KEY ("pulp vitality")) OR (TITLE-ABS-KEY (pulp)) OR (TITLE-ABS-KEY (vitality)) **#4** (TITLE-ABS-KEY (crowns)) OR(TITLE-ABS-KEY (crown)) OR (TITLE-ABS-KEY (coronal)) OR (TITLE-ABS-KEY (discoloration)) OR (TITLE-ABS-KEY (discoloured)) OR (TITLE-ABS-KEY (colour)) OR (TITLE-ABS-KEY (color)) **#1 AND #2 AND #3 AND #4**
Web of Science	**#1** TS=(primary* OR "tooth, deciduous" OR "primary dentition" OR "primary tooth" OR "primary teeth" OR "deciduous teeth" OR "deciduous tooth" OR "deciduous dentition" OR "deciduous" OR "Milk Teeth" OR "Milk Tooth" OR "Baby Teeth" OR "infant teeth" OR "primary incisors" OR "tooth injuries" OR "dental lesions" OR "dental injuries" OR "dental trauma" OR "traumatic injury" OR injuries OR injury OR trauma OR trauma OR "traumatized" OR "traumatic" OR "traumatology") **#2** TS=("dental pulp necrosis" OR necrotic OR pulp OR pulps OR pulpal OR necrosis OR "necroses") **#3** TS=("dental pulp" OR dental OR pulp OR vitality) **#4** TS=(crown OR crowns OR coronal OR discolouration OR discoloured OR discolored OR colour OR color) **#1 AND #2 AND #3 AND #4**
Cochrane Library	**#1** MeSH descriptor: [Tooth, Deciduous] explode all trees **#2** MeSH descriptor: [Tooth injuries] explode all trees **#3** "Milk teeth": ti,ab,kw **#4** "infant teeth": ti,ab,kw **#5** "baby teeth": ti,ab,kw **#6** "dental trauma": ti,ab,kw **#7** "traumatic injury": ti,ab,kw **#8** "dental lesions": ti,ab,kw **#9** "dental injury": ti,ab,kw **#10 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9** **#11** MeSH descriptor: [Dental pulp necrosis] explode all trees **#12** pulp: ti,ab,kw **#13** necrosis: ti,ab,kw **#14 #11 or #12 or #13**

	#15 MeSH descriptor: [Dental pulp] explode all trees **#16** "pulp vitality": ti,ab,kw **#17** dental: ti,ab,kw **#18** pulp: ti,ab,kw **#19** vitality: ti,ab,kw **#20 #15 or #16 or #17 or #18 or #19** **#21** MeSH descriptor: [Tooth crown] explode all trees **#22** MeSH descriptor: [Tooth Discoloration] explode all trees **#23** coronal: ti,ab,kw **#24** color: ti,ab,kw **#25** colour: ti,ab,kw **#26 #21 or #22 or #23 or #24 or #25 #27 #10 and #14 and #20 and #26**
OpenGrey	"“traumatic dental” OR trauma AND “pulp necrosis” AND “pulp vitality” AND discolored
ProQuest	**#1** all("primary dentition" OR "primary tooth" OR "primary teeth" OR "deciduous teeth" OR "deciduous tooth" OR "deciduous" OR "tooth injuries" OR "dental lesions" OR "dental injuries" OR "dental trauma" OR "traumatic injury" OR trauma OR traumatized OR traumatic) **#2** all("dental pulp necrosis" OR "necrotic" OR "pulps" OR "pulp necrosis" OR necroses) **#3** all("dental pulp" OR "pulp vitality" OR pulp OR vital OR vitality) **#4** all(crown OR coronal OR discolouration OR discoloration OR discoloured) **#1 AND #2 AND #3 AND #4**
Banco de teses e dissertações CAPES	all("primary dentition" OR "primary tooth" OR "primary teeth" OR "deciduous teeth" OR "deciduous tooth" OR "deciduous" OR "tooth injuries" OR "dental lesions" OR "dental injuries" OR "dental trauma" OR "traumatic injury" OR trauma OR traumatized OR traumatic) AND all("dental pulp necrosis" OR "necrotic" OR "pulps" OR "pulp necrosis" OR Necroses) AND all("dental pulp" OR "pulp vitality" OR pulp OR vital OR vitality) AND all(crown OR coronal OR discolouration OR discoloration OR discoloured)
Google Scholar	“traumatic dental” OR trauma AND “pulp necrosis” AND “pulp vitality” AND discoloured filetype:pdf

5. CONSIDERAÇÕES FINAIS

Diante do presente estudo, pode-se observar uma associação positiva entre a necrose pulpar e a alteração de cor da coroa em dentes decíduos traumatizados. No entanto, é importante ressaltar que ao considerar somente os estudos com inspeção visual da polpa dental durante o acesso endodôntico, os resultados encontrados mostram ausência de associação significativa entre as variáveis estudadas.

Outro fator relevante a ser considerado mediante os resultados encontrados neste estudo, refere-se ao fato de que alguns estudos incluídos na presente meta-análise utilizaram somente a avalição radiográfica como diagnóstico da necrose pulpar. Desta forma, a associação positiva entre a necrose pulpar e a alteração de cor da coroa deve ser vista com cautela, uma vez que, o diagnóstico de necrose pulpar foi realizado através de critérios limitados.

Portanto, a associação positiva entre a necrose pulpar e a alteração de cor da coroa em dentes decíduos traumatizados, fornece ao clínico mais um fator indicativo de possível alteração pulpar.

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APÊNDICE A – Artigos excluídos com as razões das exclusões.

	Autor, Ano	Razão da exclusão
1.	(CAPRIOGLIO et al., 2014)	2
2.	(CARDOSO; DE CARVALHO ROCHA, 2002)	2
3.	(CARVALHO; JACOMO; CAMPOS, 2010)	2
4.	(COSTA et al., 2016)	6
5.	(CROLL; PASCON; LANGELAND, 1987)	7
6.	(DIAB; ELBADRAWY, 2000)	1
7.	(ELOVIKOVA et al., 1995)*	
8.	(HOLAN; TOPF; FUKS, 1992)	2
9.	(HOLAN; FUKS, 1996)	7
10.	(HOLAN, 2004)	7
11.	(HOLAN, 2006)	2
12.	(JACOBSEN; SANGNES, 1978)	7
13.	(LAURIDSEN et al., 2017)	6
14.	(MACARI, 2004)	2
15.	(PUGLIESI et al., 2004)	2
16.	(QASSEM et al., 2014)	2
17.	(RAMOS-JORGE et al., 2017)	2
18.	(SANTOS; CARDOSO; ALMEIDA, 2011)	2
19.	(SOXMAN; NAZIF; BOUQUOT, 1984)	7

* Não foi obtido acesso ao texto completo.

Legenda:

1) Artigos de revisão, resumos de conferências, cartas, estudos in vitro, relato de caso;
2) Estudos com menos de um mês de acompanhamento;
3) Estudos que incluíram amostra com neoplasias malignas, desnutrição e doenças crônicas;
4) Estudos onde a alteração de cor da coroa foi identificada após o tratamento endodôntico;
5) Superposição amostral;
6) Estudos em que não apresentavam grupo controle (dentes decíduos traumatizados sem alteração de cor da coroa).

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ANEXO 1- PRISMA Checklist

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

ANEXO 2- Protocolo registrado no PROSPERO

UNIVERSITY of York
Centre for Reviews and Dissemination

NHS
National Institute for Health Research

PROSPERO International prospective register of systematic reviews

Review title and timescale

1 Review title
Give the working title of the review. This must be in English. Ideally it should state succinctly the interventions or exposures being reviewed and the associated health or social problem being addressed in the review.
Is there an association between pulp necrosis and crown discoloration in traumatized primary teeth? A systematic review

2 Original language title
For reviews in languages other than English, this field should be used to enter the title in the language of the review. This will be displayed together with the English language title.
Existe associação entre a necrose pulpar e a alteração de cor em dentes decíduos traumatizados? Uma revisão sistemática

3 Anticipated or actual start date
Give the date when the systematic review commenced, or is expected to commence.
03/04/2016

4 Anticipated completion date
Give the date by which the review is expected to be completed.
29/09/2017

5 Stage of review at time of this submission
Indicate the stage of progress of the review by ticking the relevant boxes. Reviews that have progressed beyond the point of completing data extraction at the time of initial registration are not eligible for inclusion in PROSPERO. This field should be updated when any amendments are made to a published record.

The review has not yet started ×

Review stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	Yes	Yes
Formal screening of search results against eligibility criteria	Yes	Yes
Data extraction	Yes	Yes
Risk of bias (quality) assessment	Yes	Yes
Data analysis	No	No

Provide any other relevant information about the stage of the review here.

Review team details

6 Named contact
The named contact acts as the guarantor for the accuracy of the information presented in the register record.
Dr Cardoso

7 Named contact email
Enter the electronic mail address of the named contact.
mariane_cardoso@hotmail.com

8 Named contact address
Enter the full postal address for the named contact.
Universidade Federal de Santa Catarina, UFSC, Campus Universitário, CCS-ODT-Trindade Florianópolis, Santa Catarina, Brasil

9 Named contact phone number
Enter the telephone number for the named contact, including international dialing code.
+55483721-9920

UNIVERSITY of York
Centre for Reviews and Dissemination

NHS
National Institute for Health Research

10 Organisational affiliation of the review
Full title of the organisational affiliations for this review, and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.
Federal University of Santa Catarina

Website address:
http://ufsc.br/

11 Review team members and their organisational affiliations
Give the title, first name and last name of all members of the team working directly on the review. Give the organisational affiliations of each member of the review team.

Title	First name	Last name	Affiliation
Ms	Barbara Suelen	Moccelini	MSc Student
Ms	Nashalie Andrade	de Alencar	PhD Student
Dr	Mariane	Cardoso	Adjunct Professor
Dr	Michele	Bolan	Adjunct Professor
Dr	Lucianne Cople	Maia	Adjunct Professor

12 Funding sources/sponsors
Give details of the individuals, organizations, groups or other legal entities who take responsibility for initiating, managing, sponsoring and/or financing the review. Any unique identification numbers assigned to the review by the individuals or bodies listed should be included.
Programa UNIEDU PÓS-GRADUAÇÃO/FUMDES

13 Conflicts of interest
List any conditions that could lead to actual or perceived undue influence on judgements concerning the main topic investigated in the review.
Are there any actual or potential conflicts of interest?
None known

14 Collaborators
Give the name, affiliation and role of any individuals or organisations who are working on the review but who are not listed as review team members.

Title	First name	Last name	Organisation details

Review methods

15 Review question(s)
State the question(s) to be addressed / review objectives. Please complete a separate box for each question.
Is there an association between pulp necrosis and crown discoloration in traumatized primary teeth?

16 Searches
Give details of the sources to be searched, and any restrictions (e.g. language or publication period). The full search strategy is not required, but may be supplied as a link or attachment.
The following electronic databases will be searched: PubMed/MEDLINE, Scopus, Web of Science, the Cochrane Central Register of Controlled Trials (CENTRAL), LILACS. Grey literature: OpenGrey, ProQuest Dissertations and Theses, and Google Scholar will be searched for relevant literature. In addition, a hand search will be conducted through the references of included studies, and the tables of contents of peer-reviewed international journals in the field.

17 URL to search strategy
If you have one, give the link to your search strategy here. Alternatively you can e-mail this to PROSPERO and we will store and link to it.

I give permission for this file to be made publicly available
Yes

18 Condition or domain being studied
Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes.
The aim of treatment in traumatized primary teeth is to minimize the damage to the teeth and to the germ of the permanent successor. This study aims to verify the association between pulp necrosis and crown discoloration in traumatized primary teeth.

19 Participants/population
Give summary criteria for the participants or populations being studied by the review. The preferred format includes details of both inclusion and exclusion criteria.
Patients with traumatized primary teeth.

20 Intervention(s), exposure(s)
Give full and clear descriptions of the nature of the interventions or the exposures to be reviewed
Pulp necrosis.

21 Comparator(s)/control
Where relevant, give details of the alternatives against which the main subject/topic of the review will be compared (e.g. another intervention or a non-exposed control group).
Pulp vitality.

22 Types of study to be included
Give details of the study designs to be included in the review. If there are no restrictions on the types of study design eligible for inclusion, this should be stated.
Observational studies, retrospective studies, cross-sectional studies, cohort studies, and case series studies which have clinically evaluated crown discolouration in traumatized primary teeth and pulp necrosis in healthy children, and which encompass all types of dental trauma.

23 Context
Give summary details of the setting and other relevant characteristics which help define the inclusion or exclusion criteria.
Crown discolouration in traumatized primary teeth and pulp necrosis occurring in healthy children, encompassing all types of dental trauma.

24 Primary outcome(s)
Give the most important outcomes.
Association of pulpal necrosis in discoloured primary teeth.

Give information on timing and effect measures, as appropriate.

25 Secondary outcomes
List any additional outcomes that will be addressed. If there are no secondary outcomes enter None.
None.

Give information on timing and effect measures, as appropriate.

26 Data extraction (selection and coding)
Give the procedure for selecting studies for the review and extracting data, including the number of researchers involved and how discrepancies will be resolved. List the data to be extracted.
Two reviewers will perform study selection, as well as data collection. A third reviewer will be consulted in case of disagreement between the reviewers.

27 Risk of bias (quality) assessment
State whether and how risk of bias will be assessed, how the quality of individual studies will be assessed, and whether and how this will influence the planned synthesis.
Risk of bias will be assessed according to the design of the included studies, using Fowkes and Fulton guidelines.

28 Strategy for data synthesis
Give the planned general approach to be used, for example whether the data to be used will be aggregate or at the level of individual participants, and whether a quantitative or narrative (descriptive) synthesis is planned. Where

appropriate a brief outline of analytic approach should be given.
Data will be clustered and statistical analysis will be applied if the homogeneity of the included articles is high.

29 Analysis of subgroups or subsets
Give any planned exploration of subgroups or subsets within the review. 'None planned' is a valid response if no subgroup analyses are planned.
None planned

Review general information

30 Type and method of review
Select the type of review and the review method from the drop down list.
Diagnostic, Systematic review

31 Language
Select the language(s) in which the review is being written and will be made available, from the drop down list. Use the control key to select more than one language.
English

Will a summary/abstract be made available in English?
Yes

32 Country
Select the country in which the review is being carried out from the drop down list. For multi-national collaborations select all the countries involved. Use the control key to select more than one country.
Brazil

33 Other registration details
Give the name of any organisation where the systematic review title or protocol is registered together with any unique identification number assigned. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here.

34 Reference and/or URL for published protocol
Give the citation for the published protocol, if there is one.
Give the link to the published protocol, if there is one. This may be to an external site or to a protocol deposited with CRD in pdf format.

I give permission for this file to be made publicly available
Yes

35 Dissemination plans
Give brief details of plans for communicating essential messages from the review to the appropriate audiences.
Do you intend to publish the review on completion?
Yes

36 Keywords
Give words or phrases that best describe the review. (One word per box, create a new box for each term)
Dental trauma

primary teeth

pulp necrosis

crown discoloration

37 Details of any existing review of the same topic by the same authors
Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible.

38 Current review status
Review status should be updated when the review is completed and when it is published.
Ongoing

39 Any additional information
Provide any further information the review team consider relevant to the registration of the review.

40 Details of final report/publication(s)
This field should be left empty until details of the completed review are available.
Give the full citation for the final report or publication of the systematic review.
Give the URL where available.

ANEXO 3- Manuscrito Revista International Journal of Paediatric Dentistry

International Journal of Paediatric Dentistry: Scientific papers style guide for authors

Paula Holgerson[1], Jennifer Sjöström[1], Christina Rowley[1,2](full names of each author should be given)

[1]Department of Odontology, Pediatric Dentistry, Faculty of Medicine, Umeå University, Umeå, Sweden

[2]Department of Cariology and Endodontics, School of Dentistry, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark

Running title: xylitol effects on plaque and mutans streptococci (no more than 40 characters)

Key words: Do not give these as the journal does not use keywords.

Correspondence address: Dr. Paula Holgerson

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Summary

Objective: Give only the aims and objectives in this section.

Methods: Give the main methodology behind the study but do not include any references.

Results: Give the main results presented in the paper.

Conclusion: Give the conclusions that you draw from the results. The summary should not exceed 250 words.

Introduction

The paper should be split into the following sections and the author should use Times New Roman 12pt. Please also ensure that the manuscript is double-spaced and in UK English.

Materials and methods

Subheadings should appear in italics

Statistical methods

For example: All data were processed by SPSS software (12.0, SPSS Inc., Chicago Ill, USA). The index for dental plaque were scored and categorised before evaluated with chi-square tests. Bacterial and biochemical data were subjected to analysis of variance (ANOVA) or Student's *t*-test. A *P*-value less than 0.05 were considered as statistically significant.

Style issues

Lists should appear in the main body of the text and should not be bulleted or numerical e.g.

- Point 1,
- Point 2 and
- Point 3

These should appear as: point 1; point 2; and point 3, and run on from each other.

All abbreviations should be given in full in the abstract and their first usage in the main body of the paper.

All chemicals/instruments used must have the supplier details provided, including city and country of supplier e.g. (Bio-Rad Laboratories, Hercules, CA, USA).

All references should follow the Vancouver System, and any paper that does not comply will be sent back to the author.

Results

Only give errors to the same accuracy as the findings, e.g. 1.22 ± 0.22 but not 1.22 ± 0.223.

All tables and figures should be cited in the results section.

Discussion

Do not cite tables and figures in this section. This section should discuss the findings and present your conclusions.

Bullet points:

What this paper adds

- No more than 3 bullet points.
-

Why this paper is important for paediatric dentists

- No more than 3 bullet points.
-

Acknowledgements:

Give any acknowledgements and also any funding should be stated here.

References

Journal titles should be abbreviated as seen in PubMed. Articles must be published or in press to appear here. A paper that is submitted or in preparation should only appear in the main body of the text.

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Figure legends – figure files should be supplied separately and not part of the word document. Figure files should be high resolution (≥ 300dpi) and in EPS or TIFF format. Only supply figure files in colour if you intend to pay for colour printing.

Figure 1.

Proportion of salivary mutans streptococci (MS) in relation to the total viable counts (TVC) at baseline and after 4 weeks of daily chewing on xylitol-containing gums (Group B; 6.18 g/day) or sorbitol/maltitol control gums (group A). Star denotes a statistically significant difference ($p<0.01$) compared with baseline.

Table 1.

Percentage distribution of sites with visible plaque scored according the Greene-Vermillion simplified oral debris index (OHI-S) in 128 schoolchildren. The values are based on clinical assessment after erythrosine-staining of 6 pre-determined sites from each participant.

Group/time	Score			
	0	1	2	3
A (sorbitol-maltitol)				
Baseline	30.1	41.8	23.1	5.0
4 weeks*	41.1	43.0	15.6	0.3
B (xylitol)				
Baseline	24.6	47.8	25.1	2.5
4 weeks*	44.5	40.6	14.0	0.9

* distribution significantly different from baseline, $p<0.05$, Chi-square test