Original Research Paper



Endodontics

COMPARATIVE EVALUATION OF THE EFFECT OF INTRACANAL CRYOTHERAPY ON POSTOPERATIVE PAIN AFTER SINGLE VISIT ROOT CANAL TREATMENT- AN IN VIVO STUDY

Dr. Mohit Singh Endodontist, INDC Danteshwari, Mumbai, India.					
Dr. Shahina Parvez	Professor, RUHS College of Dental Sciences, Jaipur, India.				
Dr. Rohit Khatri	Assistant Professor, RUHS College of Dental Sciences, Jaipur, India.				
Dr. Pankaj Prasad	Department of Conservative Dentistry & Endodontics, Maulana Azad Institute of Dental Sciences, Delhi, India.				

KEYWORDS:

INTRODUCTION

In general, successful endodontic treatment is governed by factors like localization, thorough bio-mechanical preparation of the root canal system, adequate shaping, proper disinfection, and three-dimensional obturation of the root canal system. To achieve this, endodontists used to perform the treatment that required multiple visits for complete disinfection of the canals for the better success of endodontic therapy¹. Single-visit endodontic therapy is defined as 'the conservative non-surgical treatment of an endodontically involved tooth consisting of complete biomechanical cleansing, shaping, and obturation of the root canal system in the same visit².

In all these years, due to the tremendous success of conventional multiple-visit endodontic therapy, single-visit endodontic therapy has until recently been a neglected mode of therapy^{3,7}. The resistance to the acceptance of single-visit treatment procedures could be attributed further to controversies such as post-operative pain, flare-ups, rate of successful healing, and patient acceptance^{8,9}. Postoperative pain is reported with a high incidence rate ranging between 3 and 58%¹¹.

The causes of postoperative pain can be classified as mechanical, chemical, and/or microbiological injuries to the periradicular tissues. Factors identified that contribute to postoperative pain after single-visit root canal treatment consist of the following: age, sex, tooth type or location, preoperative pain, periapical radiolucency, pulpal status, prophylactic drug, anesthetic agent, working length method, instrumentation, irrigation, use of lasers, obturation technique, occlusal reduction, postoperative drug, and operator¹².

There are various ways to control postoperative pain in root canal treatment & flare-ups which include each clinical step of root canal therapy (RCT) must be done with utmost perfection, some examples include, accurate working length (WL) determination, proper cleaning and shaping (crown down technique) with adequate sequencing of instruments, optimum use and judicious selection of intracanal irrigants, and use of magnifying devices, such as dental loupes and endodontic microscopes ^{14,15}. There are other adjuncts to manage postoperative pain like pretreatment analgesia, preoperative nonsteroidal anti-inflammatory steroids, preoperative single oral dose of prednisolone (30 mg) or dexamethasone (4 mg), enduring local anesthesia (bupivacaine), post-operative analgesics, intracanal cryotherapy, and occlusal reduction ¹².

In the present study, intracanal cryotherapy is taken as a mode to manage post-operative pain. In dentistry, the mechanism of action and effectiveness of cryotherapy are well described is, however strong evidence to support its use as an intracanal irrigation is limited with standardization of crucial factors such as time period, duration, application mode, and cold agent used. Therefore, the purpose of this study was to evaluate the effect of cold saline irrigation as a final irrigant following biomechanical preparation of root canals on postoperative pain in patients with irreversible pulpitis.

MATERIAL & METHODS

The institutional ethical clearance was obtained. A comparative study was carried out on 60 patients requiring root canal treatment on 60 single-rooted teeth with irreversible pulpitis or symptomatic apical periodontitis.

Inclusion Criteria:

Selection of cases for the study are

- (1) Single rooted teeth of patients' age ranged from 18 to 50 years with Vertucci type I canal configuration.
- (2) Teeth with Patients with one maxillary or mandibular tooth diagnosed with asymptomatic irreversible pulpitis or symptomatic irreversible pulpitis with either normal apical tissues or symptomatic apical periodontitis.

Exclusion Criteria:

- (1) Patients with any systemic disease i.e. diabetes, metabolic disorders.
- (2) Patients who are taking antibiotics, non-steroidal antiinflammatory drugs, or corticosteroids before the time of treatment.
- (3) Patients who need antibiotic premedication for dental treatment.
- (4) Grossly decayed teeth where rubber dam isolation is difficult,
- (5) Teeth with calcified canals and weeping canals.
- (6) Retreatment cases and teeth that had been previously accessed.
- (7) Patients with immature apices or root resorption were excluded from the study.

Preoperatively, those who fulfilled the criteria. Selected patients were randomly divided into two groups of 30 patients each:-

Group 1: **Cryotherapy group**, final irrigation was performed using 0.9% physiological saline solution at 0 degrees to 2.5 degrees Celsius Temperature (n=30 teeth)

Group 2: **Control group**, final irrigation was performed using 0.9% physiological saline solution at room temperature (n=30 teeth)

Patients were recalled at intervals of 6, 12,24 hours, 48 hours, and 7 days to evaluate the post-operative pain in the treated tooth.

METHODOLOGY

- Oral and written informed consent was obtained from the patients for the study and understood the need to attend follow-up sessions.
- Medical and dental history was recorded for all the patients selected for the study

Pre-operative Clinical Assessment

Intraoral examination was done to assess the (spontaneous pain, presence of sinus tract, swelling, mobility, periodontal probing depths greater than baseline measurements, or sensitivity to percussion or palpation). The patients who had taken medication for any systemic illness during the follow-up period were excluded from the study.

An electric pulp vitality test was performed to assess the vitality of the teeth Oral prophylaxis was done before the start of treatment.

Pre-operative Radiographic Assessment

The X-ray unit (ENDO-ACP, Villa system medical, Milano, Italy) was set at 70 kV and 7mA with an exposure time of 0.12 sec. to standardize the pretreatment and all subsequent follow-up radiographs. A long cone paralleling technique was used. Patient exposure was kept minimum by following the ALARA (as low as reasonably achievable) principle.

- The images were saved in Kodak Dental imaging software and exported in a jpeg format to the patient's file.
- During the recruitment period, a total of 60 single-rooted teeth from 60 patients with a mean age of 34 years (age range = 18-50) fulfilled the inclusion criteria.

Visual Analogue Scale (VAS)

It was instructed to the patient to point to the position on the line between the faces to indicate how much pain they are currently feeling. The far left end indicates "no pain" and the far right end indicates "worst pain ever."

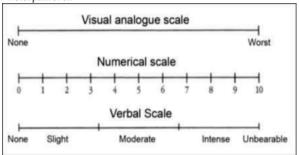


Fig 1 VAS scale

Clinical Procedure

A complete and elaborate history was taken before the start of the procedure regarding the appropriate diagnosis of pain and associated symptoms.

Preoperative VAS score was taken from the patient.

The standard procedure for both the groups at the first appointment was the infiltration of local anesthetics (2% lidocaine with 1:100000 epinephrine) as needed for patient comfort, rubber dam application was done, caries excavation if present, and access preparation made conservatively. A surgical length no. 2 and no. 4 round bur and long tapering diamond point were used laterally to eliminate pulpal horns. After the access cavity preparation, the pulp chamber was flooded with 5.25% NaOCl solution. A fine barbed broach was used for the extirpation of pulpal tissue if present. Coronal shaping and enlargement were performed 30/0.08 % Neoendo Flex Files to obtain straight-line access to the apical third of each root. Canals were then irrigated with 5.25% NaOCl and saline. RC-Help was used as a lubricant.

The working length was determined with a K-file from a coronal reference point to a distance 0.5-1 mm short of the radiographic apex i.e. apical constriction with the aid of radiovisiography and i-ROOT Electronic Apex Locator. The instrumentation was carried out using hand K-files and Neoendo Flex Files were used in sequence from the smallest to the largest starting with the initial binding file at the apical constriction. Instrumentation was done with Neoendo Flex Files and Flexicon Flex. The files were driven by an endodontic motor (DENTSPLY MAILLEFER's X-SMART) and used with a continuous brushing motion according to the manufacturer's instructions. Copious irrigation was done after alternate instruments and after filing with 5.25% NaOCl and saline. RC-Help was used as a lubricant during filing. Canal patency was maintained by passing a #10 no. stainless steel file approximately 0.5-1.0 mm beyond the working length.

Following the completion of biomechanical preparation, as the groups were randomly allocated, final irrigation was subsequently performed in **CONTROL GROUP** using 20 ml of 0.9% normal saline at room temperature approximately at the rate of 5 ml/min.

In **CRYOTHERAPY GROUP** use 20 ml of 0.9% normal saline at 0 to 2.5 degrees Celsius temperature approximately at the rate of 5 ml/min. The cold saline used in the study was preloaded in syringes and refrigerated at a controlled temperature of 0-2.5 degrees Celsius monitored via a digital thermometer until its use.

RVG image with placement of master cone was taken and then teeth were obturated in the single visit with gutta-percha cones and Sealapex as a root canal sealer, using lateral condensation technique. Permanent restoration with 3M FILTEK composite material was done after obturation and post-obturation RVG image was taken.

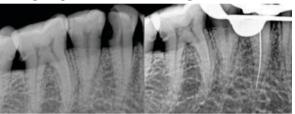
Follow Up And Evaluation Criteria:

- The patients were instructed to report immediately in case of unbearable pain or swelling.
- Patient were also asked to report prior to intake of any analgesics in case of severe pain.
- To obviate the patient-related bias, previous reference markings were taken from patients before the successive VAS score.
- For follow up patients were recalled after 6hrs, 12hrs, 24hrs, 48hrs and 7days and there post operative pain was revaluated on the basis of VAS score.



Fig 2: Digital Thermometer

Fig 3: Side vented needles





Master Cone Obturation

Fig. 4: Radiographic Representation Of Single Visit Root Canal Treatment

Statistical Analysis Statistical procedures

- Data obtained was compiled on an MS Office Excel Sheet (v 2010, Microsoft Redmond Campus, Redmond, Washington, United States).
- Data was subjected to statistical analysis using Statistical Package for Social Sciences (SPSS v 21.0, IBM).
- Descriptive statistics like frequencies and percentage for categorical data and mean & SD for numerical data has been depicted.

Since the data is coded on the VAS scale the normality of numerical data was checked using the Shapiro-Wilk test & was found that the data did not follow a normal curve; hence **non-parametric tests** have been used for comparisons.

- Inter-group comparison (2 groups) was done using Mann Whitney U test.
- Intra-group comparison was done using Friedman's (for >2 observations) followed by pair-wise comparison using the Wilcoxon Signed rank test.

For all the statistical tests, p<0.05 was considered to be statistically significant, keeping α error at 5% and β error at 20%, thus giving power to the study as 80%.

RESULTS

In the present study, 60 patients requiring root canal treatment on 60

single-rooted teeth with irreversible pulpitis or symptomatic apical periodontitis were selected to compare the effect of intracanal cryotherapy on postoperative pain on single-visit root canal treatment. Selected patients were randomly divided into two groups of 30 patients each which includes group 1 as cryotherapy group (0-2.5 °C normal saline) and group 2 as control group (normal saline at room temperature). Among 60 patients, 3 patients from the control group had to be excluded as they failed to follow up protocols and insisted on taking analgesics.

The remaining 57 patients from both groups were clinically followed after treatment for 6 hours, 12 hours, 24 hours, 48 hours, and 7 days; VAS scores were recorded at respective intervals. The observation and statistical analysis of the data for both groups are:-

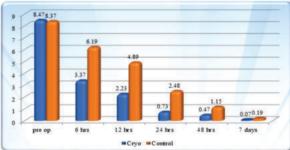
Table 1 showed there was a statistically non-significant difference seen for the values of VAS between the groups (p>0.05) at baseline & 7 days while, there was a statistically highly significant difference seen for the values of VAS between the groups (p<0.01) at 6hrs, 12 hrs, 24 hrs with higher values in the control group as compared to Cryo group. There was a statistically significant difference seen for the values of VAS between the groups (p<0.05) at 48 hrs with higher values in the control group as compared to the Cryo group

Table 1: Comparison Of VAS Scale Between The Groups

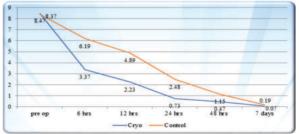
	Group s	N	Mean	Devia	Std. Error		Mann- Whitne	l .	p value
				tion	Mean		y U value		
Pre- op	Cryo	30	8.47	.629	.115	9	370	-0.62 7	0.531 #
	Control	27	8.37	.629	.121	8			
6 hrs	Cryo	30	3.37	1.351	.247	4	98.5	-4.97	0.000
	Control	27	6.19	1.733	.333	6			
12 hrs	Cryo	30	2.23	1.104	.202	2	82.5	-5.23 2	0.000
	Control	27	4.89	1.553	.299	5			
24 hrs	Cryo	30	.73	.907	.166	0	151.5	-4.19 5	0.000
	Control	27	2.48	1.553	.299	2			
48 hrs	Cryo	30	.47	.860	.157	0	267.5	-2.46 2	0.014
	Control	27	1.15	1.199	.231	1			
7 days	Cryo	30	.07	.254	.046	0	357	-1.34 9	0.177 #
	Control	27	.19	.396	.076	0			

^{* =} statistically significant difference (p<0.05)

^{#=}non significant difference (p>0.05)



Graph 1: Comparison Of VAS Scale Between The Groups

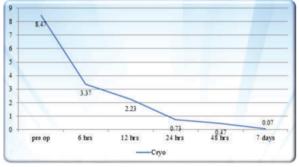


Graph 2: Comparison of VAS scale between the groups

Table 2 showed, there was a statistically highly significant difference seen for the values of VAS between the time intervals for group 1 (p<0.01) with highest values at Pre-op followed by 6 hrs and least at 7 days.

Table 2: Intra Group Comparison Of Scores Over Time Intervals In Group 1

	N	Mean	Std. Deviat ion		Maxi mum	50th (Medi an)	Chi squa re test	p value of Friedm an Test
pre op	30	8.47	.629	7	9	9.00		
6 hrs	30	3.37	1.351	1	6	4.00		
12 hrs	30	2.23	1.104	0	4	2.00	141.7 31	0.000*
24 hrs	30	.73	.907	0	3	.00		
48 hrs	30	.47	.860	0	3	.00		
7 days	30	.07	.254	0	1	.00		

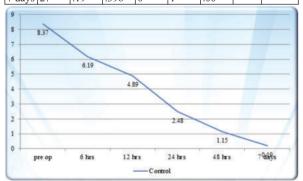


Graph 2: Intra group comparison for Cryo group

There was a statistically highly significant difference seen for the values of VAS between the time intervals for group 2 (p<0.01) with highest values at pre-op followed by 6 hrs and least at 7 days.

Table 3: Intra Group Comparison Of Scores Over Time Intervals In Group 2

	N	Mean	Std. Deviat ion	Mini mum	Maxi mum	50th (Medi an)		p value of Friedm an Test
pre op	27	8.37	.629	7	9	8.00		
6 hrs	27	6.19	1.733	3	8	6.00		
12 hrs	27	4.89	1.553	2	7	5.00		
24 hrs	27	2.48	1.553	0	5	3.00	128.6 65	0.000*
48 hrs	27	1.15	1.199	0	4	1.00		
7 days	27	.19	.396	0	1	.00		



Graph 3: Intra Group Comparison Of Scores Over Time Intervals In Group 2

Pair wise comparison using Wilcoxon Signed rank test showed, there was a statistically highly significant difference seen for the values of VAS between all pairs of time intervals for both the groups (p<0.01)

DISCUSSION

The basic biological rationale for achieving ultimate success with Root canal treatment consists primarily of eliminating microorganisms from the entire root canal system and creating an environment that is

^{** =} statistically highly significant difference (p<0.01)

most favourable for healing²⁰.

The incidence of postoperative pain and endodontic Flare-ups is one of the major concerns when evaluating endodontic treatment alternatives²¹. Root canal procedures are commonly believed to be the most painful dental treatment. Postendodontic pain most often occurs during the first 24 to 48 hours after obturation, and generally recedes in a few hours, although it occasionally persists for several days. The incidence of this post-endodontic pain (PEP) was reported to range from 3 - 58%¹¹. Pak and White concluded that the prevalence of PEP was 40% at 24 hours, whereas it reduced to 11% at 1 week and it was most intense in the first six hours following a gradual decline after a week^{22,23}.

The reasons for postoperative pain can be many including chemical, mechanical, or microbial injuries to the periapical tissues that result in acute inflammation. Mechanical factors, including over-instrumentation or extrusion of root-filling materials, have been associated with the presence of postoperative pain suggesting that root canal instrumentation and obturation techniques may influence postoperative pain. Several studies have found a correlation between the root canal instrumentation technique and postoperative pain. In step back technique; there is a high chance of pushing the debris beyond the apical foramen as stated in different studies (Ruiz et al., 1987²⁴; Al Omari and Dummer, 1995²⁵). In the step-down technique, the bulk of tissue debris and microorganisms are removed before apical instrumentation is commenced, which greatly reduces the risks of extrusion causing periapical inflammation²⁶

In the present study, a 10-cm VAS was used to assess pain. One of the major advantages of VAS is that they are perceived as a continuum, meaning that their data are considered interval-scaled. Two equally sized intervals on a VAS are always interpreted as two equally sized differences by respondents. This makes it possible to calculate the arithmetic mean. VAS should not have any markings (e.g., identifying the middle or dividing the line up into equally sized fragments), since the sensitivity of VAS without markings is higher than it is with marking²⁷.

In the present study the post-operative pain was scaled at 6,12,24 and 48 hours as previously conducted studies have shown irrelevant of technique of obturation the maximum amount of post-operative pain is experienced at 6 hours and 12 hours up to 24 hours and followed by it tends to decline after that28. In this study cryotherapy in irrigation technique is chosen as a method to check its efficacy in controlling the post-operative pain in a single-visit root canal treatment.

The term cryotherapy is derived from the Greek word cryos, meaning "cold." In physiotherapy, it means lowering or decreasing the temperature of tissues for therapeutic purposes. In reality, cryotherapy does not imply implementing cold but rather extracting heat. Previously it has been frequently used as a method to control postoperative pain in sports medicine²⁰; It was an established method when treating acute soft tissue injuries, but there was a discrepancy between the scientific basis for cryotherapy and clinical studies

It was specifically mentioned by **Swenson et al. (1996)**²⁰ in one of their article about the effect of cryotherapy on sports medicine, that pain control can be achieved in injuries to tissue via 3 specific mechanisms: 1) analgesia, 2) hypometabolism and 3) vascular response.

Analgesia can be achieved by continuous reduction of that nerve conduction by decreasing temperature until nerve fiber conduction ceases completely or also removing the causes of pain by reducing muscle spasm in the injured area, thereby reducing the effects of the secondary ischaemic injury. The decrease in inflammatory response due to hypometabolism is of greater importance than the vascular response when it comes to limiting the extent of an injury and studies have shown that the metabolic enzymatic activity is decreased by 50% when the temperature is lowered by 10°C. Lastly decreasing the temperature decreases the internal diameter of venules, maintains blood flow rate, increases erythrocyte velocity in injured tissue, and leukocytes rolling and adhesion were significantly decreased. Thus, local tissue cooling changes local circulation and reduces inflammatory reactions by inhibiting the decreased number of circulating leukocytes in venules around injured tissue.

In a systematic review, **Bleakley et al. (2004)**¹⁸ evaluated the efficiency of cryotherapy applications in acute soft tissue injuries. The study

results indicated that cryotherapy is effective in lessening short-term pain and limiting inflammation. The first physiologic tissue response to cryotherapy is a drop in local temperature, leading to reduced cellular metabolism. This causes cells to use less oxygen and reduces blood flow as induced by vasoconstriction, leading to limitation of the damage. In addition, it affects peripheral nerve endings by diminishing the threshold needed to activate the tissue nociceptors and the speed of painful nerve impulses.

To achieve the effect of cryotherapy to manage pain **Franz and Iggo** (1968)³⁰ mentioned that lowering the body temperature decreases peripheral nerve conduction, and in particular, when it reaches about 7°C, there is complete deactivation of myelinated A fibers, whereas deactivation of nonmyelinated C-fibre occurs at about 3 degrees C. As most of the pulpal fibers are nonmyelinated including periodontal pain fibers it is important to achieve the lowering temperature of the tissue to less than 3°C.

There are various ways to apply cryotherapy in an endodontic procedure including the application of a cold substance intraorally in the vestibule adjacent to the affected teeth, extraorally on the site related to the affected tooth, or intracanal irrigation with normal saline. In the present study 0-2.5 degrees Celsius saline was used as an intracanal irrigant for cryotherapy dispensed with a 31 G side vented needle 2mm short of working length at the end of biomechanical preparation.

The first clinical study on the effect of intracanal cryotherapy in endodontics was conducted by **C** Keskin., et al. (2016)³¹ who assessed the effect of 2.5°C cold saline irrigation as a final irrigant following biomechanical preparation of root canals on postoperative pain in patients with irreversible pulpitis and, reported that there was a significant pain reduction levels when compared to that of a control group and other was Al-Nahlawi., et al. (2016)³² revealed the effects of intracanal cryotherapy and negative irrigation technique (EndoVac System) on post endodontic pain after vital single visit endodontic treatment According to the results of this significant study, intracanal cryotherapy along with negative pressure irrigation system reduced PEP and resulted in elimination of post endodontic pain clinically.

In light of these observations, intracanal cryotherapy can be considered a simple, cost-effective, and non-toxic treatment option for postoperative pain control in single-visit RCT cases. However, numerous research studies should be conducted shortly to investigate the possible benefits of this technique in the treatment of other pulpal and periradicular diseases. In addition, the investigation of inflammatory markers amongst patients subjected to intracanal cryotherapy might shed further light on the action mechanism and the potential use of cryotherapy in endodontics.

CONCLUSION

Within the limitation of the present in vivo study, it can be concluded that:-

- 1) Postoperative pain was present in almost all the patients after a single visit root canal treatment; in the range of trivial to severe.
- 2) Along with other factors, the presence of pre-operative pain is strongly associated with the development of postoperative pain in single-visit root canal treatment.
- 3) In both the groups, post-endodontic pain represented with highest values after 6 hours of treatment, moderate pain after 12 hrs, mild after 24 hrs, trivial after 48 hrs, and reduced to almost nil after 1 week.
- 4) Cryotherapy applications resulted in a significant reduction in postoperative pain levels at 6hrs, 12hrs, 24hrs, and 48hrs and reduced VAS scores of pain on percussion as compared with the levels in the control group. Moreover, patients in the control group used more analyses of versus the patients in the intracanal cryotherapy groups.
- 5) As there was trivial pain after 48 hours in all the patients of both groups, it can be concluded that cold irrigation may not play a significant role in post-operative pain management after 48 hours of root canal treatment.

To control postoperative pain in Endodontics, cryotherapy seems to be an effective, practical, and cheap method. Intracanal cryotherapy can be easily included in the treatment protocol, and patients will not have an impression of an additional step in the treatment procedure. Although cryotherapy is effective in relieving postoperative pain, its effect on the long-term success of root canal treatments remains unknown. Thus, further studies examining the effect of cryotherapy applications on the long-term success of root canal treatments are required.

- Ahmed F, Thosar N, Baliga MS, Rathi N. single visit endodontic therapy: A review.
- Austin J Dent. 2016;3(2):1035. Ashkenaz PJ. One visit endodontics. Dent Clin North Am 1984; 28(4): 853-863
- Cohen S, Burns RC. One appointment root canal therapy; Case selection and treatment planning. Pathways of the Pulp, 6th Edition, Harcourt (India) Pvt. Limited, New Delhi
- 4 Roane JB. Endodontics in a single-visit, Teaching Syllabus, The University of Oklahoma Press 1979: 30-61
- Pekruhn RB. Single-visit endodontic therapy: A preliminary clinical study. J Am Dent Assoc 1981; 103: 875-877. 5.
- Roane JB, Dryden JA, Grimes EW. Oklahoma C and Tulsa 0. Incidence of postoperative pain after single and multiple-visit endodontic procedures. Oral Surg 1983; 55(1): 68-71.
- Oliet S. Single-visit endodontics: A clinical study. J Endod 1983; 9(4): 147-151. Grossman LI, Oliet S, DelRio CE. Single visit endodontics; Endodontic practice. 11th edition, Vaghese publishing house, Bombay, 1988 : 349-350.
 Taintor JF, Langeland K, Valle GF, Krasny RM. Pain: a poor parameter of evaluation in
- dentistry. Oral Surg Oral Med Oral Pathol Oral RadiolEndod 1981; 52: 299-303.

 The Visual Analog Scale for Pain: Clinical Significance in Postoperative Patients, Carol
- A Bordin, Dr.P.H.; Gordon Freedman, M.D.; Sabera Hossain, M.S.; James B. Eisenkraft, M.D.: Yaakov Beilin, M.D.
- Sathorn C, Parashos P, Messer H. The prevalence of postoperative pain and flare-up in single-and multiple-visit endodontic treatment: a systematic review. Int Endod J 2008;
- Venkateshbabu Nagendrababu, BDS, MDS, PhD1/James L. Gutmann, DDS, PhD Factors associated with postobturation pain following single-visit nonsurgical root canal
- reactions associated with postconduction pain forther meaning evisitions agreed to can treatment. A systematic review. Quintessence International 2017;48; 198-203
 Belitsky RB., et al. "Evaluation of the effectiveness of wet ice, dry ice, and cryogenic packs in reducing skin temperature". Physical Therapy 67.7 (1987): 1080-1084. 13.
- Daniel, JG. "Advanced endodonties for clinicians". 1st ed. Bangalore: J and J Publication; (1998): 202-208.
- Bystrom A and Sundqvist G. "The antibacterial action of sodium hypochlorite and EDTA in 60 cases of endodontic therapy". *International Endodontic Journal* 18.1 1985): 35-40.
- Hubbard TJ and Denegar CR. "Does cryotherapy improve outcomes with soft tissue injury?" *Journal of Athletic Training* 39.3 (2004): 278-279. 16.
- 17 Swenson C, Sw€ard L, Karlsson J. Cryotherapy in sports medicine. Scand J Med Sci Sports 1996; 6: 193-200.
- Watkins AA, Johnson TV, Shrewsberry AB. Ice packs reduce postoperative midline incision pain and parcotic use: a randomized controlled trial. J Am Coll Surg 2014: 219:
- Bleakley C, McDonough S, Domhnall MD. The Use of Ice in the Treatment of Acute Soft-Tissue Injury: A Systematic Review of Randomized Controlled Trials. Am J Sports 19 Med 2004:32:251-61.
- Swenson C., et al. "Cryotherapy in sports medicine". Scandinavian Journal of Medicine and Science in Sports 6.4 (1996): 193-200. 20.
- Malang GA, Yan N, Stark J. Mechanisms and efficacy of heat and cold therapies for 21. musculoskeletal injury. Postgrad Med 2015;127:57–65
- 22. Zook N, Hussmann J, Brown R et al. Microcirculatory studies of frostbite injury. Ann
- 23
- Zook N, Fusshaam J, Brown Ret al. Microcreditatory studies of hostone hjury. Am PlastSurg 1984; 40:246–55
 Franz DN and Iggo A. "Conduction failure in myelinated and non-myelinated axons at low temperatures". *The Journal of Physiology* 199.2 (1968): 319–345.
 Ruiz-Hubard, Eduardo E, et al. A quantitative assessment of canal debris forced periapically during root canal instrumentation using two different techniques Journal of 24.
- Endodontics, Volume 13, Issue 12, 554-558
 Al-Omari MA, Dummer PM. Canal blockage and debris extrusion with eight preparation techniques. J Endod. 1995 Mar;21(3):154-8.
 Carrotte P. Endodontics: Part 7. Preparing the root canal. Br Dent J. 2004 Nov
- 26 27;197(10):603-13.
- The visual analog scale for pain: clinical significance in postoperative patients. Bodian 27. CA, Freedman G, Hossain S, Eisenkraft JB, Beilin Y. Anesthesiology. 2001 Dec:95(6):1356-61.
- A randomized observer-blind comparison of bilateral facial ice pack therapy with no ice therapy following third molar surgery. Van der Westhuijzen AJ, Becker PJ, Morkel J, Roelse JA. Int J Oral Maxillofac Surg. 2005 May;34(3):281-6.
- Recursory. Into January Manager Surge 2005 (1984) Ed. Batrista Cl., Gouveia FM. The influence of cryotherapy on reduction of swelling, pain and trismus after third-molar extraction: a preliminary study. JAm Dent Assoc 2005;136:774–8
- Franz DN, Iggo A. Conduction failure in myelinated and non-myelinated axons at low temperatures. J Physiol 1968;199: 319–45. 30
- Cangul Keskin, et al. "Effect of intracanal cryotherapy on pain after single visit root canal treatment". Australian Endodontic Journal 42 (2016): 9-11. 31.
- Al-Nahlawi T., et al. "Effect of Intracanal Cryotherapy and Negative Irrigation Technique on Post endodontic Pain". Journal of Contemporary Dental Practice 17.12 (2016): 990-996.