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Review Article

Antibacterial Effect of Endodontic Irrigating Solutions in Pediatric Dentistry: A Systematic Review and Meta-Analysis

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Received: April 22, 2021; **Published:** May 31, 2021

Abstract

Background: Removal of diseased pulpal tissue is paramount to the success of pulp therapy in primary teeth. Biomechanical canal preparation aids in removal of pulp along with shaping of the canal. However, owing to the tortuosity of the pulp canals in primary teeth, it may not possible to eliminate the pulp tissue or organic debris completely; hence the use of irrigants has been emphasised. A pulp canal space free of microbes is essential for obturation. Antibacterial efficacy of the endodontic irrigating solutions is hence deemed to be important. However, there is no clear consensus as to which irrigating solution in primary teeth has better antibacterial properties.

Objectives: To assess the antibacterial effectiveness of root canal irrigating solutions used in primary teeth using reduction in colony forming units as an outcome measure.

Search Methods: An electronic search was undertaken on PubMed, Embase, Scopus, Prospero and Google Scholar for articles on irrigating solutions used in pulpectomy in children. All electronic searches were last updated in August 2019. Search terms used were irrigating solutions, root canal irrigating solutions, antimicrobial, antibacterial and primary teeth.

Data Collection and Analysis: Two reviewers (N.P. and A.K.) independently extracted data using single Excel data extraction form from the study described. The data form continued the following information: author names and year of publication, study design, number of participants, age, type of intervention, change in colony forming units/ml in proportion and standardization of procedure.

Main Results: 4 trials (220 participants) were included. All four studies measured the outcome in terms of reduction in colony forming units (CFU/ml). The various agents used in the studies were N. Saline, Sodium Hypochlorite, MTAD and *Morinda citrifolia*. The pooled OR showed no statistical difference between the antibacterial efficacy of any of the irrigating solutions (OR 0.45 (0.10 - 1.96)). There was a moderate heterogeneity ($p = 0.03$, $I^2 = 66\%$). The overall risk of bias was unclear.

Conclusion: All irrigating solutions have antibacterial properties when used in primary teeth; however there is inconclusive evidence regarding the superiority of any one over the other. Evidence available for assessing the effectiveness of antibacterial properties of various root canal irrigating solutions used in primary teeth is of poor quality.

Keywords: *Antibacterial Effectiveness; Primary Teeth; Root Canal Irrigating Solutions; Pulpectomy*

Abbreviations

A.J.: Ashwin Jawdekar; A.K.: Amar Katre; CFU/ml: Colony Forming Units Per Mili-Litres; CHX: Chlorhexidine; MCJ: *Morinda citrifolia* Juice; NaOCl: Sodium Hypochlorite; N.P.: Nivedita Pande; OR: Odds Ratio; RCT: Randomized Controlled Trial

Introduction

Removal of diseased pulpal tissue is paramount to the success of pulp therapy in primary teeth [1]. Accessory canals may also occur at the bifurcation of the multi-rooted primary teeth [2]. Starting with the early works of Hess and Zurcher [3] to more recent studies the anatomic complexities of the root canal systems have long been established. Prior to 1940's water was used as an irrigating material since it was inexpensive and readily available. Since then various irrigants have been tried in permanent teeth. The properties of irrigating solutions primarily useful to endodontic procedure are the flushing action, antibacterial effect and tissue dissolution [4]. The biomechanical preparation as it is commonly referred to, is a combination of chemical disinfection of the canals for eliminating the microbes and dissolution of the organic debris and flushing of the dentinal debris [5,6]. Several irrigating solutions have been in use. Sodium Hypochlorite, Normal saline, chlorhexidine, hydrogen peroxide, MTAD to name a few [7]. In a study by Peters., *et al*. it was shown that 35% or more of the root canal surfaces (including canal fins, isthmi and cul-de-sacs) remained uninstrumented [8]. AAPD guideline on pulp therapy (2020) recommends 1% Sodium hypochlorite in primary teeth [9].

Biomechanical canal preparation aids in removal of pulp along with shaping of the canal. It is practically not possible to eliminate the pulp tissue or organic debris completely; hence the use of irrigants has been emphasized. It is important to compare the antibacterial effectiveness of various irrigating solutions used in primary teeth to apply it to clinical practice. However, there is no clear consensus as to which irrigating solutions in primary teeth have better antibacterial properties. Hence, this review was undertaken.

Objectives of the Study

Primary objectives:

- To assess the anti-bacterial effectiveness of various irrigating solutions used in primary teeth.

Secondary objectives:

- Patient acceptance to taste of irrigating solutions.

Materials and Methods

This review was undertaken using PRISMA guidelines.

Criteria for considering studies for this review

Types of studies

- Clinical and controlled trials in 3 - 12 year old children involving primary teeth indicated for pulpectomy.
- Full texts articles in English.

Types of participants

3 - 12 year old children with primary teeth that were indicated for pulpectomy were included for this review.

Types of outcome measures

Primary outcomes

The antibacterial effect was measured as change in Colony forming units (CFU/ml).

Secondary outcomes

The secondary outcome measure was patient acceptance towards taste.

Search methods for identification of studies

An electronic search for articles on irrigating solutions used for pulpectomy in children was undertaken. A comprehensive search for eligible articles was undertaken from the following databases: PubMed, Cochrane library, Embase, Scopus, Prospero and Google scholar. All electronic searches were last updated in August 2019. Search terms used were irrigating solutions, root canal irrigating solutions, antimicrobial, antibacterial and primary teeth. The references listed in included articles and textbooks were also examined manually to find additional eligible studies.

Data collection and analysis

Two reviewers (N.P. and A.K.) independently extracted data using single Excel data extraction form. The data form contained the following information: author names and year of publication, title, objectives, study design, number of participants, age, intervention, change in colony forming units/ml, standardization of procedure.

Selection of studies

Records were stored in Endnote. Two reviewers independently scanned each title and abstract of the studies to narrow down and subsequently read the full articles of those that were potentially eligible. Under the circumstance that uncertainties or discrepancies emerged between the two reviewers, it was settled through discussion with a third reviewer (A.J.).

Data extraction and management

Two reviewers independently extracted data using single Excel data extraction form. The articles reported change in CFU/ml as absolute values but these were converted to proportions for comparative and statistical purposes. Hence, the change in CFU/ml was depicted as proportion. The secondary outcomes were also sought. They were patient acceptance towards taste of the irrigant. The standardization of procedure included the uniformity of pulpectomy, application of isolation agents like rubber dam, the quantity of the irrigation used and sample collection procedure pre and post the usage of irrigant.

Assessment of risk of bias in included studies

Risk of bias was assessed using the Cochrane tool for assessing the risk of bias (Version 2, 2011).

Measures of treatment effect

Proportion change of pre and post colony forming units was assessed for this review.

Dealing with missing data

For addressing the missing data, authors were contacted. Three reminders were sent via the email of the corresponding authors for obtaining the raw data and missing details of methodology.

Assessment of heterogeneity

The funnel plot was utilized to assess the heterogeneity of studies reporting the outcome measures.

Results

Description of studies

Results of the search

Identification of trials and the selection of studies are depicted in the PRISMA flowchart of studies (Figure 1).

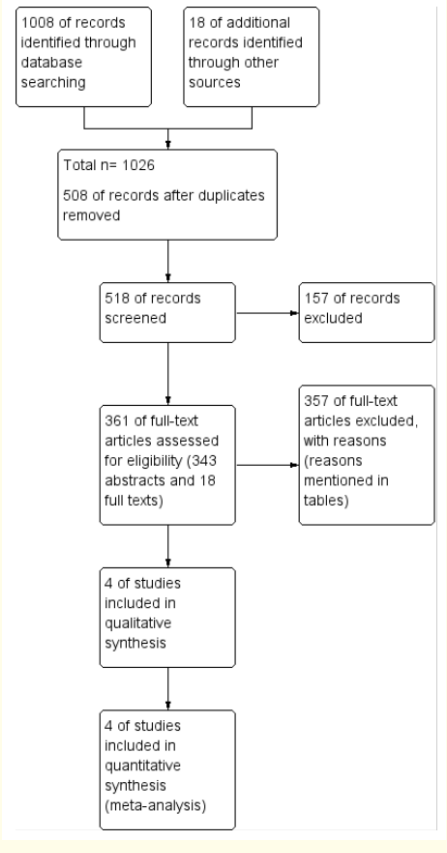

Figure 1: *PRISMA flow diagram of included studies.*

Selection of trials

1026 articles were assessed for eligibility. 518 articles were screened after eliminating duplicates. 361 were assessed (343 were abstracts and 18 were full text articles). 357 were excluded with reasons (Annexure 1). 4 were selected for the final review.

Included studies

There are 4 articles included published between 2013 and 2017. Three trials were conducted in India (Jolly 2013; Katge 2015 and Chandwani 2017) and in Mexico (Ruiz-Esparza, 2015). The irrigating solutions included in the studies were Morinda citrifolia, 2%

Chlorhexidine, 4% Calcium Hydroxide, 4% Dimethyl Sulfoxide extract of Propolis and MTAD, NaOCl and N saline. The characteristics of included studies are given in annexure 1.

Design and methods

All the included trials were parallel arm RCT. All the trials were conducted at the hospital set up of a dental school.

Participants

The trial participants ranged between 3 - 12 years. The total number of participants was 220.

Interventions

After the clinical and radiographic evaluation, those teeth indicated for pulpectomy were isolated under rubber dam. Access cavities were made using standardized protocol. A microbiological sample was taken for culturing of the endodontic microbes. Subsequent to pulp extirpation, copious irrigation was undertaken either with test or control irrigant. A second microbiological sample was taken for culture after the usage of irrigant.

Outcome measures

All the studies assessed the change in the colony forming units (CFU/ml).

Risk of bias in included studies (Table 1)

Allocation

Sequence generation

All the four studies did sequence generation. Three out of four studies mentioned that the sequence generation was done using computer assisted method (Katge 2015; Ruiz Esparza 2011; Jolly 2013). One study did not mention the method of sequence generation (Chandwani 2017). Three studies (Katge 2015; Ruiz Esparza 2011; Jolly 2013) show a low risk of bias. One study (Chandwani 2017) shows an unclear risk of bias.

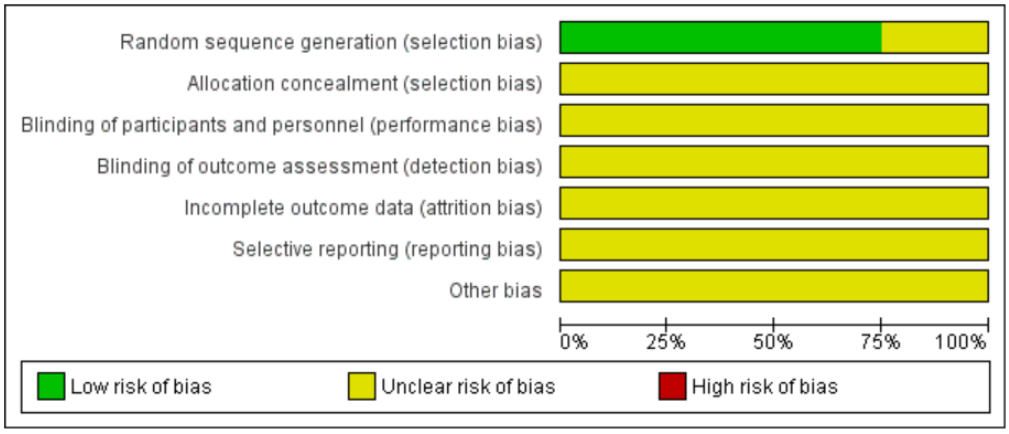

Table 1: *Risk of bias across studies.*

Allocation concealment

None of the studies have mentioned about allocation concealment. All the four studies show questionable risk of bias.

Blinding

None of the studies have mentioned about blinding. All the four studies show questionable risk of bias.

Incomplete outcome data

None of the studies have reported of attrition bias. All the four studies show questionable risk of bias.

Selective reporting

It was not possible to determine whether selective reporting was done, hence all the four studies show questionable risk of bias.

Other potential sources of bias

Baseline imbalance

There was no baseline imbalance between the pre intervention CFU/ml in all the four studies thereby indicating that both the test and control groups were adequately matched.

Overall risk of bias (Table 2)

The overall risk of bias has been assessed by Cochrane tool for risk of bias.

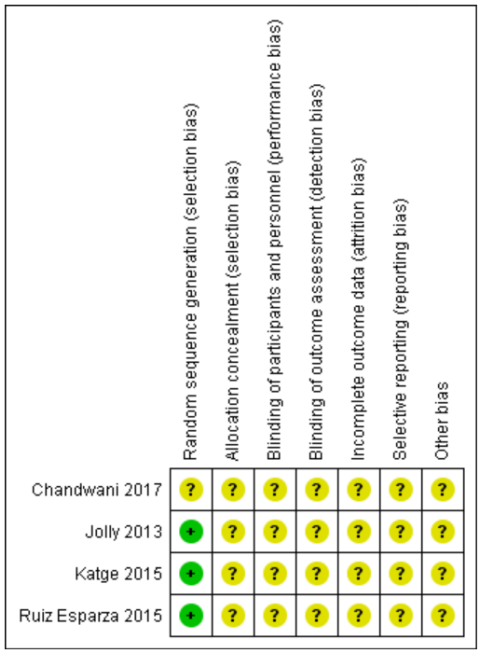

Table 2: *Risk of bias within studies.*

Effects of interventions

All four studies have measured the outcome in terms of reduction in colony forming units (CFU/ml). In the study by Chandwani (2017) [10] a proportion reduction of 50.70% was seen with the control group (NaOCl) whereas a 49.68% reduction was seen with the test group (MCJ extract). The study by Katge (2015) [11] showed a proportion reduction of 99.68% with the control group (NaOCl) whereas a 99.82% reduction with the test group (MTAD). The study by Ruiz Esparza (2011) [12] showed a proportion reduction of 36.90% with the control group (Sterile saline) whereas a 99.90% reduction in the test group (CHX). The study by Jolly (2013) [13] showed a proportion reduction of 46.70% with the control group (Normal saline) and 46.70% reduction in the test group (4% Propolis). The fixed effects model (Figure 2) showed that study by Ruiz Esparza favors the use CHX against sterile saline as the control and was statistically significant. The study by Jolly showed that the use of 4% Propolis against saline as a control does not favor test or control also not being statistically significant. The study done by Katge showed that the use of MTAD against NaOCl as a control, does not favor either of the irrigants. Lastly, the study done by Chandwani showed that the use of MCJ against NaOCl as control, does not favor either. The pooled OR shows that the test groups are favored against the control groups being statistically significant. However, when the random effects model (Figure 3) was applied, the pooled OR did not favor the test or the control groups.

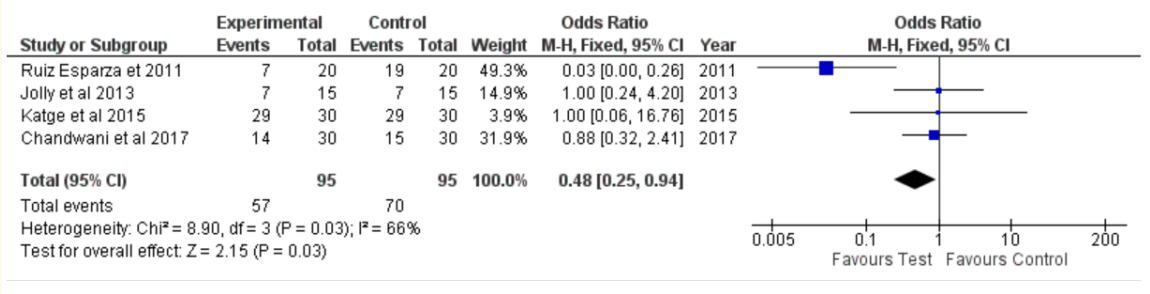

Figure 2: *Forest plot depicting proportionate change in bacterial CFU/ml counts using experimental vs control irrigating solutions (Fixed effects).*

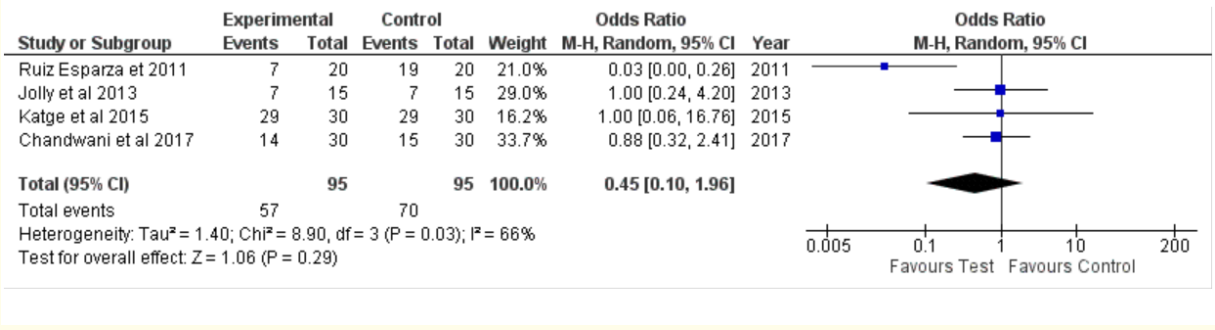

Figure 3: *Forest plot depicting proportionate change in bacterial CFU/ml counts using experimental vs control irrigating solutions (Random effects).*

The funnel plot was utilized to assess the heterogeneity of studies reporting the outcome measures. The plot showed asymmetry. 3 studies are seen to lie inside the funnel with one study outside it (Figure 4).

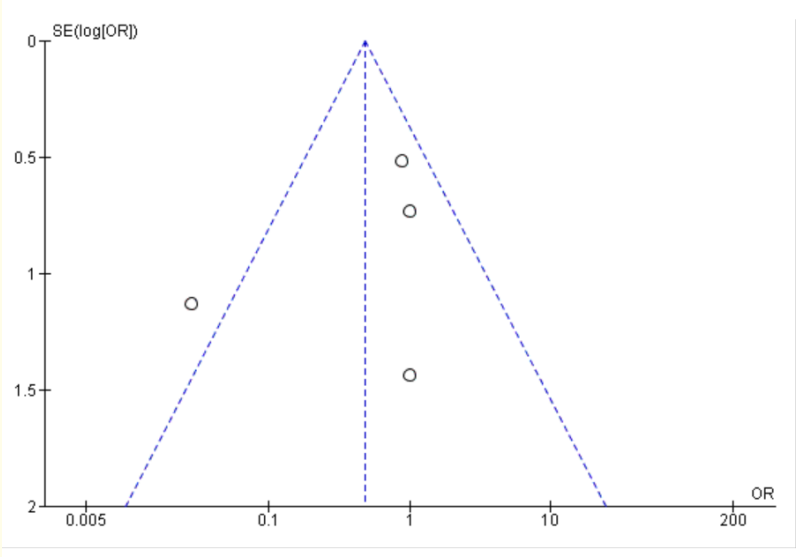

Figure 4: *Funnel plot of included studies.*

Sensitivity analysis

Sensitivity analysis consisting of 3 studies by Chandwani, Katge and Jolly M showed a pooled OR was 0.92 (0.42-2.04), being statistically non significant (Figure 5).

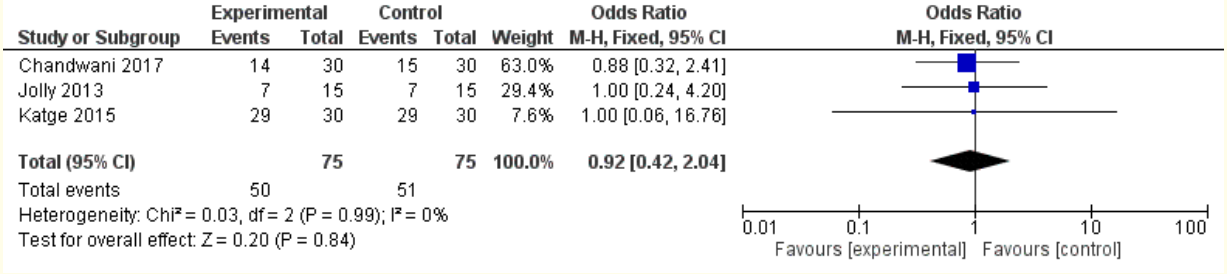

Figure 5: *Sensitivity analysis showing change in bacterial CFU/ml counts using experimental vs control irrigating solutions.*

Sub-group analyses

Sub-group analysis 1

Sub- group analysis was undertaken in 2 studies which used NaOCl as control irrigant; showed that there is no significant difference when using *Morinda citrifolia* or MTAD as experimental irrigants (OR 0.89 (0.34 - 2.31) (Figure 6).

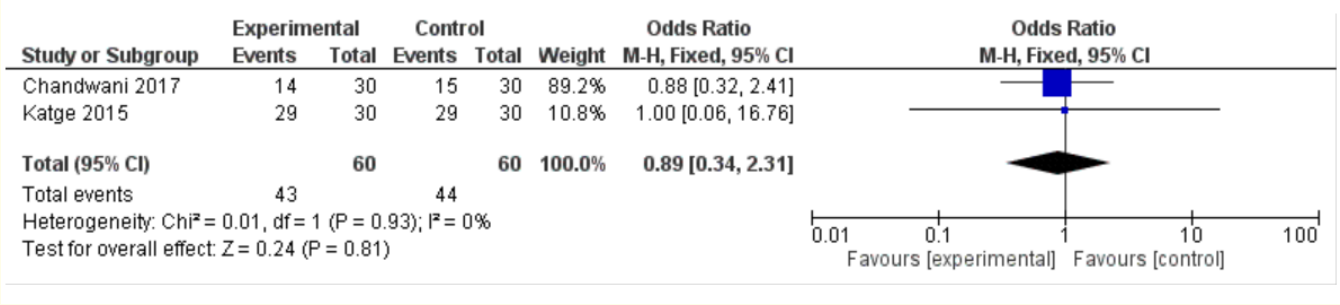

Figure 6: *Forest plot depicting proportionate change in bacterial CFU/ml counts using experimental irrigating solutions vs NaOCl as control solution.*

Sub-group analysis 2

Studies undertaken by Jolly and Ruiz Esparza included N Saline as control were included for sub-group analysis. It showed that there is statistically significant difference when using CHX and Propolis as experimental irrigants (OR 0.25 (0.09 - 0.69) (Figure 7).

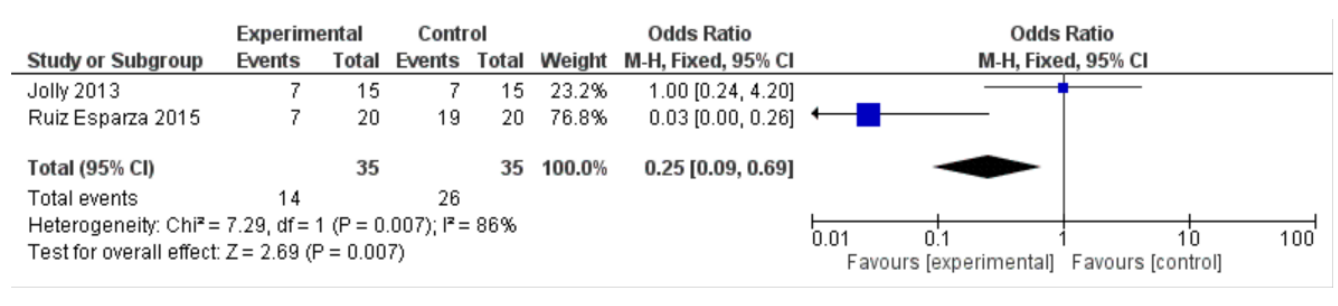

Figure 7: *Forest plot depicting proportionate change in bacterial CFU/ml counts using experimental irrigating solutions vs N Saline as control solution.*

Discussion

Summary of main results

The main question addressed in this review is the antibacterial effectiveness of various irrigating solutions used in primary teeth. 4 RCT's (220 participants) published between 2011 and 2017 participants were included. Meta-analysis of the 4 trials comparing the antibacterial effect of NaOCl, CHX, Propolis, MTAD, Morinda and N saline showed a pooled Odds Ratio of 0.45 (0.10 - 1.96) implying that there was no significant difference between the various agents. The heterogeneity was moderate. Our results are in agreement with a previous review wherein a statistically significant change in CFU/ml was not found [14]. A sensitivity analysis was undertaken excluding the outlier studies (Ruiz Esparaza) that also demonstrated no significant difference.

Overall completeness and applicability of evidence

Information on the use of irrigants in pulpectomy in primary teeth, though available was incomplete. Although we approached authors for procuring missing data, the necessary data could not be obtained despite three reminders. Hence, 5 studies with missing primary data were excluded and only 4 studies were included in the Meta analysis. This review has evaluated the effect of root canal irrigants on the reduction in colony forming units. The trials included have compared the test irrigant with a control of Sodium Hypochlorite or Normal Saline or sterile water. The trials included had conducted studies on primary teeth requiring pulpectomy. The procedure for the usage of irrigants was standardized in all the included studies. The review suggested that there is no difference between the various irrigating solutions used in primary teeth based on the meta-analysis of only these 4 studies, hence the evidence is inconclusive regarding the effectiveness of any one particular agent.

Quality of the evidence

Three studies reported low risk of bias pertaining to random sequence generation. Attrition bias was not mentioned in any of the studies. Based on the overall risk of bias assessment, we judged the overall quality of evidence as poor (Assessed as per GRADE evaluation) [15].

Potential biases in the review process

The search strategy employed was restricted to English language.

Limitations

Studies only in English language were considered for this review. Studies assessing antibacterial effectiveness were considered and success of the endodontic treatment was not studied. Only change in CFU/ml was assessed; other factors like patient's acceptance towards taste of the irrigant and cost of the irrigant to the operator could not be assessed. Access to unpublished literature was not possible; also the missing data could not be obtained from certain authors, hence, those studies had to be excluded.

Conclusion

All the irrigating solutions used in primary teeth showed reduction in the bacterial colony counts, however, no irrigant proved to be superior to the other; the quality of the evidence is poor.

Recommendation

Future studies with a larger sample size should be undertaken. The sample size should be accurately calculated based on the estimated difference. The antibacterial effect measured as CFU/ml should mention the dilution factors. Authors should be more forthcoming in sharing their data for better analysis.

Funding and Conflict of Interest

No funding was received for this undertaking this review. Authors declare no conflict of interest.

(Annexure 1)

Excluded studies

Reason	Number
Title not related to the review	157
Study design related	150
Intervention/comparison related	10 (Comparators other than irrigating solutions)
Participants related	195 (Adult population)
Outcomes related	2

Characteristics of included studies

Chandwani 2017

Methods	It is a randomised clinical trial and the procedure for carrying the pulpectomy for all the selected teeth was standardised.
Participants	The trial consisted of participants aged 6-9 years and 60 deciduous molar teeth were selected and were randomly divided into two groups; each consisting of 30 teeth.
Interventions	Experimental group was administered *Morinda citrifolia* juice and control group was administered 1% Sodium Hypochloride (NaOCl) as intra-canal irrigants.
Outcomes	The change in colony forming units (CFU/ml) was assessed for assessing the effectiveness of the intra-canal irrigating solutions. Both irrigants significantly reduce CFU/ml.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	It is mentioned that the teeth were randomly allotted to two groups. Method of randomisation is not mentioned.
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias)	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias)	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias)	Unclear risk	Not mentioned
Selective reporting (reporting bias)	Unclear risk	Not mentioned
Other bias	Unclear risk	Not mentioned

Jolly 2013

Methods	It is a randomised clinical trial and the procedure for carrying the pulpectomy for all the selected teeth was standardised.
Participants	60 children aged 6-12 years were recruited for this trial. The children were divided into 4 groups each consisting of 15 participants.
Interventions	There were 3 experimental groups; consisting of 2% Chlorhexidine (Group A), 4% Calcium Hydroxide (Group B), 4% Dimethyl Sulfoxide extract of Propolis (Group C) and control group was administered sterile saline as intra-canal irrigants.
Outcomes	The change in colony forming units (CFU/ml) was assessed for assessing the effectiveness of the intra-canal irrigating solutions. CHX superior to other irrigants.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer assisted random sequence generation
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias)	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias)	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias)	Unclear risk	Not mentioned
Selective reporting (reporting bias)	Unclear risk	Not mentioned
Other bias	Unclear risk	Not mentioned

Katge 2015

Methods	It is a randomised clinical trial and the procedure for carrying the pulpectomy for all the selected teeth was standardised.
Participants	60 children aged 3-7 years were recruited for this trial. The children were divided into 2 groups each consisting of 30 participants.
Interventions	Experimental group was administered MTAD and control group was administered 1% Sodium Hypochloride (NaOCl) as intra-canal irrigants.
Outcomes	The change in colony forming units (CFU/ml) was assessed for assessing the effectiveness of the intra-canal irrigating solutions. MTAD and NaOCl are equally effective.

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer assisted random sequence generation
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias)	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias)	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias)	Unclear risk	Not mentioned
Selective reporting (reporting bias)	Unclear risk	Not mentioned
Other bias	Unclear risk	Not mentioned

Ruiz Esparza 2015

Methods	It is a randomised clinical trial and the procedure for carrying the pulpectomy for all the selected teeth was standardized.
Participants	40 children aged 3-9 years were recruited for this trial. The children were divided into 2 groups each consisting of 20 participants.
Interventions	Experimental group was administered 2% Chlorhexidine and control group was administered sterile saline as intra-canal irrigants.
Outcomes	The change in colony forming units (CFU/ml) was assessed for assessing the effectiveness of the intra-canal irrigating solutions. CHX is superior to saline.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer assisted random sequence generation
Allocation concealment (selection bias)	Unclear risk	Not mentioned
Blinding of participants and personnel (performance bias)	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias)	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias)	Unclear risk	Not mentioned
Selective reporting (reporting bias)	Unclear risk	Not mentioned
Other bias	Unclear risk	Not mentioned

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Volume 20 Issue 6 June 2021