

CRYOTHERAPY – A GLIMPSE OF HOPE IN ENDODONTICS

ABSTRACT

Intolerable pain is the most common reason a patient seeks endodontic therapy, hence pain management becomes a prerequisite during endodontic treatment. Premedication with prophylactic analgesics such as nonsteroidal anti-inflammatory drugs, paracetamol, or corticosteroids, use of longer-acting anaesthetics, occlusal reduction of the offending tooth are some of the strategies which have been endorsed for managing endodontic pain over the past decades. Constant evolutions in the field of endodontics, requires the practitioners and researchers to sort to emerging therapies that improves the patient's comfort while being least invasive. Cryotherapy is one such evolution that is progressively becoming pervasive in the field of endodontics. Cryotherapy has already been showing promising results in other fields of dentistry. In this direction, the paper highlights a review of various scientific literatures and research work done on the implementation of cryotherapy in managing post endodontic pain and its various applications in endodontics.

KEY WORDS : *Cryotherapy; Endodontic pain; Anti-inflammatory; Intracanal cryotherapy; Extraoral cryotherapy; Cold Saline; Endo Vac;*

BREIF INTRODUCTION TO CRYOTHERAPY :

The term 'cryotherapy' is obtained from two Greek words - "cryos" meaning "cold" and "therapeia" denoting "cure". It serves as a means of lowering the temperature of tissues with therapeutic motives in physiotherapy. In actuality, cryotherapy does not infer to application of cold but rather implies to the extraction of heat from the tissues. More or less all the biological tissues, when exposed to a temperature of -20°C or below for a minute can undergo cryogenic necrosis and this forms the basis of cryotherapy. Cryotherapy effectively reduces the pain, oedema and inflammation. Hence cryotherapy has been chiefly employed to relieve musculoskeletal pain of arthritis, connective tissue distensions, muscular spasm, sports injuries, runner's knee, tendonitis, sprains, chronic pain, postoperative visceral pain and so on.¹

HISTORY

Cryotherapy has been often followed in numerous fields of medicine and dentistry. Dating back to 3000 BCE, the Egyptians were probably the first to locally apply freezing temperatures to the injured tissue as a means of analgesia. James Arnott demonstrated cryotherapy by treating malignant diseases using a combination of salt and ice. He also validated the use of cryotherapy as palliative analgesia for terminal cancer and neuralgia. Baron Lorrey signified the use of cold application as a mode of anesthesia and sedation for amputation of limbs during the Franco-Prussian Wars. Cryotherapy has been chiefly used to relieve musculoskeletal pain of arthritis, connective tissue distensions, muscular spasm, sports injuries, runner's knee, tendonitis, sprains, chronic pain, postoperative visceral pain and so on.^{1,2}

From the early 1960's, Cryotherapy was implied in various fields of dentistry. Its uses evolved from the local application of liquid nitrogen swabs for inflammatory papillary hyperplasia of the palate, to cryosurgical treatments of angiomas, hyperplasias of palate, leukoplakia, lichen planus and so on. Cryotherapy has been widely recommended after extractions, intraoral excisional surgeries, periodontal surgeries and implant placement to counter the inflammation. Cryotherapy was also found to be beneficial in alleviating pain, swelling, trismus and arthritis associated with temporomandibular joint disorders.³

PHYSIOLOGICAL EFFECTS OF CRYOTHERAPY

Subjecting the tissues to freezing temperatures results in lowering of the conduction velocity of nerve impulses, reduced hemorrhage, edema, and local inflammation. The three basic physiological effects of cryotherapy are exerted on vascular tissue, neurologic tissue, and tissue metabolism.

1. Vascular effects :

Cold application triggers vasoconstriction and lowers the vascular permeability, which in-turn limits the amount of fluid seepage into periapical tissue, henceforth reducing tissue edema and the related swelling. This forms the basis of cold application to surgical sites and has become the recommended protocol in postsurgical supportive therapy. The intensity of the vasoconstriction reaches the maximum at a temperature of 15°C. Cryotherapy has also been shown to diminish the number of white blood cells adhering to the endothelial lining of capillaries, leading to a weaker inflammatory response.⁴

2. Neurologic effects :

Cooling induces analgesia by slowing the conduction velocity of the nociceptive sensory nerve fibers. Local application of cold temperatures also lowers the activation threshold of tissue nociceptors and produces a local anesthetic effect. Furthermore, it also prompts the release of endorphins – a neuroeffective agent that hinders the transmission of nociceptive impulses to the central nervous system.

3. Effects on tissue metabolism :

Tissue injury leads to added utilization of oxygen, leading to consequent tissue hypoxia and necrosis. Cryotherapy lessens the blood flow and brings down the rate of biochemical reactions by more than 50%, thus curbing the formation of free radicals in tissues and thereby reducing the oxygen consumption and preventing further tissue hypoxia followed tissue injury.⁵

ENDODONTIC PAIN AND IT'S MANAGEMENT :

In the endodontic practice, one of the most deleterious and disheartening event for both the patient and clinician is commencement of pain, which could set in during the course or even after the completion of endodontic intervention. The situation turns more devastating if the patient was devoid of pain, to begin with. Flare-ups or pain after endodontic treatment may occur despite of carrying out the root canal therapy with utmost care and asepsis.⁶

There are multiple factors that could provoke pain during or after endodontic treatment, the most usual factor being - the extrusion of irritants like microorganisms or their toxins, dentin debris, irrigants, sealers, obturating materials etc into the periradicular tissue.

The incidence of post-endodontic pain reports to range from 3 - 58%. Studies have stated that symptomatic teeth more often produce flare ups than asymptomatic teeth.⁷ Study conducted by Sundquist

inferred that in most of the flare up cases, *Bacterioides melanninogenicus* was present.⁸ This conclusion was backed-up by Griffee et al who stated that, asymptomatic infected teeth did not harbor *Bacterioides melanninogenicus*. This gram negative anaerobic rod releases collagenolytic, fibrinolytic enzymes and endotoxins that in turn stimulates release of bradykinin- a potential pain mediator.^{9,10}

Besides managing the preoperative pain, several strategies have been put forward in concern to alleviate the potential pain that could arise during or after the endodontic treatment. One of the most widely sorted ways to counter the pain and inflammation is to prescribe analgesic medications. This improves the patient's confidence and faith in their dentists, increases their pain threshold, and creates a positive attitude towards further dental treatment. Despite being relatively safe, these drugs can often cause adverse effects such as gastrointestinal irritation. Overdosage or long term consumption of these drugs can potentially manifest renal, hepatic, and respiratory disorders.¹¹

ROLE OF CRYOTHERAPY IN ENDODONTICS:

In endodontics, the use of cryotherapy had been recommended as postoperative and palliative care following periradicular surgeries. The implementation of cryotherapy in endodontic treatment is gradually becoming ubiquitous. Numerous studies have been carried out to validate the use of Cryotherapy in managing Endodontic pain and inflammation.

A review of various scientific literatures and research work is summarized below :

Vera et al. were first among the researchers to uplift the concepts of cryotherapy in endodontics. They conducted an in-vitro study that aimed to substantiate a method that could reduce and maintain a low external root surface temperature so as to minimize the inflammation of periradicular tissues and associated pain. A novel protocol of irrigation using saline at 2.5°C along with EndoVac negative pressure irrigation system was followed. The results proved that intracanal irrigation with cold (2.5°C) saline lowered the temperature of external root surface at the apical third by more than 10°C and maintained the same for a minimum of 4 minutes, which could be sufficient to produce a local anti-inflammatory effect in the periradicular tissues. EndoVac system was used to carry the irrigant upto the apical third, as irrigants scarcely reach the root apices due to apical vapor lock.¹²

Transmission of cold temperatures to the periodontium differs from coronal to apical thirds of the root due to variations in dentinal properties like mineralization and width of dentin at both the thirds. More number of larger dentinal tubules are present in cervical third of root dentin that could make the transmission of therapeutic effect more difficult. Contrarily, apical root dentin is more dense and mineralized, with lesser dentinal tubules that would enhance more efficient cold transmission to adjacent tissues.^{12,13}

A randomized multicenter clinical trial conducted by the same researchers, Vera et al., used a final 20ml, 2.5°C cold saline irrigation with the EndoVac. The results were in accordance to their previous studies which emphasized the efficacy of intracanal cryotherapy in lowering post endodontic pain. The trial resulted in significantly reduced incidence and intensity of postoperative pain and lesser need for analgesics in patients diagnosed with necrotic pulp and symptomatic apical periodontitis.¹³

Cryotherapy was first introduced into clinical endodontics by Keskin et al in 2016 to assess the effect of final irrigation with 2.5°C cold saline on the postoperative pain after single-visit root canal treatment. This study used a side-vented, positive-pressure 31-G NaviTip needle, in place of EndoVac to nullify its additional effect on lowering the postoperative pain. The outcome of this study denoted that final irrigation with cold saline resulted a significantly lesser postoperative pain in the experimental cryotherapy group

than compared to the control group.¹⁴ These findings were affirmed in another similar study conducted by Al Nahlawi et al., signifying the use of intracanal cryotherapy in adjunct with negative pressure technique to minimize postoperative pain following single visit endodontics.¹⁵

A randomized control trial compared the outcome of cryotherapy on postoperative pain in patients with irreversible pulpitis with or without apical periodontitis. The study revealed that intracanal cryotherapy resulted in statistically lower postoperative pain in patients diagnosed with irreversible pulpitis and apical periodontitis. In patients having irreversible pulpitis without apical periodontitis, inflammation remains confined only to the root canal system without extension into periapical tissues, and once the inflamed pulp tissue gets extirpated, the source of inflammation also gets eliminated in both control and cryotherapy groups. This validates the reason that cold saline did not produce a statistically significant difference from normal saline in reducing the inflammation.¹⁶ This finding was similar to the results of two other In-vivo studies, suggesting that intracanal cryotherapy with 2.5°C saline does not produce much help in teeth with healthy periapical tissue, but turns out to be significantly effective in teeth with apical periodontitis. These studies validate the usefulness of intracanal cryotherapy in cases with apical periodontitis.^{7,17}

The results of an in-vitro study conducted by Mandras et al., indicate that cryo-instrumentation followed by NaOCl irrigation could significantly lower the colony forming unit of *Enterococcus faecalis* in the root canal compared to NaOCl irrigation alone.²⁰ One of the most common pathogen isolated in abundance from the canals of teeth having persistent post-treatment disease is the *Enterococcus faecalis*. These pathogens deeply penetrate into the dentinal tubules and are protected from irrigants and instrumentation, thereby causing difficulty in their eradication.^{18,19} Cryotherapy implemented in this study could significantly lower the microbial load. The equipment used for cryotherapy in this study had a conduit of conveyor that was connected to the cryogenic fluid (liquid nitrogen) source and a cryogenic needle. The freezing-thawing cycle induced altered protein conformation, cell wall disruption of the *E.faecalis*, causing leakage of intracellular components and their sequential cryodestruction.²⁰

Intracanal, intraoral and extraoral are the various modes of cryotherapy application, all of which are comparable in relieving postoperative pain as inferred by a randomized clinical control. In this study, Intracanal cryotherapy was carried out with 20ml of 2.5°C saline for 5 min, intraoral cryotherapy was carried out by placing small ice packs wrapped with gauze on the vestibular surface of offending tooth, and patients were asked to leave the pack in place for 30min. Extraoral cryotherapy was performed by placing ice packs on the cheek surface of the treated side for 30min. All of the above modes could lower postoperative pain and VAS score of tenderness on percussion. The patients in the control group who did not receive cryotherapy sorted to more analgesics than the experimental cryotherapy group. The Intracanal mode of cryotherapy had an added advantage of being included in the treatment procedure and that the patients can be more comfortable without having to carry intra/extraoral ice packs.²¹

A randomized clinical trial tested the effect of intracanal cryotherapy on the expression of interleukin-6 expression using different irrigation protocols.²⁴ Cytokines such as interleukin-1 (IL-1) β , IL-6, tumor necrosis factor regulate the development of apical periodontitis. IL-6 is a primary mediator cytokine that provokes the synthesis of prostaglandins and proteolytic enzymes, potentiates neutrophils and mediates periapical bone resorption.^{22,23} Results of this study revealed that Intracanal cryotherapy minimized the migration and adhesion of leukocytes, limits the formation of free radicals and pro-inflammatory mediators, thus resulting in reduced expression of IL-6 in the periapical tissues and associated inflammation.²⁴

APPLICATION OF CRYOTHERAPY ON ROTARY NITI INSTRUMENTS :

Wear resistance, cyclic fatigue resistance, cutting efficiency of rotary files can be enhanced by subjecting the rotary files to different surface treatment methods such as, physical vapor deposition of titanium nitride, electropolishing, thermal nitridation, boron ion implantation, cryogenic treatment and so on.^{25,26}

During cryogenic treatment the NiTi rotary files are subjected to subzero temperatures and then the metal is allowed to slowly warm up to the room temperature. In comparison with untreated files, the NiTi files that have undergone cryogenic treatment shows significant improvement in terms of cyclic fatigue resistance. This improvement was seen due to the complete transformation to the martensitic phase, from the austenitic phase of the alloy. Hence reduced internal stress and increased wear resistance are the chief advantages of cryogenic treatment on NiTi rotary files.^{27,28}

APPLICATION OF CRYOTHERAPY IN VITAL PULP THERAPY

Recently Cryotherapy has been proven to be successful in controlling the hemorrhage from the pulp tissue during direct pulp capping procedures. Sterile shavings of ice at 0°C is placed directly on vital pulp tissue that could directly or indirectly be exposed by a caries. After a minute approximately, the molten ice was suctioned out with a high-speed suction, following which 17% EDTA was used to rinse the area exposed.²⁹ EDTA is to be chosen over sodium hypochlorite as EDTA has the potential to synthesize numerous growth factors that aids matrix secretion, differentiation of odontoblasts, and tertiary dentin formation. Besides it also enhances the adhesion, migration, and differentiation of dental pulp stem cells.³⁰ After treatment with EDTA, the exposed dentin is covered with bioceramic materials, overlaid by a permanent restoration. 12–18 months follow up the tooth revealed vital pulp, completely asymptomatic and functional tooth. Further studies are required so as to determine and signify the long term results of cryotherapy during vital pulp therapy.^{29,31}

CONCLUSION

Intracanal cryotherapy is an easy, cost-effective, and non-invasive therapeutic option for managing postoperative pain. Due to its anti-inflammatory potential it is considered a viable option to reduce pain, swelling and discomfort related to periradicular inflammation that could be encountered during or after endodontic treatment and surgeries. Its ability to control the pulpal hemorrhage during pulp capping procedure has upgraded the success and the survival rates of vital pulp therapies. Further research should be carried out in the coming future to validate the efficacy, possible benefits of cryotherapy in the treating pulpal and periradicular diseases and to derive evidence based treatment outcomes.

REFERENCES

1. Bansal A, Jain S, Gupta S. Cryosurgery in the treatment of oro-facial lesions. *Indian J Dent Res* 2012;23:297.
2. Aggarwal N, Ahuja K, Pal N, Pannu R and Berwal V Neeraj. Cryosurgery: A Therapeutic Modality for Orofacial Lesions *HECS Int J Com Health and Med Res* 2017;3(3):42 (3):66-73
3. Asrani S, Reddy PB, Dhirawani RB, Jain S, Pathak S, Asati P. Cryosurgery: A simple tool to address oral lesions. *Contemp Clin Dent* 2018;9:S17-22

4. Vandana Gade, Digesh Barfiwala, Reema Asani, Rachana Gawande, Jaykumar Gade: Cryotherapy: An Emerging Trend in the Field of Endodontics *Int. J. Drug Res. Dental Sci.*, 2020; 2(3): 70-76.
5. Fayyad DM, Abdelsalam N, Hashem N. Cryotherapy: A New Paradigm of Treatment in Endodontics. *J Endod.* 2020 Jul;46(7):936-942.
6. Sathorn C, Parashos P, Messer H. The Prevalence of Postoperative Pain and Flare-Up in Single- And Multiple-Visit Endodontic Treatment: A Systemic Review. *Int Endod J* 2008; 41:91-9
7. Jain A, Davis D, Bahuguna R, et al. Role of cryotherapy in reducing postoperative pain in patients with irreversible pulpitis. an in-vivo study. *Int J Den Med Sci* 2018;2:43-9.
8. Bystrom A, Sundquist G, The antibacterial action of sodium hypochlorite and EDTA in 60 cases of endodontic therapy, *international Endodontic Journal*, 18, 1985, 35-40
9. Griffie M Patterson SS, Miller CH, Kafrawy AH, DeObrrio, *Bacteriodesmelanogenicus and Dental Infections, Oral Surgery* ,54, 1982, 486
10. J.F Siqueira, Microbial Causes Of Endodontic flare ups, *International Endodontic Journal*, 36, 2003, 453- 463
11. Smith EA, Marshall JG, Selph SS, Barker DR, Sedgley CM. Nonsteroidal Anti-inflammatory Drugs for Managing Postoperative Endodontic Pain in Patients Who Present with Preoperative Pain: A Systematic Review and Meta-analysis. *J Endod.* 2017 Jan;43(1):7-15.
12. Vera J, Ochoa-Rivera J, Vazquez-Carcaño M, Romero M, Arias A, Sleiman P. Effect of Intracanal Cryotherapy on Reducing Root Surface Temperature. *J Endod.* 2015 Nov;41(11):1884-7.
13. Vera J, Ochoa J, Romero M, Vazquez-Carcaño M, Ramos-Gregorio CO, Aguilar RR, Cruz A, Sleiman P, Arias A. Intracanal Cryotherapy Reduces Postoperative Pain in Teeth with Symptomatic Apical Periodontitis: A Randomized Multicenter Clinical Trial. *J Endod.* 2018 Jan;44(1):4-8.
14. Keskin C, Özdemir Ö, Uzun İ, Güler B. Effect of intracanal cryotherapy on pain after single-visit root canal treatment. *Aust Endod J.* 2017 Aug;43(2):83-88.
15. Al-Nahlawi T, Abo Hatab T, Abd Alrazak M, Al-Abdullah A. Effect of Intracanal Cryotherapy and Negative Irrigation Technique on Postendodontic Pain. *J Contemp Dent Pract* 2016;17(12):990-996
16. Bazaid DS, Kenawi LM. The effect of intracanal cryotherapy in reducing postoperative pain in patients with irreversible pulpitis: a randomized control trial. *Int J Health Sci* 2018;8:83-8.
17. Alharthi AA, Aljoudi MH, Almaliki MN, et al. Effect of intra-canal cryotherapy on post- endodontic pain in single-visit RCT: A randomized controlled trial. *Saudi Dent J* 2019;31:330-5
18. Gomes, B.P., Souza, S.F., Ferraz, C.C., Teixeira, F.B., Zaia, A. A., Valdrighi, L. and Souza-Filho, F.J. (2003) Effectiveness of 2% chlorhexidine gel and calcium hydroxide against *Enterococcus faecalis* in bovine root dentine in vitro. *Int Endod J* 36, 267-275
19. Oliveira, D.P., Barbizam, J.V., Trope, M. and Teixeira, F.B. (2007) In vitro antibacterial efficacy of endodontic irrigants against *Enterococcus faecalis*. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 103, 702-706.
20. Mandras N, Allizond V, Bianco A, Banche G, Roana J, Piazza L, Viale P, Cuffini AM. Antimicrobial efficacy of cryotreatment against *Enterococcus faecalis* in root canals. *Lett Appl Microbiol.* 2013 Feb;56(2):95-8.
21. Gundogdu EC, Arslan H. Effects of Various Cryotherapy Applications on Postoperative Pain in Molar Teeth with Symptomatic Apical Periodontitis: A Preliminary Randomized Prospective Clinical Trial. *J Endod.* 2018 Mar;44(3):349-354.
22. Ataoğlu T, Ungör M, Serpek B, Haliloğlu S, Ataoğlu H, Ari H. Interleukin-1beta and tumour necrosis factor-alpha levels in periapical exudates. *Int Endod J* 2002;35:181-5
23. Nair PN. Pathogenesis of apical periodontitis and the causes of endodontic failures. *Crit Rev Oral Biol Med* 2004;15:348-81.

24. Emad A, Abdelsalam N, Fayyad DM. Influence of intracanal cryotherapy on postendodontic pain and interleukin-6 expression using different irrigation protocols: A randomized clinical trial. *Saudi Endod J* 2021;11:246-51
25. Mohammadi Z, Soltani MK, Shalavi S, Asgary S. A review of the various surface treatments of NiTi instruments. *Iran Endod J* 2014;9:235-40.
26. Ruiz-Sanchez C, Faus-Matoses V, Alegre-Domingo T, et al. An in vitro cyclic fatigue resistance comparison of conventional and new generation nickel-titanium rotary files. *J Clin Exp Dent* 2018;10:805-9.
27. Vinothkumar TS, Miglani R, Lakshminarayanan L. Influence of deep dry cryogenic treatment on cutting efficiency and wear resistance of nickel-titanium rotary endodontic instruments. *J Endod* 2007;33:1355-8
28. Vinothkumar TS, Kandaswamy D, Prabhakaran G, Rajadurai A. Effect of dry cryogenic treatment on Vickers hardness and wear resistance of new martensitic shape memory nickel-titanium alloy. *Eur J Dent* 2015;9:513-7.
29. Bahcall J, Johnson B, Xie Q, et al. Introduction to vital pulp cryotherapy. *Endod Pract US* 2019;1:14.
30. Galler KM, Buchalla W, Hiller KA, et al. Influence of root canal disinfectants on growth factor release from dentin. *J Endod.* 2015;41:363-368.
31. Bahcall J, Xie Q, Baker M, et al. New approaches in endodontics: cryotherapy for vital pulp treatment. *Decisions in Dentistry.* 2019;5:14-18.