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CRYOTHERAPY IN ENDODONTICS: A REVIEW

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Endodontic post- operative pain is a common concern following root canal treatment, and it can significantly impact the patient's quality of life. Various strategies have been implemented to minimize or alleviate post- operative pain, including the use of non-steroidal anti- inflammatory drugs (NSAIDs), opioids, and local anesthetics. However, these approaches may have limitations, such as potential side effects and patient discomfort or allergy. Therefore, there is a need for alternative techniques that can effectively manage pain while ensuring patient's comfort and safety.

Recently, cryotherapy has emerged as a potential effect on reducing post-operative pain in various medical fields, including dentistry. It involves the use of cold temperatures to induce therapeutic effects. The application of cryotherapy in dentistry has shown promising results in reducing pain, inflammation, and swelling after oral surgical procedures. However, its efficacy in endodontics have not been extensively explored.

One aspect of interest is the effect of cryotherapy on endodontic post-operative pain and its potential impact on the level of substance P. Substance P is a neuropeptide involved in pain transmission, and its release is associated with the perception of pain. By modulating the release or activity of substance P, cryotherapy could potentially influence the level of pain experienced by patients following endodontic procedures.

1. Pain

The main purpose of endodontic treatment is to provide 3D- hermetic seal to the root canal system, after eliminating any microorganisms by preforming chemo-mechanical disinfection. The aim is to prevent the sequelae of inflamed pulp and allow an existing lesion to heal. [1] Endodontic post-operative pain is one of the common side effects that encounters huge concern to the clinician and the patient. Postoperative pain or "flare up" as it is referred to by this term is defined as "unpleasant sensory and emotional experience associated with actual or potential tissue damage". [1]

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Based on literature postoperative pain prevalence ranges from 3% to 58%, which gradually decreases over time. Having a close look to the reasons causing post-operative pain we will find that it is multifactorial. It depends on systemic health condition, age, gender, pulp and periapical statues, preparation and types of instruments used, irrigation and obturation technique. It is also influenced by failure to access extra or accessory canals, apical extrusion of debris and not establishing apical patency during endodontic treatment.[1,2]

Presence of preoperative pain is one of the critical reasons of occurrence of post-operative pain as it was found that patients with pre-operative pain are five times more likely to suffer from post-operative pain [3]. Pain could be evaluated by questionnaires and rating scales; more than one type of rating scale is available. Numeric scale, visual analogue scale and categorization scale. Visual analogue scale (VAS) is one of the most common scales used among them. A 10-centimeter line indicates severity of pain where 0 refers to no pain and 10 refers to worst pain ever.[2,4]

Because evaluating pain through rating scales is subjective and patients may tend to exaggerate, it's preferred to evaluate pain through level of neuropeptides in gingival crevicular fluid (GCF) or apical fluid. According to literature, symptomatic teeth with pulpitis releases inflammatory mediators which evoke blood flow and pro- inflammatory neuropeptides such as substance P. [5] For a clinician to address patient's complain a thorough diagnosis should be held with proper history as pain can manifest itself in many ways. Without knowing the true underlying cause of pain no relieving approach will be effective. Dental pain could be relieved by pharmacological and non-pharmacological strategies.

Pharmaceutical strategies for pain management often begin with premedication. This approach involves the administration of analgesics prior to the procedure to preemptively manage pain. The delivery of these drugs can be achieved through either an intramuscular or intra-oral route. The intra-oral approach is more commonly used, with the drug being administered anywhere from 20 minutes to 3 hours before the procedure.[6] The second strategy involves the use of analgesics, specifically non-opioids, which are typically used for dental pain. NSAIDs and aspirin are the most common drugs used in this context. Ibuprofen, at a dose of 400mg, is considered the safest over-the-counter drug used for this purpose. Alternatively, acetaminophen is used when aspirin is contraindicated. These strategies together form the cornerstone of pharmaceutical pain management in dentistry.[7,8]

Behavioral management and audio analgesia are two non-pharmaceutical approaches to pain management. Anxiety, which can decrease the pain threshold, is common among patients who are nervous about medical procedures, especially when they are not fully informed about the procedure. By providing information and a sense of control, we can help reduce their anxiety, thereby increasing the pain threshold [9].

Audio analgesia, on the other hand, involves the use of music or noise to relieve pain. During treatment sessions, patients are given earphones and a control box, allowing them to increase the volume of the music if they feel any discomfort [6]. Home remedies also play a significant role in pain management. For instance, clove has been found to be effective in relieving pain and discomfort. Patients often chew clove on the side where they feel pain, and it typically takes about 10 minutes to relieve their pain. Additionally, tannic acid, which is found in black tea bags, is very effective in relieving pain and reducing swelling. It is recommended to bite on the tea bag for about 15 minutes.[6]

Cold application, or cryotherapy, is another strategy used for pain relief, especially after surgeries. Applying ice packs decreases blood flow by causing vasoconstriction, which results in decreased inflammatory discomfort. [6]. Cryotherapy is a simple therapeutic process used in medicine and sports medicine to relieve pain, control edema, and decrease muscle spasms. It's a testament to the variety of non-pharmaceutical approaches available for pain management. [10].

2. Cryotherapy

The nomenclature "cryosurgery" originates from the Greek word "kryos," signifying "frost" or "iciness." The act of applying extreme cold to induce the controlled destruction of unwanted tissue is denoted by the term "cryosurgery." This specific treatment modality utilizes local cryogenic temperatures to achieve targeted tissue ablation.[1] While cryotherapy is conventionally understood as the therapeutic application of low temperatures, a more nuanced perspective recognizes it as a process of heat extraction.[11] Due to minimal discomfort, negligible bleeding, and minimal to no scarring, cryotherapy exhibits high patient acceptability.[3] Cryotherapy presents compelling clinical advantages due to its inherent user-friendliness, minimal impact on the inorganic structure of bone tissue, and exceptionally low incidence of infection. Additionally, unlike radiotherapy or chemotherapy, it allows for repeated applications without permanent side effects and boasts superior localization of action.[12] For individuals contraindicated for surgery due to geriatric considerations or underlying medical issues, this technique offers a valuable alternative. The therapeutic application of cryotherapy is limited by the challenges of uncontrolled tissue swelling, lack of fine-tuned depth control, and significant dependence on the operator's skill and experience.[2]

2.1 History

The therapeutic application of localized cold, documented as early as ancient Egypt, served the dual purpose of pain relief and tissue ablation. Notably, during the Franco-Prussian War, this cryogenic property facilitated the surgical removal of injured appendages[5] John Hunter, in 1777, described the local tissue response to cryotherapy as characterized by necrosis, vascular stasis, and subsequent optimal healing. This highlights the initial understanding of tissue destruction and subsequent regenerative processes initiated by cold exposure. James Arnott, in 1851, pioneeringly utilized a salt and ice mixture to freeze and ablate malignant breast tumors. This marked a significant milestone in the practical application of cryosurgery for oncological purposes. Campbell White, in 1899, became the first to employ cryogenic agents in clinical settings. He successfully treated warts and other dermatological conditions with liquid air, demonstrating the versatility of cryotherapy for addressing various skin lesions.[1]

In 1908, A.W. Pusey coined the term "cryotherapy" to refer to the treatment of skin lesions with intense cold. Presently, cryosurgery freezes diseased tissues to death, while cryotherapy cools the body's surface without damaging tissue. In Japan, Yamauchi and his colleagues opened the world's first cryogenic temperature chamber in 1978.(Farah & Savage, 2006) The magnitude of tissue temperature alteration and subsequent biophysical responses are governed by a multi-factorial interplay of parameters. These include the pre-existing temperature differential between the applied thermal modality (heat or cold) and the target tissue, the duration of exposure, the intrinsic thermal conductivity of the tissue itself, and the specific characteristics of the employed agent. Ultimately, the therapeutic implications of this approach in human tissues manifest through the resulting localized temperature change.[8]

The effectiveness of cryotherapy, both in terms of tissue cooling and the body's response, is influenced by four key factors [8,13,14]:

1. Temperature difference between target tissue and cryotherapy (Fourier's Law)

Fourier's law, which states that "per unit area the transfer of heat in a given direction is proportional to the temperature gradient,". this implies that a lower-temperature cryotherapy modality provides more heat energy transfer opportunities, which should subsequently lead to a lower Tsk.

2. Exposure duration
3. Tissue characteristics: The thermal conductivity and specific heat capacity of the treated area determine how easily heat is transferred within the tissue, impacting cooling depth and rate.
4. Cooling agent characteristics: The thermodynamic properties of the chosen agent [10].

2.2 Cryotherapy Principles

Cryotherapy relies on a scientific principle called Joule-Thomson expansion. This essentially means that when a substance moves from a high-pressure zone to a lower-pressure one, its molecules expand and lose energy, resulting in a temperature drop 2. The rapid release of nitrous oxide from the high-pressure cryoprobe environment to the lower-pressure cryotip triggers an adiabatic expansion, leading to a pronounced temperature decrease and subsequent tissue freezing. Cryotherapy employs a multistep protocol involving this rapid freeze-thaw cycle, with repetition further potentiating tissue destruction through cellular disruption 12. Cryotherapy evokes a cascade of biophysical changes, including vasoconstriction (constriction of blood vessels), which diminishes hemorrhage and alleviates secondary hypoxic injury, inflammatory response, and edema formation through decreased fluid extravasation. Further promoting tissue repair. Sustained tissue temperature reduction below 15°C initiates a biphasic vasoconstriction-vasodilation response known as the "hunting phenomenon." Initial vasoconstriction minimizes heat loss but necessitates a compensatory mechanism. Subsequently, vasodilation mediated by the release of "substance H," a histamine-like molecule, rewarms the tissue. This influx of warm blood triggers another round of vasoconstriction, resulting in an oscillating pattern of blood flow characterized by alternating phases of constriction and dilation. This adaptive cycle ensures continued tissue perfusion despite prolonged cold exposure. Cryotherapy induces peripheral nerve hypofunction via modulation of transmembrane ionic currents, leading to altered conduction velocity and synaptic transmission efficacy. Furthermore, it facilitates alpha-motor neuron excitability while dampening gammamotor neuron activity, resulting in a transient reduction in spastic muscle tone [8].

2.3 The basic physiological reactions that occur with heat or cold application:

Following the application of heat or cold application, local blood flow can either increase or decrease, and neural receptors can be stimulated or inhibited in the skin and subcutaneous tissues. Additionally, there can be a change in the metabolic activity of the cells [15].

In accordance with Van't Hoff's principle, cryotherapy induces vasoconstriction and suppresses cellular metabolic activity via reduced biochemical reaction rates. This cascade of effects minimizes tissue injury by decreasing cellular oxygen consumption and mitigating free radical generation. Vasoconstriction exerts antiedemic action by decreasing interstitial fluid extravasation. Additionally, cold application directly inhibits nociceptor activity at nerve terminals, leading to analgesia. The maximal degree of vasoconstriction occurs at 15°C. Reduced body temperature progressively impairs peripheral nerve conduction velocity. At 7°C, myelinated A-delta fibers, responsible for fast pain transmission, undergo complete deactivation, while nonmyelinated C-fibers, mediating slower nociceptive and thermal sensations, cease function at 3°C. These findings were established by Franz and Iggo [11].

2.4 Cryotherapy in Medicine

Cryotherapy, also known as cryosurgery, employs the destructive power of freezing and thawing to eradicate unwanted tissues. This technique finds potent applications in medicine, from eliminating various skin lesions and cervical precancers to tackling certain prostate carcinomas. Additionally, cryotherapy encompasses the therapeutic use of ice or cold packs to combat inflammation following injuries [16].

2.5 Cryotherapy in Dentistry

Though cold application is a common post-surgical pain management tool in dentistry, its efficacy, particularly in endodontics, lacks strong confirmation. The existing literature delves into potential mechanisms and advantages, but definitive evidence remains elusive. Crucially, standardization of factors like timing, duration, application technique, and cooling agent is paramount for robust assessment. Encouragingly, recent studies exploring intracanal cryotherapy as a post-endodontic pain management strategy present a promising path for further investigation.[17,18]

2.5.1 Technique for Using Cryotherapy in a Root Canal

For precise tissue treatment, the dental cryotherapy device utilizes a controlled flow path connected to a source of cryogenic fluid. A slender, adaptable needle (0.25 mm), designed to navigate the narrow confines of the root canal, delivers the cold liquid directly to the targeted area [19].

2.5.2 Cryotherapy in Endodontics

2.5.2.1 Effect on Post-Endodontic Pain

Vera et al. were the first to explore cryotherapy's potential in endodontics. Their protocol utilized a final irrigation with 2.5°C saline solution augmented by Endovac, maintained for 5 minutes. Subsequently, they employed precise measurements to evaluate the temperature changes induced on the external root surfaces of extracted teeth. They suggest that exceeding a 10°C reduction in external root surface temperature for a duration of 4 minutes, facilitated by their cryotherapy protocol, may be sufficient to induce localized anti-inflammatory effects within the peri-radicular tissues. This study confirmed that cryotherapy significantly lowered the incidence of postoperative pain and medication use in patients undergoing root canal treatment for necrotic pulp and symptomatic apical periodontitis[18].

Keskin et al. further elucidated the analgesic potential of cryotherapy in endodontics. Their investigation evaluated the efficacy of final irrigation with 2.5°C cold saline via a side-vented, positive-pressure NaviTip needle (31-gauge) in single-visit root canal treatments of vital teeth. To isolate the cryotherapy effect, they opted for a non-negative apical pressure technique. Their findings corroborated the pain-reducing effect of cryotherapy in vital teeth, suggesting its utility for postoperative pain management in single-visit root canal procedures. However, the study's generalizability is hindered by the undifferentiated inclusion of cases with and without apical periodontitis, potentially confounding the observed pain reduction [17].

Study demonstrated that combining intracanal cryotherapy, involving the application of extreme cold within the root canal, with negative pressure irrigation effectively eliminated post-operative pain after single-visit root canal treatment 20. Nevertheless, another study found that controlling post-endodontic pain could be achieved by finalizing the canal flushing with cold or room temperature saline [21].

Bazaid et al. (2018) evaluated the analgesic efficacy of intracanal cryotherapy using 27gauge side-vented needle delivery of cold saline as a final irrigant in single-visit root canal treatments for irreversible pulpitis. Their results demonstrated that this approach markedly reduced postoperative pain in patients diagnosed with apical periodontitis, characterized by inflammation at the root tip. However, no significant pain reduction was observed in patients lacking apical periodontitis [22].

A previous study suggests intracanal cryotherapy offers a promising immediate pain relief solution after root canal procedures. Although its effect weakens over time, it significantly reduces discomfort within the crucial first 24 hours, offering substantial patient benefit [23]. In a recent systematic review, report that intracanal cryotherapy application leads to a statistically significant reduction in postoperative endodontic pain at 6 and 24 hours following root canal procedures [24].

2.5.2.2 Effect of Cryotherapy on Enterococcus faecalis

With its multifaceted array of virulence factors, Enterococcus faecalis stands as the most prevalent and recalcitrant pathogen in persistent root canal infections. These factors endow the bacterium with a remarkable ability to resist eradication strategies within the complex anatomy of the canals [25].

In accordance with Mandras et al, cryo-instrumentation implemented subsequent to NaOCl irrigation exhibited a statistically significant decrease in root canal bacterial count compared to NaOCl alone, albeit failing to completely eliminate Enterococcus faecalis. The cryogenic fluid, liquid nitrogen, employed with controlled treatment duration, can achieve desired depth penetration and induce immediate bacterial cell freezing, leading to cryodestruction [26]. Microorganisms suffer during freeze-thaw cycles due to a cascade of events. The initial break in their protective barriers (membranes or cell walls) triggers the leakage of vital molecules, ultimately rendering proteins dysfunctional, which collectively compromises cellular integrity and survival [27]. Employing a cyclic freezing and thawing regimen (30 seconds cryogenic exposure, 30 seconds rewarming, and subsequent 30 seconds cryogenic exposure) utilizing liquid nitrogen, Yamamoto and Harris observed a significant decrease in in vitro bacterial population compared to baseline [28].

2.5.2.3 Cryotherapy effect in vital pulp therapy

Direct or indirect carious exposure necessitates pulpal bleeding control during vital pulp therapy. Shaved sterile water ice at 0°C (vital pulp cryotherapy) has emerged as a potential intervention. The ice is applied topically to the exposed pulpal tissue and the entire tooth. Sterile shaved ice, prepared by freezing sterile water and subsequent processing in an ice shaving device, was applied to the vital pulpal tissue for approximately one minute. Following gentle removal of the ice with a high-speed suction, the exposed area was thoroughly rinsed with 17% ethylenediaminetetraacetic acid (EDTA) solution [29]. In the context of promoting dentin regeneration and pulp healing, EDTA irrigation presents a compelling alternative to sodium hypochlorite. While the latter excels at disinfection, recent studies suggest EDTA possesses unique properties that actively stimulate tissue repair. EDTA's efficacy stems from its ability to chelate calcium ions, a crucial component of dentin matrix. This chelation process triggers the release of growth factors from the dentin itself, promoting crucial cellular activities like matrix secretion, odontoblastic differentiation (the development of mature dentin-forming cells), and even tertiary dentin formation (a reparative layer deposited within the pulp chamber) [30,31]. Following application of cryotherapy with sterile shaved ice and EDTA irrigation to the exposed or indirectly exposed pulp tissue, a bio-ceramic material was placed as a protective barrier. This was then further sealed with a permanent restoration. Remarkably, within two weeks, all treated teeth reported no symptoms, and this positive outcome persisted for the entire 12-18-month follow-up period. The teeth remained vital, asymptomatic, and functional, indicating successful pulp preservation. However, despite these promising short-term findings, further research with larger sample sizes is crucial to definitively establish the long-term efficacy and predictability of this novel therapeutic approach [22].

2.5.2.4 Cryotherapy effect on endodontic instruments

Traditionally, cryogenic treatment of metals, particularly superelastic NiTi and stainless steel, has been employed during manufacturing to enhance their surface hardness and thermal stability. This practice involves exposing the metal to subzero temperatures followed by a controlled warming to ambient temperature [32]. The classification of cryogenic treatment based on treatment temperature distinguishes between shallow and deep approaches. Deep cryogenic treatment demonstrably offers greater advantages compared to the conventional shallow method [33].

Two studies investigated cryogenic treatment for stainless steel endodontic instruments. Both found no significant changes in cutting efficiency before or after treatment, nor in wear resistance [34] [35]. Concisely, cryogenic treatment seems ineffective for enhancing performance or durability of stainless-steel endodontic instruments.

Investigating the potential benefits of cryogenic treatment on NiTi endodontic instrument performance, a study reported a statistically significant increase in microhardness. However, this change failed to manifest as a discernible improvement in cutting efficiency when assessed under clinical conditions[36]. While this study suggests limitations on the influence of cryogenic treatment on super elastic NiTi files, Vinothkumar et al. reported a clear improvement in their cutting efficiency without impacting wear resistance, highlighting the potential benefits of this technique [37]. Variations in both technique and duration of cryogenic treatment might be responsible for the observed disparities. The later study implemented a 24-hour dry deep cryogenic process, in contrast to the prior brief immersion in liquid nitrogen for 10 minutes [38].

Vinothkumar, et al. investigated the use of supplementary deep cryogenic treatment (DCT) to elevate the martensite volume and, consequently, improve cyclic fatigue resistance and cutting efficiency in novel, small-diameter martensitic NiTi alloys. Results indicated a remarkable 13% increase in cyclic fatigue resistance for specimens subjected to a 24-hour DCT soak, compared to a marginal 1% increase for a 6-hour soak. Notably, cutting efficiency remained largely unaffected by DCT duration [39].

2.5.3 Cryotherapy effect as local Anesthetic

Despite its established role as the standardized injection technique for regional anesthesia of mandibular molar teeth, the inferior alveolar nerve block (IANB) exhibits limitations in providing reliable pulpal anesthesia, particularly in patients diagnosed with symptomatic irreversible pulpitis (SIP), a condition characterized by significant tooth pain due to advanced inflammatory processes within the dental pulp. While preoperative intraoral cryotherapy following inferior alveolar nerve block (IANB) failed to achieve consistent profound pulpal anesthesia in nearly half of mandibular molars with symptomatic irreversible pulpitis (SIP), its simplicity and low cost suggest potential as an adjunctive method to improve IANB success rates in this population. Cryotherapy modulates pain through a multipronged approach. It directly influences nociceptor function by suppressing chemical mediator release and lowering the activation threshold and conduction velocity of pain signals. This cascade of effects effectively inhibits pain transmission, culminating in local anesthesia [15].

Vera et al. held a randomized clinical trial to assess the effect irrigation with cold saline on post-operative pain in patients diagnosed with pulp necrosis and symptomatic apical periodontitis. Total of 210 patients were enrolled all diagnosed with necrotic uni-radicular teeth with periapical periodontitis. All recorded on VAS above 7. Patients were randomly allocated in control or experimental group. Experimental group received final irrigation with 20 mL cold 2.5°C saline delivered to working length by the use of Endo-Vac for 5 minutes. Results showed that control group patients were presented with higher incidence and intensity of pain and needed to take analgesics [18].

Vieyra et al. tried to assess the reduction of post-operative pain after the use of three different irrigation regimens with different temperatures. Total of 240 patients were enrolled in this study, they were presented with vital pulp designated to conventional root canal treatment for prosthetic reasons. 80 of the complete sample were randomly allocated to one of the 3 groups. Group 1 received final flush with cold (4°C) 17 % EDTA and distilled saline, Group 2 received final flush with cold (2.5°C) 17% EDTA and distilled saline and for the control group they received same irrigation regimen but in room temperature. Results showed that patients in groups 1 and 2 suffered significantly less pain in compare to the control group and needed fewer analgesics. On the other hand, patients in control group suffered higher intensity of pain and for longer duration [40].

Keskin et al. investigated the level of inflammatory biomarkers in periapical exudates of asymptomatic apical periodontitis mandibular premolars and evaluate post-operative pain in correlation to biomarkers. 44 patients were enrolled in the study aged between 18-35 years and diagnosed with asymptomatic apical periodontitis. Root canal treatment was held in two visits, baseline periapical exudate samples were taken then patients were assigned to control group were final flush with distilled water at room temperature or cryotherapy group were final flush with distilled water at 2.5 °C. Canals were dressed with calcium hydroxide between visits. In the second visit calcium hydroxide was removed with passive ultrasonic irrigation and second periapical exudate sample was taken. Results showed positive relation between post-operative pain and IL-1β and PGE2. Cryotherapy group showed less levels of IL-1β, IL-2 and IL-6 levels compared with the control group. Also, intracanal cryotherapy was effective in reducing post- operative pain [41].

REFERENCES

1. Bansal A, Jain S, Gupta S. Cryosurgery in the treatment of oro-facial lesions. Vol. 23, Indian Journal of Dental Research. 2012. p. 297.
2. Farah CS, Savage NW. Cryotherapy for treatment of oral lesions. Vol. 51, Australian Dental Journal. 2006. p. 2–5.
3. Emmings FG. The use of liquid nitrogen cryotherapy in the management of locally aggressive bone lesions. Journal of Oral and Maxillofacial Surgery. 1993 Mar;51(3):274.
4. Salmassy DA, Pogrel MA. Liquid nitrogen cryosurgery and immediate bone grafting in the management of aggressive primary jaw lesions. Journal of oral and maxillofacial surgery. 1995;53(7):784–90.
5. Leopard PJ. CRYOSURGERY, AND ITS APPLICATION TO ORAL SURGERY. Vol. 13, British Journal of Oral Surgery. 1975.
6. Zehravi M, Maqbool M, Ara I. An Update on Pain Control in Conservative Dentistry and Endodontics: A Review. Indian J Nutr Diet [Internet]. 2022 Feb 25;59(1):114–25. Available from: https://doi.org/10.21048/ijnd.2022.59.1.28600
7. Zehravi M, Maqbool M, Ara I. An Update on Pain Control in Conservative Dentistry and Endodontics: A Review. Indian J Nutr Diet. 2022;114–25.
8. Hubbard TJ, Denegar CR. Does cryotherapy improve outcomes with soft tissue injury? J Athl Train [Internet]. 2004;39(3):278–9. Available from: www.journalofathletictraining.org
9. Edwards RR, Doleys DM, Fillingim RB, Lowery D. Ethnic Differences in Pain Tolerance: Clinical Implications in a Chronic Pain Population. Psychosom Med [Internet]. 2001;63(2):316–23. Available from: https://doi.org/10.1097/00006842-200103000-00018
10. Selfe J, Hardaker N, Whitaker J, Hayes C. Article in Thermology International [Internet]. 2009. Available from: https://www.researchgate.net/publication/232947219
11. Belitsky RB, Odam SJ, Hubley-Kozey C. Evaluation of the Effectiveness of Wet Ice, Dry Ice, and Cryogen Packs in Reducing Skin Temperature.
12. Salmassy DA, Pogrel MA. Liquid Nitrogen Cryosurgery and Immediate Bone Grafting in the Management of Aggressive Primary Jaw Lesions [Internet]. Vol. 53, J Oral Maxillofac Surg. 1995. Available from: https://doi.org/10.1016/0278-2391(95)90333-X

13. Jutte LS, Merrick MA, Ingersoll CD, Edwards JE. The relationship between intramuscular temperature, skin temperature, and adipose thickness during cryotherapy and rewarming. Arch Phys Med Rehabil [Internet]. 2001;82(6):845–50. Available from: https://doi.org/10.1053/apmr.2001.23195

14. Malanga GA, Yan N, Stark J. Mechanisms and efficacy of heat and cold therapies for musculoskeletal injury [Internet]. Vol. 127, Postgraduate Medicine. Taylor and Francis Inc.; 2015. p. 57–65. Available from: https://doi.org/10.1080/00325481.2015.992719

15. Gade V, Barfiwala D, Asani R, Gawande R, Gade J. Cryotherapy: An Emerging Trend in the Field of Endodontics. International Journal of Drug Research and Dental Science [Internet]. 2:2020. Available from: https://doi.org/10.36437/ijdrd.2020.2.3.J

16. Bouzigon R, Grappe F, Ravier G, Dugue B. Whole- and partial-body cryostimulation/cryotherapy: Current technologies and practical applications. Vol. 61, Journal of Thermal Biology. Elsevier Ltd; 2016. p. 67–81.

17. Keskin C, Özdemir Ö, Uzun İ, Güler B. Effect of intracanal cryotherapy on pain after single-visit root canal treatment. Australian Endodontic Journal [Internet]. 2017 Aug 1;43(2):85–90. Available from: 10.1111/aej.12175

18. Vera J, Ochoa J, Romero M, Vazquez-Carcaño M, Ramos-Gregorio CO, Aguilar RR, et al. Intracanal Cryotherapy Reduces Postoperative Pain in Teeth with Symptomatic Apical Periodontitis: A Randomized Multicenter Clinical Trial. J Endod [Internet]. 2018 Jan 1;44(1):4–8. Available from: 10.1016/j.joen.2017.08.038

19. Mohammadi Z, Shalavi S, Jafarzadeh H. C.E. Credit. Cryotherapy in Endodontics: A Critical Review. J Calif Dent Assoc. 2022 Dec 1;50(12):727–32.

20. Al-Nahlawi T, Hatab TA, Alrazak MA, Al-Abdullah A. Effect of intracanal cryotherapy and negative irrigation technique on postendodontic pain. Journal of Contemporary Dental Practice. 2016;17(12):990–6.

21. Alharthi AA, Aljoudi MH, Almaliki MN, Almalki MA, Sunbul MA. Effect of intra-canal cryotherapy on post-endodontic pain in single-visit RCT: A randomized controlled trial. Saudi Dental Journal. 2019 Jul 1;31(3):330–5.

22. Bazaid DS, Kenawi LMM. The Effect of Intracanal Cryotherapy in Reducing Postoperative Pain in Patients with Irreversible Pulpitis: A Randomized Control Trial. Int J Health Sci Res. 2018;8(2).

23. Sadaf D, Ahmad MZ, Onakpoya IJ. Effectiveness of Intracanal Cryotherapy in Root Canal Therapy: A Systematic Review and Meta-analysis of Randomized Clinical Trials [Internet]. Vol. 46, Journal of Endodontics. Elsevier Inc.; 2020. p. 1811-1823.e1. Available from: https://doi.org/10.1016/j.joen.2020.08.022

24. Pena Braga Monteiro L, Yasmin Reis Guerreiro M, de Castro Valino R, Baraúna Magno M, Cople Maia L, Melo da Silva Brandão J. Effect of intracanal cryotherapy application on postoperative endodontic pain: a systematic review and metaanalysis. Available from: https://doi.org/10.1007/s00784-020-03693-8

25. Mohammadi Z, Dummer PMH. Properties and applications of calcium hydroxide in endodontics and dental traumatology. Vol. 44, International Endodontic Journal. 2011. p. 697–730.

26. Mandras N, Allizond V, Bianco A, Banche G, Roana J, Piazza L, et al. Antimicrobial efficacy of cryotreatment against Enterococcus faecalis in root canals. Lett Appl Microbiol. 2013;56(2):95–8.

27. Yamamoto SA, Harris LJ. The effects of freezing and thawing on the survival of Escherichia coli O157:H7 in apple juice [Internet]. Vol. 67, International Journal of Food Microbiology. 2001. Available from: www.elsevier.nlrlocaterijfoodmicro

28. Keskin C, Sariyilmaz E, Keleş A, Güler DH. Effect of intracanal cryotherapy on the fracture resistance of endodontically treated teeth. Acta Odontol Scand. 2019 Feb 17;77(2):164–7.

29. Bahcall James, Xie Qian, Baker Mark, Weeks Steve. Introduction to vital pulp Cryotherapy. Endodontic Practice US. 2019;14(1).

30. Casagrande L, Demarco FF, Zhang Z, Araujo FB, Shi S, Nör JE. Dentin-derived BMP-2 and odontoblast differentiation. J Dent Res. 2010 Jun;89(6):603–8.

31. Galler KM, Buchalla W, Hiller KA, Federlin M, Eidt A, Schiefersteiner M, et al. Influence of root canal disinfectants on growth factor release from dentin. J Endod. 2015 Mar 1;41(3):363–8.

32. Bensely A, Senthilkumar D, Mohan Lal D, Nagarajan G, Rajadurai A. Effect of cryogenic treatment on tensile behavior of case carburized steel-815M17. Mater Charact. 2007 May;58(5):485–91.

33. Moore K, Collins DN. Cryogenic treatment of three heat-treated tool steels. Key Eng Mater. 1993;86:47–54.

34. Vinothkumar TS, Miglani R, Lakshminarayananan L. Influence of Deep Dry Cryogenic Treatment on Cutting Efficiency and Wear Resistance of Nickel-Titanium Rotary Endodontic Instruments. J Endod. 2007 Nov;33(11): 1355–8.

35. Berls RW. Effect of cryogenic tempering on the wear resistance of two types of stainless steel files. . Journal of Endodontics . 2003;300(29).

36. Kim JW, Griggs JA, Regan JD, Ellis RA, Cai Z. Effect of cryogenic treatment on nickel-titanium endodontic instruments. Int Endod J. 2005 Jun;38(6):364–71.

37. Vinothkumar TS, Miglani R, Lakshminarayananan L. Influence of deep dry cryogenic treatment on cutting efficiency and wear resistance of nickel–titanium rotary endodontic instruments. J Endod. 2007;33(11):1355–8.

38. Fayyad DM, Abdelsalam N, Hashem N. Cryotherapy: A New Paradigm of Treatment in Endodontics [Internet]. Vol. 46, Journal of Endodontics. Elsevier Inc.; 2020. p. 936–42. Available from: 10.1016/j.joen.2020.03.019

39. 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(4):513–7.

40. Vieyra JP, J Enriquez FJ, Acosta FO, Guardado JA. Reduction of postendodontic pain after one-visit root canal treatment using three irrigating regimens with different temperature. Niger J Clin Pract. 2019;22(1).

41. Keskin C, Aksoy A, Kalyoncuoğlu E, Keleş A, İlik AA, Kömeç O, et al. Effect of intracanal cryotherapy on the inflammatory cytokine, proteolytic enzyme levels and post-operative pain in teeth with asymptomatic apical periodontitis: A randomized clinical trial. Int Endod J [Internet]. 2023;56(8):932–42. Available from: https://doi.org/10.1111/iej.13937