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Comparative evaluation of postoperative pain with different intracanal medicaments – A Systematic Review

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ABSTRACT

Patients as well as clinicians have been apprehensive of pain of endodontic origin for many years¹. Pain during root canal treatment can be attributed to inflammation in the periapical tissues due to exudation of irritants from the root canal². The persistence of microorganism due to improper disinfection of root canal is the most important cause of pain¹. The eradication of microorganism from the root canals is therefore vital during root canal treatment. Thus, an antimicrobial dressing in root canals is advocated after root canal preparation¹. To evaluate the effectiveness of different intra canal medication in reducing the post operative pain in nonsurgical root canal treatment. The following databases were searched: PubMed CENTRAL, MEDLINE and Cochrane Databases of Systemic Reviews, Bibliographies of Clinical Studies and Reviews identified in the electronic search were analysed for studies published outside the electronically searched journals. Trials were selected if they met the following criteria: Clinical trials or in-vivo studies that evaluated the post operative pain after using different intracanal medicament in patients undergoing root canal treatment. All the studies included, were based on the data extraction and analysis of the studies for quality and publication bias. The primary outcome measure was to evaluate the reduction in post operative pain after using different intra canal medicaments in patients undergoing root canal treatment. The reviews some clinical evidence that use of intra canal medicaments can reduce postoperative pain. There is no enough evidence to prove that calcium hydroxide is effective in reduction of pain. Corticosteroids antibiotic combination and calcium hydroxide combination with chlorhexidine and camphorated paramonochlorophenol were effective in reducing pain. From this systematic review it can be concluded that, certain intra canal medicaments can be used to reduce postoperative pain during root canal treatment. Most of the studies proved that, corticosteroid antibiotic solution or combination of calcium hydroxide with other medicine like camphorated paramonochlorophenol or chlorhexidine is effective in reducing post operative pain. There is no evidence that, use of calcium hydroxide is effective in relieving pain. Further clinical trials are required to evaluate the efficacy of intra canal medicaments in reducing postoperative pain.

Keywords : Post operative pain, calcium hydroxide, intracanal medicament, antimicrobial

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INTRODUCTION

Patients and clinicians are widely concerned of pain of endodontic origin^{3,4,5}. Root canal procedures are commonly believed to be the most painful dental treatment⁶. Pain can occur before, during or after root canal procedures.

Various factors predisposes to pain such as microbial factors, chemical mediators, change in cyclic mediators, change in periapical tissue pressure and various psychological factors. The persistence of microorganism due to improper disinfection of root canal is the most important cause of pain¹. In a study done by Torabinejad et al, approximately 50% of 2000 patients who had undergone root canal treatment in pulpless teeth had interappointment emergencies⁷.

In order to ensure eradication of as many bacteria as possible from the entire root canal system, dissolution of organic and inorganic substance and the removal of smear layer, a combination of instrumentation done mechanically and irrigating solutions has been commonly used⁸. However, only 50-70 percent of infected canals were rendered free of micro organism after mechanical instrumentation with antibacterial irrigation. Therefore, placement of an effective antimicrobial agent in root canal after preparation is recommended to predictably eliminate any remaining bacteria⁸.

Since micro organisms are considered as the major cause for postoperative pain, intracanal procedure based on antimicrobial dressing might reduce the incidence of pain in root canal treatment.

Aim

The aim of this systematic review was to evaluate the effectiveness of different intra canal medicaments in reducing the post operative pain in non surgical root canal treatment.

Structured Question

Is the use of intracanal medicaments effective in reducing post operative pain in patients undergoing root canal treatment?

PICO Analysis

Population – Patients undergoing root canal treatment

Intervention – Intracanal medicaments

Outcome – Postoperative pain

Null Hypothesis

There is no difference in the post operative pain with the use of different intra canal medicaments.

MATERIALS AND METHOD

Sources Used

For included studies identification or considered for this review, search strategies were carried in detail on the following databases.

- PubMed
- PubMed Advanced search
- MEDLINE
- Cochrane Database of Systemic Review

Language

There was no language restriction during the electronic search.

Hand Searching

The following journals were hand searched

- 1) Journal of Interdisciplinary Dentistry
- 2) Journal of Khyber College of Dentistry
- 3) Advanced Materials Research
- 4) Journal of Liaquat University of Medical and Health science
- 5) Pakistan Oral and Dental Journal

Recent queries				
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Inclusion Criteria

Criteria for considering studies for this review.

Types of Studies

Randomized controlled trial or clinical trials evaluating and comparing the effectiveness of different intracanal medicaments in reducing postoperative pain.

Types of Participants

All participants undergoing root canal treatment.

Type of Intervention

Various intracanal medicaments.

Types of Outcome Measures

To check the post operative pain with various intracanal medicaments.

Exclusion Criteria

The following studies were excluded for this review,

- Case reports / case series
- Animals studies
- In vitro studies
- Studies involving primary teeth
- Systematic reviews (Chart 1)

RESULTS AND DISCUSSION

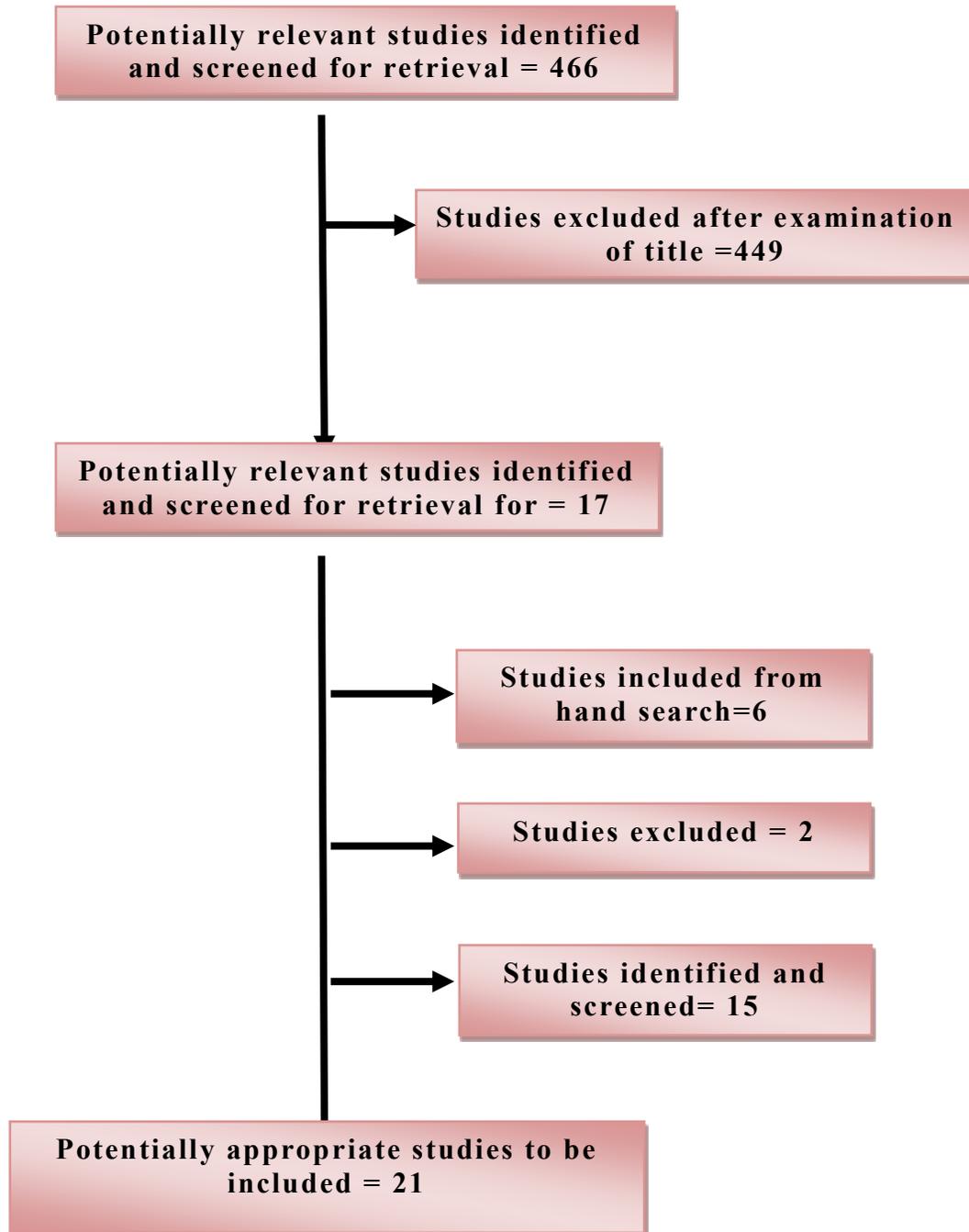


Chart 1: Search Flow Chart

Description of Studies

The search identified 466 publications, out of which 449 were excluded after reviewing the title. Full articles were obtained for 17 studies, 2 of these were excluded after reading the abstract and full text article [Table 2]. 6 hand searched articles fulfilled the inclusion criteria. Therefore, a total of 21 publications fulfilled all criteria for inclusion. [Table1] shows the variable of interest for this systematic review. [Table 3] details the general information of the selected articles. Search flow

chart is given in chart 1. Graph 1 and 2 shows the number of studies conducted in different time period and the sample size respectively.

Table 1: Variables of Interest

SI No:	Variable of Interest
1	Post operative pain

Table 2: Characteristics Of Excluded Studies

SI No:	Author	Year	Reason for Exclusion
1	Torabinejad et al.	1994	Oral medications are given and no intra canal medicaments.
2	Arias et al.	2013	Single visit root canal treatment; no medicament placed.

Table 3: General Information of Selected Articles

Sl No	Author	Year	Country	Study Design	Sample Size	Age	Set- Up	Intra-Canal Medicament Used	Methods Of Evaluation
1	M Kundabala et al.	2014	India	Clinical Study	30	Irrespective of age	University	Group 1 : Ledermix Group 2 : Eugenol soaked cotton	Pain evaluated as : no pain , mild pain , moderate pain , severe pain
2	Yasir Khan Khattak et al.	2014	Pakistan	Randomized Control Trial	80	16-50 years	University	Group 1 : Calcium Hydroxide mixed with 2% chlorhexidine Group 2 : calcium hydroxide mixed with 0.9% saline	Visual Analog Scale
3	Swathi Pai et al.	2014	India	Invivo Study	50	18-60 yrs	University	Group 1 : No intracanal medicament Group 2 : Calcium hydroxide Group 3 : Triple antibiotic paste	Verbal Rating Scale
4	Ripu Daman Singh et al.	2013	India	Double Blinded Randomized Clinical Trial	64	20-40 years	University	Group 1: Calcium hydroxide + 2% chlorhexidine Group 2: 2% Chlorhexidine Group 3 : Calcium hydroxide paste Group 4 : No dressing	Visual Analog Scale
5	Bestoon Mohammed Faraj.	2013	Iraq	Prospective Randomized Clinical Trial	860	Not mentioned	Private clinic	Pulpotec	Descriptive pain intensity scale
6	Hui-Xiao Yang.	2013	Switzerland	Clinical Trial	118	24-56 years	University	Group 1 : 2% Chlorhexidine mixed with calcium hydroxide Group 2: Formocresol	Pain evaluated as : no pain/discomfort, slight discomfort , mild pain , moderate to severe pain
7	Naveed Ahmed Menon et al.	2013	Pakistan	Randomized Clinical Trial	60	14-60 years	University	Group 1: Ledermix Group 2: Calcium hydroxide	Visual Analog Scale
8	Abdul QadirDall et al.	2011	Pakistan	Randomized Control Trial	222	14-60 years	University	Group 1 : Ledermix paste Group 2 : No intracanal medicament	Visual Analog Scale
9	Shafqat et al.	2010	Pakistan	Randomized Clinical Trial	100	15- 50 years	University	Group 1 : Calcium hydroxide Group 2 : Creosote	Visual Analog Scale
10	Tulio G V Gama et al.	2008	Brazil	Clinical Trial	138	9-72 years	University	Group 1: Calcium hydroxide/camphorated	Pain evaluated as : no pain , mild pain , moderate pain

								paramonochlorophenol / glycerine paste Group 2 : Chlorhexidine	, severe pain
11	Jamileh Ghoddusi et al.	2006	Iran	Prospective Randomized Clinical Trial	60	Not mentioned	University	Group A : Single visit Group B : No medicament Group C : Calcium hydroxide	Modified Visual Analog Scale
12	E H Ehrmann et al.	2003	Australia	Prospective Randomized Clinical Trial	223 teeth in 221 patients	Not mentioned	University	Group 1 : Ledermix paste Group 2 : Calcium hydroxide Group 3 : No medicaments	Visual Analog Scale
13	Walton et al.	2003	U.S.A	Randomized Clinical Trial	140	Mean age of 38 years	University	Group 1 : Calcium hydroxide Group 2 : No medicament	Pain evaluated as : no pain , mild pain , moderate pain and severe pain
14	Jose F Siqueira et al.	2002	U.S.A	Prospective Study	627	18-75 years	University	Calcium hydroxide / camphorated paramonochlorophenol paste	Pain evaluated as : none , mild, moderate, severe
15	Maged M Negm.	2001	Egypt	Randomized Double Blind Study	988	15-75 years	Not mentioned	Group 1 : Corticosteroid – antibiotic compound Group 2 : Placebo	Pain evaluated as : none , mild, moderate, severe
16	Martin J Rogers et al.	1999	U.S.A	Randomized Control Trial	48	18-65 years	University	Group 1 : Oral ibuprofen Group 2 : Oral placebo Group 3 : Intracanal dexamethasone Group 4 : Intracanal ketorolac	Visual Analog Scale
17	L R G Fava et al.	1998	Brazil	Randomized Clinical Trial	60 maxillary central incisors from 48 patients	28-64 years	Private practice	Group 1 : Calcium hydroxide Group 2 : Corticosteroid antibiotic solution	Pain evaluated as none/slight , moderate , severe
18	Maged M Negm.	1994	Egypt	Randomized Control Trial	760 patients	18-78 years	Not mentioned	Group 1: Diclofenac Group 2 : Ketoprofen Group 3 : Hyaluronidase BP Group 4 : Saline	Pain evaluated as : none , mild, moderate, severe
19	L R G Fava.	1992	Brazil	Clinical Trial	60 maxillary central incisors	15-62 years	Not	Group 1 : Corticosteroid antibiotic solution Group 2 : Calcium hydroxide paste	Pain evaluated as : none /slight, moderate, severe

					from 45 patients				
20	Trope M.	1990	U.S.A	Clinical Trial	474 teeth	Not mentioned	Private practice	Formocresol – 156 Ledermix – 160 Calcium hydroxide – 158	Pain evaluated as presence or absence of flare up
21	Kenneth Chance et al.	1987	U.S.A	Clinical Trial	300 patients	Not mentioned	University	Group 1 : Corticosteroid Group 2 : Saline	Pain evaluated as : none , slight, moderate, severe

Table 4: Results And Summation

SL No	Author	Year	Material Used	Method Of Evaluation	Statistical test used	P value	Results	Conclusion	Summation
1	M Kundabala et al.	2014	Group 1 : Ledermix Group 2 : Eugenol soaked cotton	Pain evaluated as : no pain , mild pain , moderate pain , severe pain	Fischers exact test	0.017	Ledermix – 100% after 72hrs Eugenol -100% after 2 weeks	Ledermix reduced pain faster than eugenol.	Ledermix is better than eugenol
2	Yasir Khan Khattak et al.	2014	Group 1 : Calcium Hydroxide mixed with 2% chlorhexidine Group 2 : Calcium hydroxide mixed with 0.9%saline	Visual Analog Scale	Chi-square test	0.001	After 6 hrs , mean pain score in Group 1 : 3.65+/-2.293 Group 2 : 5.6 + 2.590	Mean pain score after 6,12, 24 and 48 hrs is lesser in group 1	Calcium hydroxide chlorhexidine mixture is better than calcium hydroxide saline mixture.
3	;	2014	Group 1 : No intracanal medicament Group 2 : Calcium hydroxide Group 3 : Triple antibiotic paste	Verbal Rating Scale	Chi – square test	0.002 between group I and III , 0.07 between group I and II , 0.23 between group II and III	Group 1 – 50% Group 2 – 15% Group 3 – 0%	Statistical difference between group 1 and 3 Difference between (group 1 and 2) and (group 2 and 3) were not significant.	Triple antibiotic paste is better than calcium hydroxide and no medicament group.
4	Ripu Daman	2013	Group 1: Calcium hydroxide + 2%	Visual Analog Scale	Dunnett's test.		At 96hrs Group 1 :	Group 1 and group 2	Calcium hydroxide chlorhexidine mixture is

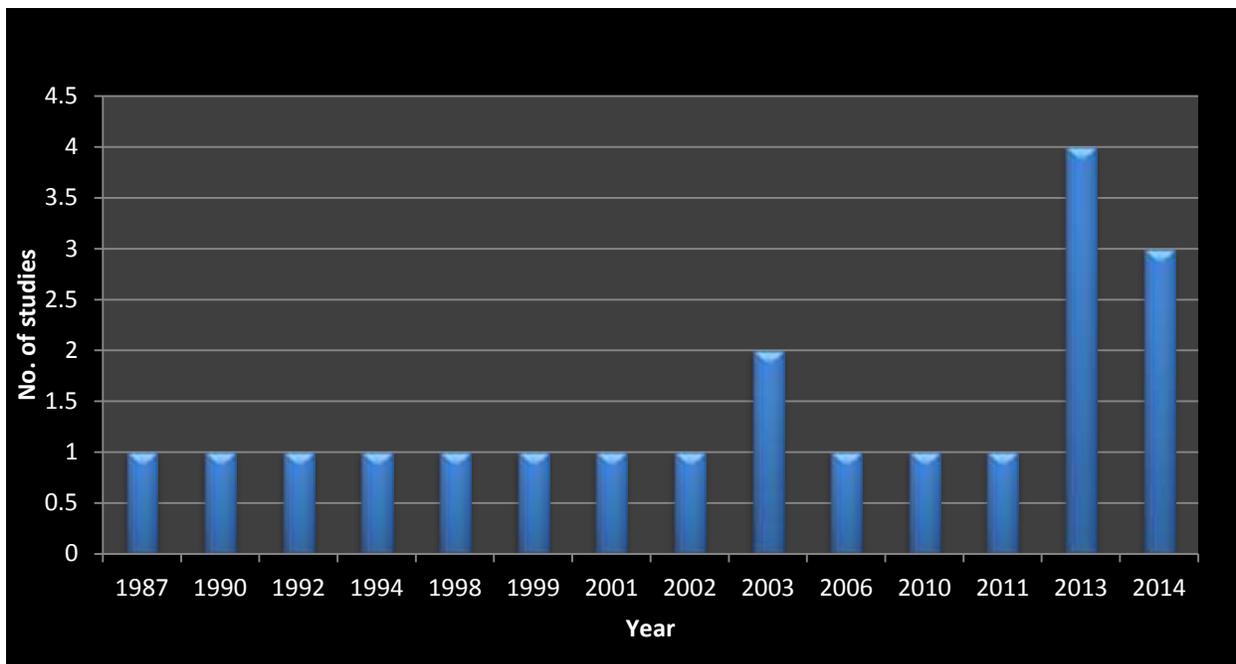
	Singh et al.		chlorhexidine Group 2: 2% Chlorhexidine Group 3 : Calcium hydroxide paste Group 4 : No dressing				1.31+/-1.53 Group 2 : 2.00+/-1.86 Group 3 : 12.3+/-7.92 Group 4: 12.8+/- 10.6	differed significantly from control . No significant difference between group 3 and control group.	better than chlorhexine alone , calcium hydroxide and no medicament group.
5	Bestoon Mohammed Faraj.	2013	Pulp /otec	Descriptive pain intensity scale	Chi – square test	0.000 for 8,24 , 48 and 3 days and 0.065 for 1 week.	No pain at 8hrs- 67.67% No pain at 1 week – 96.63% Mild pain at : 8 hrs- 32.33% 24hrs – 22.09% 48hrs – 17.09% 3 days – 10.93% 1 week – 3.37% Moderate pain at: 24hrs – 7.90% 3days – 5.81% 7days – 2.21% Severe pain: 24 hrs – 1.16% 48hrs – 0.69%	Intracanal irrigation with 5%NaOCl accompanied by pulpotec intracanal dressing is beneficial in rapid resolution of pain and/or swelling in emergency root canal treatment.	Pulpotec is useful in rapid resolution of pain .
6	Hui-Xiao Yang.	2013	Group 1 : 2% Chlorhexidine mixed with calcium hydroxide Group 2: Formocresol	Pain evaluated as : no pain/discomfort, slight discomfort , mild pain , moderate to severe pain	Analysis of variance and chi- square test.	<0.05	After 1 st visit : Group A : 3.4% incidence Group B : 15.3% incidence After 2 nd visit : Group A : 0% incidence Group B : 1.7%incidence	Calcium hydroxide can significantly alleviate the pain response in residual pulpitis patients.	Calcium hydroxide is better than formocresol.
7	Naveed	2013	Group 1: Ledermix	Visual Analog	Fisher	0.999	No pain	Ledermix is	Ledermix is better than

	Ahmed Menon et al.		Group 2: Calcium hydroxide	Scale	Exact test		experienced Group 1 : 1week – 43.3% Group 2 : 1week – 26.6%	significantly better than calcium hydroxide.	calcium hydroxide.
8	Abdul QadirDall et al.	2011	Group 1 : Ledermix paste Group 2 : No intracanal medicament	Visual Analog Scale	Unpaired t test	0.005	Mean interappointment pain Group 1 : 9.0+/- 0.71 Group 2 : 12.26+/-0.90	Ledermix group significantly experienced less pain than with no intracanal medicament at 48hrs.	Ledermix is better than no medicament group.
9	Shafqat et al.	2010	Group 1 : Calcium hydroxide Group 2 : Creosote	Visual Analog Scale	Chi – square test.	Before treatment – 0.405 4hours – 0.00 12 hours – 0.395 24 hours – 0.00 48 hours – 0.000	At 48hrs : Group 1 : 0.38+/-0.7 Group 2 : 1.72+/- 1.51	Calcium hydroxide is significantly better than creosote.	Calcium hydroxide is better than creosote.
10	Tulio G V Gama et al.	2008	Group 1: Calcium hydroxide/camphorated paramonochlorophenol / glycerine paste Group 2 : Chlorhexidide	Pain evaluated as : no pain , mild pain , moderate pain , severe pain	Fischer's test. Chi – square test	0.6 0.8	No pain. Group 1 -89.7% Group 2 – 78%	No significant difference between medications.	Chlorhexidine is equally effective as calcium hydroxide/CPMC
11	Jamileh Ghoddusi et al.	2006	Group A : Single visit Group B : No medicament Group C : Calcium hydroxide	Modified Visual Analog Scale	Chi – square test	<0.05	Pain occurrence Group c : 15% Group B : 47.5 %	Calcium hydroxide is significantly better than no medicament group.	Calcium hydroxide is better than no medicament group.

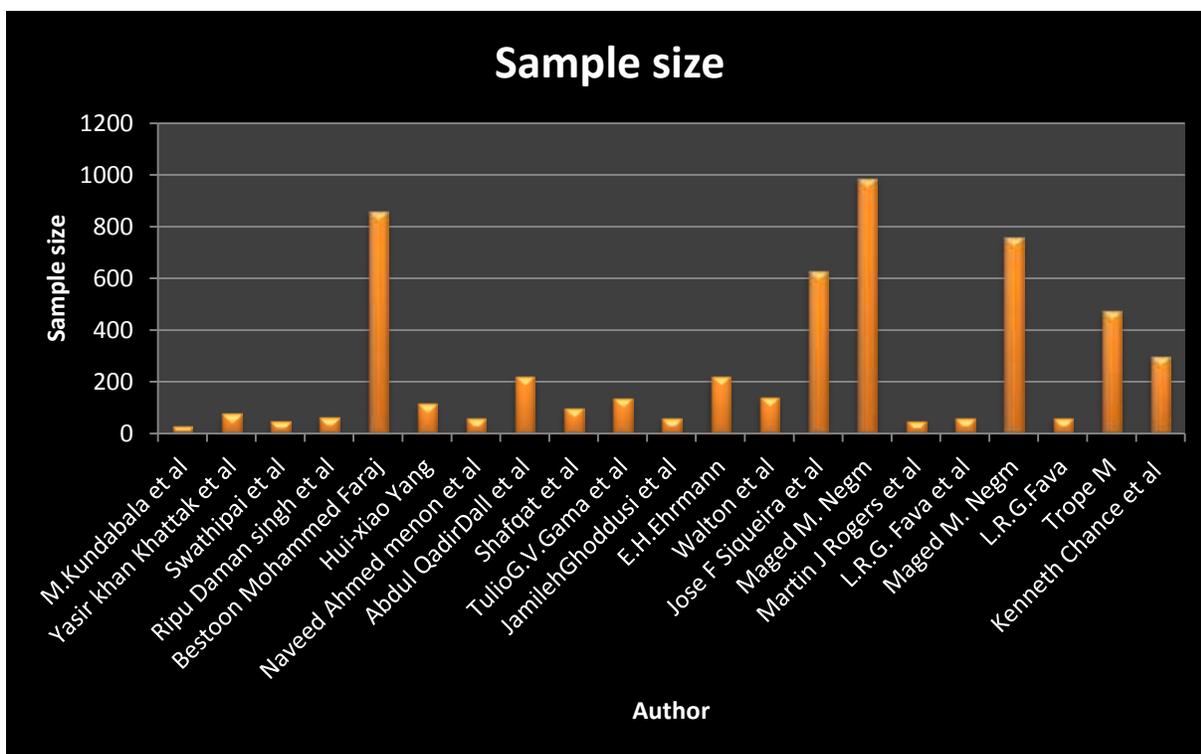
12	E Ehrmann et al.	2003	Group 1 : Ledermix paste Group 2 : Calcium hydroxide Group 3 : No medicaments	Visual Analog Scale	One way ANOVA Repeated measures ANOVA	0.4	At 96 hrs Group 1 : 4.3 ± 8.8 Group 2 : 8.8 ± 17.5 Group 3 : 9.0 ± 17.4	Group 1 is significantly better than group 2 and 3 . No significant difference between group 2 and 3.	Ledermix is better than chlorhexidine and no medicament group.
13	Walton et al.	2003	Group 1 : Calcium hydroxide Group 2 : No medicament	Pain evaluated as : no pain , mild pain , moderate pain and severe pain	Multiple regression analysis	>0.05	Moderate to severe pain 4hrs : 30% 24hrs : 16% 48hrs : 8%	No significant difference between 2 groups.	Calcium hydroxide is no better than no medicament.
14	Jose F Siqueira et al.	2002	Calcium hydroxide / camphorated paramonochlorophenol paste	Pain evaluated as : none , mild, moderate, severe	Chi – square test	<0.05	Absence of pain – 15.2%	Antimicrobial intracanal dressing reduce post operative pain.	Calcium hydroxide/CMPF/glycerine paste is effective in reducing pain.
15	Maged M Negm.	2001	Group 1 : Corticosteroid – antibiotic compound Group 2 : Placebo	Pain evaluated as : none , mild, moderate, severe	Chi – square test. Analysis of variance	<0.01	Mean pain difference Group 1 : 1.77 ± 0.96 Group 2 : 0.21 ± 0.50	Group 1 is significantly better than placebo in controlling post treatment pain.	Corticosteroid antibiotic paste is better than no medicament group.
16	Martin J Rogers et al.	1999	Group 1 : Oral ibuprofen Group 2 : Oral placebo Group 3 : Intracanal dexamethasone Group 4 : Intracanal ketorolac	Visual Analog Scale	ANCOVA	<0.05	At 12hr : Group 1 : 22.1 Group 2 : 28.3 Group 3 : 13.9 Group 4 : 14.1	Dexamethasone and ketorolac showed statistically significant relief in pain at 12hr when compared to placebo. No significant difference between	NSAID is equally effective as corticosteroid.

								ibuprofen and either dexamethasone or ketorolac.	
17	L R G Fava et al.	1998	Group 1 : Calcium hydroxide Group 2 : Corticosteroid antibiotic solution	Pain evaluated as none/slight , moderate , severe	-	- ---ksdc	Moderate pain after 48hrs Group 1 : 2 pts Group 2 : 1 pt	No significant difference between the two groups.	Calcium hydroxide is equally effective as corticosteroid antibiotic solution.
18	Maged M Negm.	1994	Group 1: Diclofenac Group 2 : Ketoprofen Group 3 : Hyaluronidase BP Group 4 : Saline	Pain evaluated as : none , mild, moderate, severe	ANOVA	<0.05	Mean pain experienced 1)For asymptomatic tooth a) Group 1 : 1.35 ± 0.15 b) Group 2 : 1.12 ± 0.33 c) Group 3 : 1.50 ± 0.78 d) Group 4 : 1.34 ± 0.56 e) Group 5 : 1.78 ± 1.00 f) Group 6 : 1.80 ± 1.01 2) For symptomatic tooth difference between before and after a) Group 1: 1.20±1.04 b) Group 2 : 1.47 ± 0.99 c) Group 3 : 1.10 ± 1.03	Post treatment use of diclofenac and ketoprofen was effective in controlling pain and was superior to placebo. Addition of hyaluronidase to medications even reduced pain , but it was not significant.	NSAIDs are effective in reducing pain.

							d) Group 4 : 1.21 ± 1.03 e) Group 5 : 0.39 ± 0.76 f) Group 6 : 0.41 ± 0.77		
19	L.R.G.Fava.	1992	Group 1 : Corticosteroid antibiotic solution Group 2 : Calcium hydroxide paste	Pain evaluated as : none /slight, moderate, severe	-	-	48hrs : Moderate pain : Group 1 : 1pt Group 2 : 1pt	No difference in incidence of pain between 2 groups.	Calcium hydroxide is equally effective as corticosteroid antibiotic solution.
20	Trope M.	1990	Formocresol – 156 Ledermix – 160 Calcium hydroxide – 158	Pain evaluated as presence or absence of flare up	Chi square	>0.05	Flare ups Group 1 : 1.92% Group 2: 3.12% Group 3 : 2.53%	No statistical difference among the three groups.	Ledermix is equally effective as calcium hydroxide and formocresol.
21	Kenneth Chance et al.	1987	Group 1 : Corticosteroid Group 2 : Saline	Pain evaluated as : none , slight, moderate, severe	Chi square test	0.05	Severe pain Group 1 : 2.7% Group 2 : 6.8%	Reduced incidence of severe pain was significant in group 1 when compare to group 2.	Corticosteroid is better than steroid.



Graph 1: No of studies



Graph 2: Sample size

Quality Assessment

The quality assessment of included trials was undertaken independently as a part of data extraction process. Four main quality criteria were examined.

1. Method of Randomization , recorded as
 - a) Yes – adequate as described in the text
 - b) No – inadequate as described in the text
 - c) Unclear in the text
2. Allocation Concealment , recorded as
 - a) Yes – adequate as described in the text
 - b) No – inadequate as described in the text
 - c) Unclear in the text
3. Outcome assessor blinded to intervention, recorded as
 - a) Yes – adequate as described in the text
 - b) No – inadequate as described in the text
 - [c) Unclear in the text
4. Completeness of follow-up (was there a clear explanation for withdrawals and dropouts in each treatment group) Assessed as :
 - a) Yes – dropouts were explained
 - b) No – dropouts were not explained
 - c) None – no dropouts or withdrawals
 Other methodological criteria examined included:
 1. Presence or absence of sample size calculation
 2. Comparability of groups at the start
 3. Clear inclusion / exclusion criteria

Presence/absence of estimate of measurement error. The validity and reproducibility of the method of assessment.

Risk of Bias in Included Studies

The assessments for the four main methodological quality items are shown in table 6,7,ans 8. The study was assessed by to have a “high risk” of bias if it did not record a “yes” in 3 or more of the 4 main categories , “moderate” if 2 out of 4 categories did not record a “yes” and “low” if randomization , assessor blinding and completeness of follow up were considered adequate.

Table 6: Evidence of Selected Studies

Sl No	Study	Year	Study Design	Level of Evidence
1	M Kundabala et al.	2014	Clinical Study	3
2	Yasir Khan Khattak et al.	2014	Randomized Control Trial	2
3	Swathi Pai et al.	2014	In Vivo Study	3

4	Ripu Daman Singh et al.	2013	Double Blinded Randomized Clinical Trial	2
5	Bestoon Mohammed Faraj.	2013	Prospective Randomized Clinical Trial	2
6	Hui-Xiao Yang.	2013	Clinical Trial	3
7	Naveed Ahmed Menon et al.	2013	Randomized Clinical Trial	2
8	Abdul Qadir Dall et al.	2011	Randomized Control Trial	2
9	Shafqat et al.	2010	Randomized Clinical Trial	2
10	Tulio G V Gama et al.	2008	Clinical Trial	3
11	Jamileh Ghodduzi et al.	2006	Prospective Randomized Clinical Trial	2
12	E H Ehrmann et al.	2003	Prospective Randomized Clinical Trial	2
13	Walton et al.	2003	Randomized Clinical Trial	2
14	Jose F Siqueira et al.	2002	Prospective Study	3
15	Maged M Negm.	2001	Randomized Double Blind Study	2
16	Martin J Rogers et al.	1999	Randomized Control Trial	2
17	L R G Fava et al.	1998	Randomized Clinical Trial	2
18	Maged M Negm.	1994	Randomized Control Trial	2
19	L R G Fava.	1992	Clinical Trial	3
20	Trope M.	1990	Clinical Trial	3
21	Kenneth Chance et al.	1987	Clinical Trial	3

Table 7: Risk of Bias – Major Criteria

SI No	Study	Year	Randomization	Allocation Concealed	Assessor Blinding	Dropouts Described	Risk of Bias
1	M Kundabala et al	2014	Yes	No	No	No	High
2	Yasir Khan Khattak et al	2014	Yes	No	No	No	High
3	Swathi Pai et al	2014	No	No	No	No	High
4	Ripu Daman Singh et al	2013	Yes	No	No	Yes	Moderate
5	Bestoon Mohammed Faraj	2013	Yes	No	No	Yes	Moderate
6	Hui-Xiao Yang	2013	No	No	No	No	High
7	Naveed Ahmed Menon et al	2013	Yes	No	No	Yes	Moderate
8	Abdul QadirDall et al	2011	Yes	No	No	Yes	Moderate
9	Shafqat et al	2010	Yes	No	No	Yes	Moderate
10	Tulio G V Gama et al	2008	No	No	No	No	High
11	Jamileh Ghodduzi et al	2006	Yes	No	No	Yes	Moderate
12	E H Ehrmann et al	2003	Yes	No	No	Yes	Moderate
13	Walton et al	2003	Yes	No	No	Yes	Moderate
14	Jose F Siqueira et al	2002	No	No	No	No	High
15	Maged M Negm	2001	Yes	Yes	Yes	Yes	Low
16	Martin JRogers et al	1999	No	No	No	No	High
17	L R G Fava et al	1998	Yes	No	No	Yes	Moderate
18	Maged M Negm	1994	No	No	No	Yes	High
19	L R G Fava	1992	No	No	No	No	High
20	Trope M	1990	No	No	No	Yes	High
21	Kenneth Chance et al	1987	Yes	No	No	Yes	Moderate

Table 8: Risk of Bias – Minor Criteria

S:no	Study	Year	Sample Justified	Baseline Comparison	I/E Criteria	Method Error
1	M Kundabala et al.	2014	No	Yes	Yes	No
2	Yasir Khan Khattak et al.	2014	Yes	No	yes	No
3	Swathi Pai et al.	2014	No	No	Yes	No
4	Ripu Daman Singh et al.	2013	No	Yes	Yes	No
5	Bestoon Mohammed Faraj.	2013	No	No	No	No
6	Hui-Xiao Yang.	2013	No	No	Yes	No
7	Naveed Ahmed Menon et al.	2013	No	Yes	Yes	No
8	Abdul QadirDall et al.	2011	Yes	No	No	No
9	Shafqat et al.	2010	No	Yes	Yes	No
10	Tulio G V Gama et al.	2008	No	No	Yes	No
11	Jamileh Ghoddsi et al.	2006	Yes	Yes	Yes	No
12	E H Ehrmannet al.	2003	No	Yes	Yes	No
13	Walton et al.	2003	No	Yes	Yes	No
14	Jose F Siqueira et al.	2002	No	No	No	No
15	Maged M Negm.	2001	No	No	Yes	No
16	Martin J Rogers et al.	1999	No	No	Yes	No
17	L R G Fava et al.	1998	No	Yes	Yes	No
18	Maged M Negm.	1994	No	No	Yes	No
19	L R G Fava.	1992	No	No	No	No
20	Trope M.	1990	No	Yes	Yes	No
21	Kenneth Chance et al.	1987	No	No	Yes	No

DISCUSSION

Interpretation of Results

First Trial by Kundabala et al (2014)²⁴, 30 symptomatic teeth were grouped into two. Group I: Ledermix and group II: eugenol liquid. Pain relief was faster in Ledermix than eugenol. All patients in group I became asymptomatic after 72 hours, whereas patients in group II became asymptomatic only after 2 weeks [Table 4].

Second trial by Yasir Khan Khattak (2014)²³, 80 subjects were randomly divided into two groups. Group 1: calcium hydroxide mixed with 2% chlorhexidine and Group 2: calcium hydroxide mixed with normal saline. The mean pain after 12, 24 and 48 hours showed lesser pain in group 1 compared to group 2 [Table 4].

Third trial by Swathi Pai et al (2014)²⁵, 50 patients were divided into 3 groups. Group I: No intracanal medicament, group II: chlorhexidine and group III: Triple antibiotic paste. No flare up occurred in group III, whereas 50% of group 1 and 15% of group II had flare up [Table 4].

Fourth trial by Ripu Daman Singh et al (2013)¹, 64 mandibular were randomized into four groups (n=16), group I: calcium hydroxide paste mixed with 2% chlorhexidine gel, group II: 2%

chlorhexidine gel, group III: calcium hydroxide paste and group IV received no dressing. Groups I and II were significantly more effective than groups III and IV at all time period in reducing the postoperative pain values [Table 4].

Fifth trial by Bestoon Mohammed Faraj (2013)²², pulpotec paste was used as intra canal medicament in 860 teeth. Pulpotec intracanal dressing was effective in reducing postoperative pain[Table 4].

Sixth trial by Hui-Xiao Yang (2013)²¹, 118 patients were randomly distributed into two groups. Group A: 2% chlorhexidine mixed with calcium hydroxide and group B formocresol was used. Group A showed, lower incidence of pain after 1st visit when compared to group B[Table 4].

Seventh trial by Naveed Ahmed Menon et al (2013)²⁷, 60 patients were divided into 2 groups (n=30). Group 1 was medicated with Ledermix paste and group 2 was medicated with calcium hydroxide. Significant reduction in pain was found in group 1 than in group 2 after 1 week[Table 4].

Eight trial by Abdul QadirDall et al (2011)²⁰, 222 patients were divided into two groups. Ledermix paste was placed in group 1 and in group 2, no medicament was placed. Ledermix paste experienced significantly less postoperative pain than with no intra canal medicament and may be used to reduce the inter appointment pain[Table 4].

Nineth trial by Shafqat et al (2010)²⁶, 100 patients were equally divided into 2 groups (n=50). In group 1 calcium hydroxide was placed as intra canal medicament and in group 2 creosote was placed . Postoperative pain in group 1 was 38% and group 2 was 50%. They concluded that, calcium hydroxide is better than creosote in reducing pain[Table 4].

Tenth trial by Tulio G V Gama et al (2008)¹⁹, 138 patients were divided into 2 groups. In one group, 0.12% chlorhexidine in natrosol gel was placed and in other group calcium hydroxide/CPMC/glycerine paste was used. There was no significant difference between the two medications with regard to postoperative pain[Table 4].

Eleventh trial by Jamileh Ghoddusi et al (2006)¹⁸, 60 were divided into 3 equal groups. Group 1 patients were treated in single visit, group 2 in 2 visit without intra canal medicament and group 3 treated in 2 visit with calcium hydroxide as medicament. Two visit endodontic treatment with calcium hydroxide as intra canal dressing can decrease the incidence of flare up[Table 4].

Twelfth trial by E H Ehrmann et al (2013)², 223 teeth were divided into 3 groups. Group 1 – Ledermix paste, group 2 – calcium hydroxide and group 3 – no dressing. Dressing with a corticosteroid/antibiotic paste experienced less pain when compared to calcium hydroxide/no dressing.

Thirteenth trial by Walton et al (2003)¹⁷, 140 samples were divided into 2 groups, one group received calcium hydroxide and other group received dry cotton pellet with no intra canal medicament. There was no significant between the 2 groups in post treatment pain [Table 4].

Fourteenth trial by Jose F Siqueira et al (2002)¹⁶, 627 teeth were used for the study. After canal preparation, canals were medicated with calcium hydroxide/CMCP paste. Postoperative pain was recorded after 1 week. Absence of pain was noted in 84.8% cases. This study concludes that the reduction in pain level might be due to the antimicrobial properties of the medicament [Table 4].

Fifteenth trial by Maged M Negm (2001)¹⁵, 988 subjects were divided into 2 groups. In one group they placed kenacomb and in another they placed placebo. 93% of cases treated with kenacomb showed complete relief of pain within 24hrs whereas 18% in the placebo group experienced complete relief of pain during the same period [Table 4].

Sixteenth trial by Martin J Rogers et al (1999)¹⁴, 48 patients were randomly assigned into 4 groups. Group1- oral ibuprofen, group 2 – placebo, group 3 – dexamethasone, group 4 – ketorolac tromethamine. Dexamethasone and ketorolac was better in relieving pain at 12hour over placebo. Ibuprofen was equally effective as either dexamethasone or ketorolac in relieving pain [Table 4].

Seventeenth trial by L R G Fava et al (1998)¹³, 60 teeth were randomly distributed into 2 groups. one group was medicated with calcium hydroxide and other group was medicated with corticosteroid antibiotic solution. There was no significant difference between calcium hydroxide and corticosteroid paste in pain reduction [Table 4].

Eighteenth trial by Maged M Negm (1994)¹², 760 subjects were divided into 6 groups: diclofenac, diclofenac- hyaluronidase, ketoprofen, ketoprofen – hyaluronidase, placebo, placebo–hyaluronidase. When hyaluronidase was added to medications, the percentage of cases with no pain was higher. Use of ketoprofen and diclofenac was effective in controlling pain in symptomatic and asymptomatic cases and they were superior to placebo [Table 4].

Nineteenth trial by L R G Fava (1992)¹¹, 45 patients were divided into 2 groups. Group 1: corticosteroid antibiotic solution (otosporin) and group 2:calcium hydroxide. There was no significant difference between both medication [Table 4].

Twentieth trial by Trope M (1990)¹⁰, 474 samples are grouped into 3 groups. In one group formocresol was placed. In other group Ledermix (n=160) was placed in root canal and in the 3rd group calcium hydroxide (n=158) was placed. Incidence of flare up was independent of intra canal medicament used [Table 4].

Twenty first trial by Kenneth Chance et al (1987)⁹, 300 patients were randomly entered in the study. In one group, they placed corticosteroid (n=147) and in another group they placed saline

(n=133). They concluded that, to reduce the incidence of postoperative pain after initial instrumentation in teeth where vital pulp tissue was removed, intra canal use of corticosteroid is recommended [Table 4].

DEFENDING THE RESULTS

Studies with Corticosteroids

Out of 21 studies, 2 studies compared corticosteroid intra canal medications with other medications. In one study, they found that meticortilone (prednisolone), when used as an intracanal medicament was better than saline. In other study they found that, corticosteroids and NSAIDs were equally effective in relieving pain [Table5].

These studies show that, corticosteroids are effective in relieving pain. Corticosteroids acts by inhibiting prostaglandin release which mediates pain. Also in one study, corticosteroid and NSAIDs have shown to be equally effective. The mode of NSAIDs is inhibition of cyclo-oxygenase pathway that metabolizes arachidonic acid to prostaglandins and thromboxanes. Equal effectiveness of corticosteroid and NSAIDs may be due to the similar mode of action.

Studies with other Medicament Combined with Corticosteroid

9 studies tested corticosteroid combinations as intra canal medicament. 5 studies were done with Ledermix paste in which 4 studies concluded Ledermix paste is superior. In one study they concluded Ledermix paste is equally effective as formocresol and calcium hydroxide. In 2 studies done by Fava, corticosteroid – antibiotic combination was equally effective as calcium hydroxide. In study conducted by Negm, corticosteroid – antibiotic combination was better than placebo. Bestoon stated that use of pulpotec resulted in rapid resolution of pain. Swathi Pai et al founded that use of triple antibiotic paste is more effective in controlling flare up in diabetic patients than calcium hydroxide and no medicament [Table 5].

Table 5: Studies with Various Medicaments

S.NO	Author	Studies	Medicaments	Medicaments Compared with Corticosteroids
1.	Kenneth Chance et al.	Corticosteroid used	Meticortelone (Prednisolone)	Saline
2.	Martin J Rogers et al	Corticosteroid used	Dexamethasone	Oral ibuprofen, Oral placebo, Intracanal ketorolac.
3	Trope M.	Corticosteroid combination used	Ledermix	Formocresol, Calcium hydroxide
4	L R G Fava.	Corticosteroid combination used	Otosporin	Calcium hydroxide paste
5	L R G Fava.	Corticosteroid combination used	Polymixin B, Neomycin sulphate, Hydrocortisone	Calcium hydroxide paste
6	Maged M Negm.	Corticosteroid combination used	Kenacomb	Placebo
7	E H Ehrmann et al.	Corticosteroid combination used	Ledermix	Calcium hydroxide No medicaments
8	Abdul QadirDall et al.	Corticosteroid combination used	Ledermix paste	No intracanal medicament
9	Naveed Ahmed Menon et al.	Corticosteroid combination used	Ledermix paste	Calcium hydroxide
10	M Kundabala et al.	Corticosteroid combination used	Ledermix	Eugenol soaked cotton
11	M Kundabala et al.	Phenol used	Eugenol	Ledermix
12	Hui-Xiao Yang.	Phenol used	Formocresol	Chlorhexidine mixed with calcium hydroxide
13	Shafqat et al.	Phenol used	Creosote	Calcium hydroxide
14	Trope M.	Phenol used	Formocresol	Ledermix Calcium hydroxide
15	Swathi Pai et al.	Medicament used	Calcium hydroxide	No intracanal medicament Triple antibiotic paste
16	Ripu Daman Singh et al.	Medicament used	Calcium hydroxide paste	Calcium hydroxide + 2% chlorhexidine 2% Chlorhexidine No dressing
17	Naveed Ahmed Menon et al.	Medicament used	Calcium hydroxide	Ledermix
18	Shafqat et al.	Medicament used	Calcium hydroxide	Creosote
19	Jamileh Ghodduzi et al.	Medicament used	Calcium hydroxide	No medicament
20	E H Ehrmann et al.	Medicament used	Calcium hydroxide	Ledermix paste No medicaments
21	Walton et al.	Medicament used	Calcium hydroxide	No medicaments
22	L R G Fava et al.	Medicament used	Calcium hydroxide paste	Polymixin B, Neomycin sulphate Hydrocortisone
23	L R G Fava.	Medicament used	Calcium hydroxide paste	Otosporin
24	Trope M.	Medicament used	Calcium hydroxide	Formocresol Ledermix

25	Yasir Khan Khattak et al.	Calcium hydroxide combinations	Calcium Hydroxide mixed with 2% chlorhexidine	Calcium hydroxide mixed with 0.9% saline
26	Ripu Daman Singh et al.	Calcium hydroxide combinations	Calcium hydroxide + 2% chlorhexidine	2% Chlorhexidine Calcium hydroxide paste No dressing
27	Hui-Xiao Yang.	Calcium hydroxide combinations	2% Chlorhexidine mixed with calcium hydroxide	Formocresol
28	Tulio G V Gama et al.	Calcium hydroxide combinations	Calcium hydroxide/camphorated paramonochlorophenol / glycerine paste	Chlorhexidine
29	Jose F Siqueira et al.	Calcium hydroxide combinations	Calcium hydroxide/camphorated paramonochlorophenol paste	-
30	Maged M Negm.	NSAIDS	Diclofenac Ketoprofen	Hyaluronidase BP Saline
31	Martin J Rogers et al.	NSAIDS	Intracanal ketorolac	Oral placebo, Oral ibuprofen Intracanal dexamethasone
32	Ripu Daman Singh et al.	Chlorhexidine	2% Chlorhexidine	Calcium hydroxide + 2% chlorhexidine Calcium hydroxide paste No dressing
34	Tulio G V Gama et al.	Chlorhexidine	Chlorhexidine	Calcium hydroxide/camphorated paramonochlorophenol / glycerine paste

In all studies using corticosteroid combinations, corticosteroids combinations are found to be superior or equally effective to other medicaments. None of the medicaments were superior to corticosteroid combinations. Mostly corticosteroids are combined with antibiotics. Use of corticosteroids alone can interfere with immune response, which could disseminate bacteria leading to infectious disease. The use of antibiotics along with corticosteroids prevents dissemination of bacteria.

Studies with Phenol

Phenol (formocresol) was equally effective as Ledermix paste and calcium hydroxide in a study conducted by Trope. In a study done by Shafqat et al, phenol (creosote) was found to be less effective than calcium hydroxide. Hui-Xiao compared phenol (formocresol) with calcium hydroxide and formocresol was less effective in relieving pain [Table 5]. In all the studies except one, phenol was found to be inferior. In one study it was equally effective as that of Ledermix paste and calcium hydroxide. This may be because the author placed intra canal medicament irrespective of whether patient is symptomatic or asymptomatic.

Studies with Calcium Hydroxide

In 3 studies, calcium hydroxide was better than no medicament, but in 2 studies there was no difference between calcium hydroxide and no medicament. 3 studies reveal calcium hydroxide is less effective than corticosteroid antibiotic solution where as in 3 studies calcium hydroxide was equally effective as corticosteroid-antibiotic solution. In 2 studies calcium hydroxide was better than phenol where as in one study it was equally effective as phenols. In one study it was better than chlorhexidine in relieving pain [Table 5].

The pain relief in some studies may be due to its antibacterial and anti-inflammatory properties. Antibacterial property may be explained by its ability to maintain high pH by release of hydroxyl ions and its ability to detoxify lipopolysaccharides. But in some studies, calcium hydroxide is ineffective in relieving pain. This may be due to the buffering action exerted by dentine over calcium hydroxide or resistance of certain bacteria in root canals towards calcium hydroxide. Also calcium hydroxide is ineffective in removing bacteria penetrated deep into the dentinal tubules.

Studies with calcium Hydroxide as Combination

One study used calcium hydroxide camphorated paramonochlorophenol glycerine paste and they found there was reduction in pain. Another study compared calcium hydroxide camphorated paramonochlorophenol glycerine paste with chlorhexidine and found that both were equally effective. In another study comparing calcium hydroxide chlorhexidine mixture with calcium hydroxide , chlorhexidine and no medicament, calcium hydroxide chlorhexidine mixture was

effective in reducing pain. Calcium hydroxide chlorhexidine mixture and calcium hydroxide mixed with saline were used as medicaments in another study and calcium hydroxide chlorhexidine mixture was found to be effective [Table 5].

Association of calcium hydroxide with CPMC has a broader antibacterial spectrum and higher radius of antibacterial action. Combination of calcium hydroxide and chlorhexidine produces a pH of 12.8 and it also improves the wettability of the medication on the root canal by lowers its contact angle. The equal effectiveness of CPMC calcium hydroxide combination with chlorhexidine may be due to the decreased concentration of chlorhexidine used.

Studies using NSAIDs

In one study, diclofenac and ketoprofen were equally effective in reducing pain. In another study ketorolac was equally effective as corticosteroid but better than placebo [Table 5]. Equal effectiveness of diclofenac and ketoprofen may be due to the similarity in mode of action ie inhibition of COX pathway that metabolizes arachidonic acid to prostaglandins and thromboxanes.

Studies using Chlorhexidine

In one study, chlorhexidine was equally effective as calcium hydroxide camphorated paramonochlorophenol glycerine paste. In another study chlorhexidine was less effective than calcium hydroxide chlorhexidine mixture but better than calcium hydroxide[Table 5].

The less effectiveness of chlorhexidine when compared to calcium hydroxide chlorhexidine mixture may be due to the synergistic effect of calcium hydroxide and chlorhexidine. Equal effectiveness of chlorhexidine when compared to calcium hydroxide CPCM paste may be due to the lower concentration of chlorhexidine used in that study.

Quality of Evidence

INFERENCE

There are many intra canal medicaments used in endodontics. Though calcium hydroxide is commonly used as intra canal medicament, there is no substantial evidence that it is better in reducing postoperative pain. From this systematic review, it is concluded that certain medicaments such as corticosteroids antibiotic combination and calcium hydroxide chlorhexidine combinations might be effective in reducing pain.

Implications for Practice

Calcium hydroxide is the commonly used intra canal medicament during root canal treatment. But recent systematic reviews states that calcium hydroxide is not effective in reducing postoperative pain. So new medicaments has to be tried for reducing postoperative pain.

Implications for Research

Since the number of good quality randomized controlled clinical trials included in this review is limited, more clinical trials are required to prove the efficacy of various medicaments.

Report of Outlier Data

No outlier data obtained.

SUMMARY

The aim of this systematic review was to evaluate effectiveness of various medications in reducing postoperative pain. Trials were selected if they met the following criteria: clinical trials or in-vivo studies that evaluated the efficacy of various intra canal medicaments in reducing postoperative pain during root canal treatment. For identification of studies considered in this review, detailed search strategies were carried out on the following databases. PubMed (until July 2015), PubMed Advanced search (until July 2015), Medline and Cochrane Database of Systematic reviews. The search identified 414 publications, out of which 397 were excluded after reviewing the title. Full articles were obtained for 17 studies, 2 of which are excluded after reading the full text article. So a total of 15 studies were included. 6 hand searched publications fulfilled the inclusion criteria. Therefore a total of 21 publications fulfilled all criteria for inclusion.

CONCLUSION

From this systematic review, it can be concluded that certain intra canal medicaments can be used to reduce postoperative pain during root canal treatment. Most of the studies proved that corticosteroid antibiotic solution or combination of calcium hydroxide with other medicine like CMPC or chlorhexidine is effective in reducing post operative pain. There is no evidence that use of calcium hydroxide is effective in relieving pain. Further clinical trials are required to evaluate the efficacy of intra canal medicaments in reducing postoperative pain.

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