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Cryotherapy: A paragon for endodontic therapy

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Abstract
Patients undergoing endodontic treatment may develop post-endodontic pain, leading to pain and inflammation. Cryotherapy is a remedial procedure widely used in the field of medicine and dentistry, considered to be effective at reducing edema, pain, bleeding and inflammation. In endodontics, it is relatively new and may be beneficial in the prevention and treatment of post-endodontic pain. Additionally, cryogenic treatment is considered a key factor in strengthening rotary NiTi endodontic files. Further well-designed clinical studies will be conducted to establish the effective use of cryotherapy in the control of post-endodontic pain in clinical practice. This article describes the concept of cryotherapy and its potential clinical implications in endodontics.

Keywords: Cryotherapy, cold application, post-endodontic pain, rotary endodontic NiTi files

Introduction
Preventing and managing post-endodontic pain is an essential step of Root canal therapy. The prevalence of pain during and after endodontic therapy ranges between 3-58% [1, 2]. In the field of endodontics, cryotherapy has been proven to help to reduce postoperative pain and inflammation. The term cryotherapy comes from the Greek word "cryos", meaning "cold". The concept of cryotherapy not only causes cooling of the target tissue but rather extracts heat from the tissue of elevated temperature to the subject of lower temperature [4]. Cryotherapy can refer to the direct application of ice, ice chips, melted ice water, ice massage, coolant sprays, whirlpools, ice baths or a pre-packaged chemical ice pack at the site of injury to reduce pain and inflammation [5].

Cryotherapy is widely used as a curative treatment in medicine and dentistry and is believed to be effective in reducing edema, pain, bleeding and inflammation [3]. Application of this freezing therapy by using a mixture of salt and ice to destroy cancerous growths was first reported and demonstrated by James Arnott in 1851 [6].

In medicine, the Cryosurgery form of cryotherapy is used to remove, destroy and treat the cancerous and pre-cancerous lesions of the skin, uterine cervix tissues, and prostate cancer. Also, Cryoneurotomy is used to produce an extended, but reversible, nerve block in the management of uncontrollable neurogenic pain in the pre-auricular area [7].

Cryotherapy has been used in dentistry after intraoral excisional surgical procedures, periodontal surgery, extractions, and implant placement and showed positive effects in reducing swelling, pain and arthritis associated with temporomandibular joint disorders [4, 8].

Endodontics uses cryotherapy during vital pulp therapy, nerve block, periradicular surgeries, and root canal treatment to minimize preoperative, and postoperative pain and inflammation. Cryogenic treatment plays a vital role in improving the strength of rotary endodontic files, which offer enhanced cyclic fatigue resistance and thus, reduce potential file separation. Also, it has a major impact on improving the cutting efficiency of superelastic NiTi endodontic files. More recently, cryotherapy in combination with bioceramic materials has been shown to be useful as an adjunct to hemostasis in vital pulp therapy [4].

Even though cryotherapy is widely used in medicine and dentistry, research on its specific usage in endodontics is still sparse in the literature. Hence, the objective of this pioneer review is to understand the concept of cryotherapy in endodontics and to sketch out a prospective future for the application of cryotherapy in endodontics.

Cryotherapy physiology

The basic physiological responses are [4, 9]

1. Temperature change.
2. Changes in local blood flow.
3. Nerve stimulation or inhibition of cutaneous neuroreceptors.
4. Cellular tissue metabolic activity.

Temperature changes in tissue treated with cryotherapy are dependent on the temperature difference between the tissue and the coolant, the size and shape of the cold pack, the duration of cooling, the thickness of the tissue, the anatomical location of the intended cryotherapy, and mode of therapy [5, 10].

Hunting response occurs when cold is applied to the tissue for more than 15 minutes causing vasoconstriction of blood vessels followed by cold-induced vasodilatation[11]. Vasoconstriction reduces vascular permeability, thereby reducing the amount of fluid that exits the periapical tissue as exudate or transudate, resulting in a reduction of tissue edema which is commonly associated with periapical tissue after biomechanical preparation and thus reduces swelling[5]. Postsurgical application of cold delays local blood flow and counteracts the rebound phenomenon that occurs after the application of local anesthetics, including vasoconstrictors. Therefore, the application of cold to lower the temperature of the surgical site has been suggested as a good postoperative supportive therapy [8].

Neurologic effect on cryo-treated tissue, analgesia is closely related to the nerve conduction velocity of the nociceptive sensory nerve fibers [12, 13]. Cold reduces nerve conduction velocity and provides an analgesic effect. According to Franz and Iggo [10], complete inactivation of myelinated nerve fibers also known as A-delta fibers occurs at ~7 °C while unmyelinated fibers also known as C fibers are completely inactivated at ~3 °C. The larger myelinated A fibers provide faster sensory input resulting in pain relieving effect of cryotherapy by temporarily closing the gate and impeding the transmission of the unendurable impulses of the unmyelinated C fibers stated by the gate control theory which is considered to be responsible for the pain control [14].

Furthermore, cold application releases neuro-effective agents such as endorphins that bind to opioid receptors in the medullary dorsal horn and modulate nociceptive transmission to the central nervous system inducing an analgesic effect [15]. Also, the application of cold results in cold-induced neuropraxia by inhibiting the threshold potential of tissue nociceptors [16]. Thus, a combination of a decreased release of chemical mediators of pain and inhibition of the propagation of neural pain signals due to cooling causes an analgesic effect.

Effect of cryotherapy on cellular tissue metabolic activity, consumption of oxygen is more in injured tissue resulting in tissue hypoxia and necrosis. Cryotherapy decreases tissue blood flow and cell metabolism by more than 50% and reduces the rate of biochemical reactions, which minimizes the oxygen demand of cells and prevents tissue hypoxia and further tissue injury [4, 17].

Implications of cryotherapy during endodontic procedures

1. Post-endodontic pain management

Pain is not a simple sensation but rather a complex neurobehavioral event involving physical or emotional behavior and an unpleasant situation. Managing postoperative pain is critical in endodontics, even after adherence to standard treatment protocols.

Inflammation of periapical tissue is considered one of the major causes of postoperative pain. Pain after endodontic therapy may be influenced by factors such as pulpal and apical tissue condition, presence of periapical radiolucency, preoperative pain, microbial factors etc. [10, 14, 17]. Other factors responsible for post-endodontic irritation and pain are inadequate root canal cleaning and shaping, improper working length determination leading to over or under-instrumentation, hyper-occlusion, missed canals, extrusion of apical debris, irrigants, guttapercha, endodontic sealer and intracanal medication [18, 19].

Correct working length determination, proper cleaning and shaping of canal space, judicious selection and adequate use of intracanal irrigants, prolonged and profound anesthesia, occlusal reduction, and use of a negative apical pressure irrigation device give a significant reduction of post-endodontic pain [20, 21]. An alternative approach to pain management is the prescription of pre- or postoperative medications (prophylactic analgesics and corticosteroids). Laser and cryotherapy have also been suggested to prevent pain after endodontic therapy [4].

Vera *et al.* [22] first described the effectiveness of cryotherapy in endodontics. They used a final rinse of 5 min with cold saline at 2.5 °C associated with Endovac a negative pressure irrigation device to measure the temperature change of the external surface of the root in an extracted tooth. They found a more than 10 ºC reduction in the temperature of the external surface of the root which is sustained for 4 minutes, which may be enough to produce a local anti-inflammatory effect in periradicular tissues. This is in accordance with Al-Nahlawi, *et al.* (2016) [24], who evaluated the effects of intracanal cryotherapy and negative pressure irrigation (Endo Vac) on postoperative pain after vital single-sitting endodontic treatment and concluded that clinically intracanal cryotherapy eliminated postoperative pain and negative pressure improved its effect.

In 2016, cryotherapy was first clinically used in endodontics by Keskin *et al.* [23] for minimizing post-operative pain. Their study included teeth with vital inflamed pulps; used 2.5 °C cold saline irrigation as a final irrigant following biomechanical preparation of root canals and concluded that the use of intracanal cryotherapy reduced the postoperative pain after single sitting root canal treatment in patients with irreversible pulpitis. However, they did not differentiate between asymptomatic and symptomatic pulpitis nor did they differentiate between cases with and without apical periodontitis [4].

Randomized multicentre clinical studies compared the effect of cryotherapy on reducing post-endodontic pain in teeth presenting irreversible pulpitis with and without apical periodontitis. As a result, cryotherapy made a difference only in patients diagnosed with apical periodontitis, and in patients with irreversible pulpitis only, there was no significant difference in the incidence of postoperative pain between the cryotherapy and control groups [25]. It was shown that there was no effectiveness of cryotherapy in previously asymptomatic cases without periapical pathosis, according to a study conducted by Alharthi *et al.* [26]. This is in accordance with Jain *et al.* [27] who concluded the use of cryotherapy for reducing post-endodontic pain only in teeth presenting symptomatic irreversible pulpitis with apical periodontitis.

2. Vital pulp therapy

In cases of direct pulp capping, cryotherapy has shown positive results when applied for the control of pulpal bleeding. After direct application of Shaved sterile water ice (0 °C) over tissue and tooth surfaces for 1 minute and then removed by high-speed aspiration and rinsed with EDTA. Ethylenediamine tetraacetic acid also known as EDTA is a chelating agent, commonly used as an endodontic irrigating solution. Studies showed that EDTA plays an important role in the removal of the smear layer and odontoblast differentiation as it releases bioactive growth factors from the dentin resulting in reparative dentin formation. Additionally, EDTA helps to promote the adhesion, proliferation, and differentiation of dental pulp stem cells. Later, the exposure site was sealed with a bioceramic material followed by permanent restoration. After the follow-up at intervals of 2 weeks, 12 months, and 18 months, the treated teeth became asymptomatic and remained asymptomatic, vital, and functional [28]. However, further clinical studies are needed to determine the long-term outcome of viable pulp cryotherapy.

3. Nerve block

Most recently, preoperative cold application increased the potency of inferior alveolar nerve blocks as stated by Topcuoglu *et al*. [29]. However, in cases of symptomatic irreversible pulpitis, additional anesthetic techniques may often be required to achieve extensive pulpal anesthesia.

4. Effects of cryotherapy on endodontic instruments

The most critical step in root canal therapy is biomechanical preparation and is considered a key factor for the success of endodontic therapy [30]. The advent of NiTi rotary instruments is greatly advantageous in modern endodontics. But have their own limitations such as the unwarned separation of an endodontic rotary NiTi instrument within a root canal is a difficult clinical situation.

There is markable improvement noticed in the surface hardness and thermal stability of the metals when they are subjected to Cryogenic treatment during manufacturing [4]. This is an additional process of slowly warming the metal to room temperature after exposure of stainless steel and superelastic NiTi to subzero temperatures [31-33]. Depending upon the treatment temperature cryogenic treatment are of two types shallow and deep cryogenic treatment. Shallow cryogenic treatment has been tried at conventional sub-zero temperatures of approximately -80 ºC. However, deep cryogenic treatment (DCT) using liquid nitrogen at temperatures -185 ºC and -196 ºC improves the life of the instruments [4]. Immersing the material in liquid nitrogen, the process is called as wet. The dry method is a method in which the material is not immersed in liquid nitrogen and is held above the liquid nitrogen [34].

When compared to shallow cryogenic treatment, deep cryogenic treatment is considered to be more advantageous due to its better cutting efficiency, strength, and lowering of the internal stresses of alloy. Furthermore, low-temperature processing affects the entire cross-section, not just the surface of the metal. Therefore, cryogenic treatment is thought to be useful in strengthening rotary endodontic files [4].

The following factors influence the properties of rotary NiTi instruments after cryogenic treatment:

1. Titanium nitride is formed on the surface of NiTi alloys by a reaction between nitrogen and titanium atoms [36].
2. Formation of lattice strain because of deposition of nitrogen atom the atomic lattice of NiTi alloy [37].
3. Complete transformation into a martensitic phase from the austenite phase of the NiTi alloy [35].
4. Finer carbide particles deposition throughout the crystal lattice phase [32].

The above-mentioned mechanisms have been proposed to explain the cryogenic transformation in steel alloys [35]. The absence of carbon in NiTi alloys rules out the fourth mechanism [38].

According to Bramipour *et al*., [39] the cutting efficiency of stainless-steel endodontic instruments is not affected by cryogenic treatments. Whereas Berls [40] concluded wear resistance of the stainless-steel hand instruments (S-type and K-type) remains the same after cryogenic treatments. The effect of cryogenic treatment on microhardness and cutting efficiency of NiTi instruments was investigated by Kim *et al*. [38] and found that there is an increase in microhardness, but cutting efficiency and the structural composition remains unaffected. Whereas, the cryogenic treatment showed a significant increase in the cutting efficiency of superelastic NiTi files, with no change in its wear resistance according to Vinothkumar *et al*. [34]. This discrepancy may be due to the cryogenic treatment procedure and timing.

Following are the two crystallographic forms of NiTi alloys

Austenite phase	Martensite phase
▪ Also known as the Parent phase ▪ **Examples:** Conventional superelastic NiTi, M-Wire and R phase.	▪ Also known as the Daughter phase. • **Examples:** CM-Wire and Gold and Blue heat-treated NiTi files.
Advantages ▪ Super elasticity. ▪ Ability to revert back to their original shape on the release of stress.	**Advantages** ▪ Shape memory effect ▪ Super flexible instruments ▪ Increased cyclic fatigue resistance

Super elastic group 2 smaller-size instruments was treated with cryogenic treatment in order to increase the volume of martensite and increase cyclic fatigue resistance and cutting efficiency [41]. Application of DCT at -185 ºC with 2 different soaking times one for 24 hours and another for 6 hours, and the result showed that there is a significant increase in the cyclic fatigue resistance by 13% with a 24-hour soaking time and only 1% with a 6-hour soaking time. However, the cutting efficiency remain unaffected [42]. This may be due to the fact that retained austenite has sufficient time to fully transform to martensite [43].

Effect of cryotherapy on fracture resistance of tooth

Keskin *et al*. conducted a study on endodontically treated teeth and evaluated the impact of intracanal cryotherapy on their fracture resistance. They concluded that there is a decline in vertical fracture resistance after using intracanal cold normal saline as a final irrigant when compared with the standard group. This is because the application of cold normal saline within the pulp space may bring about a more uniform thermal stress in the dentin as a result of the absence of enamel structure and the microtubular structure of the dentin closer to the pulp space [44].

Antibacterial efficacy of cryotherapy against *Enterococcus faecalis*

Antibacterial properties of cryotherapy treatment along with 5% NaOCl against E. faecalis were evaluated by Mandras *et* *al*. [44], Cryogenic treatment was performed on a dental instrument equipped with a duct and associated with liquid nitrogen (cryogenic liquid), with a cooling needle receiving the cryogenic fluid. They concluded that the cryo-treated instrument along with Sodium Hypochlorite irrigation substantially decreases the quantity of *E. faecalis* (p<0.01) in the root canal. Hence, cryo treatment suppositiously reduces the microbes, using standard NaOCl as the final irrigant.

Conclusion

The present review thoroughly identifies, summarises and appraises the clinical implications of cryotherapy in endodontics. In the endodontic literature, Cryotherapy is relatively new and considered to be a effortless and cost-efficient, non-irritating supplementary method for minimizing pain during and after endodontic treatment, inflammation, and controlling pulpal bleeding during vital pulp therapy. Nonetheless, further studies have to be conducted to clarify the effects of cryogenic treatment on NiTi endodontic instruments. Also, additional well-designed clinical studies are to be conducted to establish and avail all the possible benefits of cryotherapy in the field of endodontics and day-to-day clinical practice.

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