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Review Article

An Emerging Alternative for Pain Control: Mechanism and Applications of Cryotherapy in Endodontics

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Abstract: Patient discomfort after conventional root canal therapy remains inevitable in endodontic practices. It depends on the clinician to lessen the postoperative pain encountered by the patient. This review article aims to get acquainted with Cryotherapy, a current modality designed to reduce patients' anxiety, pain, and inflammation levels. Extensive studies have been provided on the applications of cryotherapy in the fraternity of medicine, but its utilization has been restricted in the Endodontic regime. Cryotherapeutic agents benefit in the regard that they eliminate the need for prescribing supplementary medications. The application of cryo-therapeutic agents is technique sensitive and requires the clinician to have thorough and correct knowledge regarding its underlying mechanism of action. Several expected outcomes can be derived after cryotherapy application. It is proven that intracanal application of the cryotherapeutic agent provides anodyne–like action serving as an essential tool for pain control. The concept of frozen tissues is related to ancient times, such as treating sports injuries, while its recent introduction into endodontics has been a boon to already practicing clinicians. Although it is a slow process requiring multiple appointments of visits to the clinician, its long-term benefits can be a breakthrough in meeting the benefits of delivering quality patient care. This article sheds light on its recent applications in endodontics, focusing on the chemistry behind freezing cells to newer advancements. However, significant and valid trials need to be carried out to reach evidence of certainty about the therapeutic benefits and additional tools of delivery. It will pave the way for further scientific work to broaden its range of applications in dentistry.

Keywords: Cryotherapy; freezing; postoperative pain; endodontics; cryo-therapeutic agents.

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1. INTRODUCTION

One of the major reasons for a patient to visit a dentist in routine dental practice today is to alleviate the pain and discomfort caused throughout and after a root canal treatment. Amongst all clinical procedures, endodontic pain is most commonly linked to patients for an unscheduled dental visit.[1] The review article aims to focus on the benefits of cryotherapy in assessing the demands of routine pain control measures in endodontics. Only a few has been tried and tested in incorporating the principles of Cryotherapy in routine endodontic practices. The novelty of this method is a boon in itself to eliminate pain and inflammation from the target tissue. Several etiological factors are enlisted for pain, amongst which chemical, mechanical, and microbiological injuries occurring at the periphery of the tooth root-periapex region comprise a vast majority. These are majorly iatrogenic and arise due to the routine act of vigorous canal preparations which occur during treatment procedures. Common factors affecting post-root canal pain include incomplete removal of vital or necrotic pulpal tissue, periapical extrusion of irrigating solutions, intracanal medicaments and endodontic sealers, and failure to diss occlude the tooth post-endodontic treatment. Microorganisms remain the greatest cause of menace in root canal systems. To reduce the patient's discomfort and enhance the faster healing of tissues, numerous non-steroidal anti-inflammatory drugs (NSAIDs) are routinely prescribed by clinicians. Ibuprofen is an effective analgesic drug to control post-endodontic pain. [2] Applying cold is a novel method to reduce post-operative pain in patients undergoing routine root canal treatment. In reality, the notion behind Cryotherapy is not to lower the heat of the region upon which it is applied; rather, it intends to extract the heat from tissues of higher temperature, eventually rendering them vulnerable to the benefits of a lower temperature. Orthopedics and other domains of medicine have applied cryo-therapeutic agents to reduce inflammation at injury sites to speed up healing. It has been proven to alleviate pain and discomfort encountered during sports injuries. Using this beneficial property of Cryotherapy has yet to be explored in endodontics. Hence, This article sheds light on its mechanisms of applications and potential benefits. [3] The impact of this review lies in providing the knowledge and underlying mechanisms of cryotherapy and the various agents which cause the freezing of tissues. Also, it is a novel resort to pain control modalities in dental setups, offering faster pain relief without much investment in other sophisticated mechanisms.

1.1. Historical Background

At around 3000 BCE, the early Egyptians were believed to be the ancestral predecessors of cold application for the cure of injuries and to decrease tissue inflammation at the site of trauma. Cryotherapy relates to lowering the temperature of the tissues for healing and therapeutic purposes. The word was, however, imitative of the Greek words "cryo," which denoted 'cold' & 'therapeia, which denoted 'cure'[3]. Later Arnott, in the 19th Century, first described the procedure of application of a salt solution supercooled to a temperature of –18°C to –24°C for effective pain control and cure of advanced cancers. For appropriate utilization and adequate delivery of the cryotherapeutic agent to the desired site, it is foremost for a clinician to comprehend the underlying mechanisms behind freezing cells and eventually procure its benefits of reducing pain and inflammation. It generates work dependent on cryoplasty, derived from basic science and clinical research. The latest advancements in this area are related to using chilled irrigation s solutions and sterile shaved ice to lower the tissue site temperatures. A study on vital pulpal stumps claims that placing sterile ice shavings directly or indirectly reduces the swelling and pain in the affected area. The pulpal tissues lose their inflamed state, and new vascularisation initiates, thus, helping to restore the vitality status of the tooth. It utilizes additional pulp capping materials to recreate the dentinal bridge formation in hard tissues. Various modalities of cold application in the form of gel packs, foam, liquid solvents, and several others have been utilized in medical and sports fields to reduce post-operative pain in patients. Another innovation is the utilization of chilled cold saline to flush into the canal as a final irrigant to lower tissue temperatures. The saline is flushed as a final endodontic rinse at 2-4 degrees Celcius using a 27-Gauge side vented needle. The benefits achieved are incredible in terms of reducing symptoms of post-operative pain.

2. DISCUSSION

2.1. Applications of Cryotherapy

The applications of cryotherapy are widespread in the health and medicine sectors. Acute Athletic injuries and other musculoskeletal diseases have shown good clinical results upon treatment using this novel method. It comes under Cryokinetics, which has been used to relieve pain due to various sports injuries like the runner's knee, tendonitis, sprains, arthritis pain, and swelling [4]. Furthermore, it has been used to destroy potentially malignant cells and dysplastic tissues to cure cancer. For treating malignant lesions, cryotherapy is not a first-line remedy and is typically set aside for those patients who cannot sustain excisional surgery. However, in dentistry, cryotherapy has been used after intraoral excisional surgical procedures, periodontal surgery, and after extractions and implant placement and was found to be effective in reducing swelling, pain, and arthritis associated with temporomandibular joint disorders [5]. Amongst the turf of endodontics, most periradicular surgeries envisage large amounts of tissue destruction accumulating enormous amounts of inflammatory modulators to trigger the cascade of inflammation. Cryotherapy comes to the rescue after such periapical to curtail pain and inflammation generated after such treatments. Other implementations include projecting nickel-titanium (NiTi) endodontic files to thermal variations to enhance their cyclic fatigue resistance threshold, thus creating a version more resistant to potential file separation. Another lesser explored frontier is its role as a beneficial adjunct for achieving cessation of blood flow in a vital pulp when used in aggregation with a bioceramic material. Another therapeutic benefit is using chilled saline solution (2.5 degrees Celcius) as a final irrigant to reduce the root surface temperature externally. A root surface temperature of more than 10 degrees Celcius can be maintained effectively for 4 minutes, sufficient to activate a local anti-inflammatory effect in the periapex region of tooth [6]. The delivery of the cryotherapeutic agent to this zone of a tooth is achieved through negative pressure irrigation, but its exact mechanism is lesser explored as of now.

2.2. Physiologic Effects following After Cold Application

Pain control in endodontics remains a major concern for all clinicians. Moderate to severe post-operative pain is invariably associated with root canal treatment and other routine dental operative procedures. Thus successful pain management is crucial in alleviating this pain. The cascade of inflammation occurring in the periarticular region is typical and similar to the inflammatory reactions in any other body connective tissue. Vasodilation occurs initially, causing increased vascular permeability, followed by migration of leucocytes from blood vessels to the injury site [7,8]. These migrating cells comprise primarily neutrophils and large macrophages. The biological activities involved in cell destruction and produced by these inflammatory mediators result in excruciating pain, sometimes accompanied by swelling [9], for effective pain control regimes like the usage of long-lasting anesthesia and occlusal reduction are recommended [10]. Many nonsteroidal anti-inflammatory drugs are relatively safe for use, and treatments like lasers and cryotherapy have been further suggested if these fail to provide relief [11,12,13,14,15]. The benefits of Cryotherapy have been depicted in the process flow diagram as shown in "Figure 1".

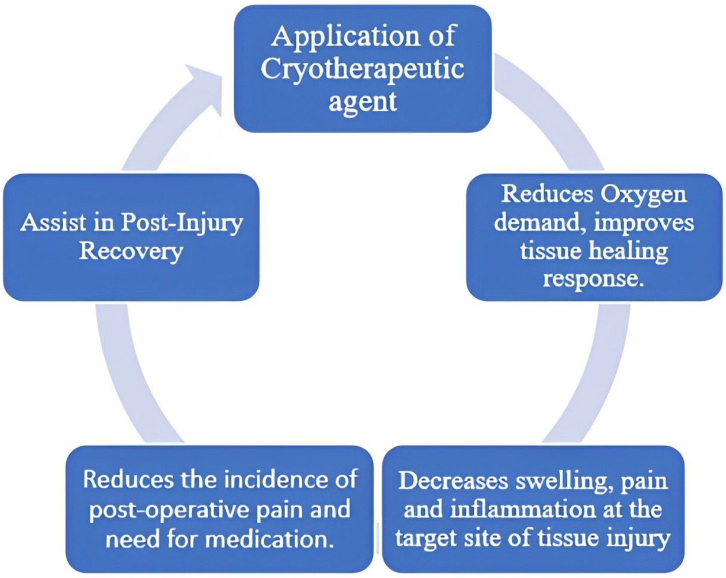

Fig 1: Process flow Depicting the benefits of Cryotherapy after application onto the tissues

2.3. The chemistry behind Cold Application

Cryotherapy acts on the target tissues through three basic physiologic effects: vascular, neurologic, and tissue metabolism. A typical "hunting response" response occurs, described as a cycle of initial vasoconstriction followed by vasodilation. After exposure to lower temperature ranges for more than 15 minutes, a tissue evokes initial vasoconstriction. Vasodilation follows this and is mediated by releasing a histamine-like substance called 'H' [16]. This cycle continues as a complex neural reflex triggered by adrenergic components in the blood vessel network [17,18,49]. Cell permeability is reduced significantly in the periradicular area, thus reducing the volume of liquefied material escaping as exudate or transudate. This fluid accumulation in the periapex commonly occurs after chemo-mechanical preparation, sometimes visibly seen as a swelling [19]. Achieving enhanced healing rates simultaneously and minimizing post-surgical complications is crucial to significant pain control. Cold application hinders blood flow and thwarts the rebound phenomena using vasoconstrictor-containing anesthetic solutions. Thus, reducing the temperature at the surgical spot by applying cold has become the endorsed protocol in providing better postsurgical supportive therapy [20,49].
Regarding the neurologic effect produced by the cold application, it is devised that cooling initiates analgesia by slowing the conduction velocity in a nerve [21,22]. However, this result is more marked in the myelinated nerve fibers (A-delta fibers) paralleled with the unmyelinated fibers (C fibers) [23], as Franz and IggoZ [24] prove. According to the assumption, gate control theory is responsible for endorsing this analgesic outcome of cryotherapy, given that a faster sensory input by the larger myelinated A fibers momentarily closes the gate and hinders the communication of more excruciating impulses of the unmyelinated C fibers [25,26]. In addition, cold application induces neuropraxia, which will further decline the activation threshold of tissue nociceptors, resulting in a transient local anesthetic effect. Thus, the analgesic effect of cooling is produced by an amalgamation of a decreased release of chemical mediators of pain superadded to a slower dissemination of painful neuronal signals [27]. The consequence of cryotherapy on cell metabolism is that the damaged tissue becomes liable to devour more oxygen, eventually leading to hypoxia of tissues causing necrosis. Furthermore, Cryotherapy tends to cut off tissue blood flow and cellular metabolism by a further 50%. It consequently slackens the rates of biochemical reactions, limiting free radical production in tissues, and reducing oxygen consumption, thereby preventing tissue hypoxia and further tissue injury [28,29].

2.4. Modes of Delivery

Several authors have reported that crushed or moistened ice is the most effective cryo-therapeutic agent. Still, when the same is condensed in gel packs, it becomes the least efficacious in lowering the skin temperature (Tsk). This phenomenon can induce an anodyne-like response to compensate for the increased intramuscular temperature (Tim) and tissue inflammation (Tim) [8,30]. Several methods of delivering cryo-therapeutic agents include

2.5. Sprays

An efficient method for delivering the liquid cryogen to the site of action is the usage of Self-pressurizing spray guns which transport a mixture of vapor and drops of liquid cryogenic material. As soon as the liquid Nitrogen associates with the tissue, it evaporates into the gas phase. This phenomenon removes a larger amount of heat from tissue. These are useful for treating benign and neoplastic lesions [31]. The amount of cryogen to be delivered at the site of the lesion is effectively regulated by the needle orifice diameter and the pressure by which the agent is being pushed out of the needle. Runoff of the cryogen from the treatment site is prevented by packing the surrounding area with Vaseline-impregnated sponges [32].

2.6. Cryoprobes

Unlike spray and solid delivery of a cryogenic agent into the localized area, another method uses hollow probes, which are used for direct contact penetration and initiate freezing. It makes it easiest to control, although, depending on the configuration of the probe. Several attachments have been used as adjuncts to these probes to serve as modalities of thermal conduction. A metal commonly used is Copper due to its high conductivity [33,34]. The application of cryo-therapeutic agents in endodontics also relates to using rotary Ni-Ti endodontic files. The versatile nature of endodontic Ni-Ti lies in its unique property of shape memory, better adaptability, increased torsional resistance, and enhanced flexibility. Several investigations have been tried to evaluate the cutting efficacy, cyclic fatigue, and fracture resistance on the impact of NiTi endodontic instruments. They concluded that cold treatment enhances these values leading to an overall increase in physical properties.

2.7. Dipstick Applicator Method

The direct application of liquid nitrogen to lesions can be made with the help of a Dipstick applicator method. The cryotherapeutic agent is delivered by firmly pressing against the lesion for the stipulated time. However, it is difficult to achieve low temperatures by using this method [35].

2.8. Thermo Couple Device

A probe conjoined with a temperature probe that can read to -75 degrees treats malignant lesions. The method of application of the probe into the lesion lies in estimating the depth of the temperature probe and gradual insertion into the lesion [33,36].

2.9. Cryotherapeutic agents

2.9.1. Liquid Nitrogen

The commonest method for freezing lesions is liquid nitrogen as the coolant. The chilled liquid at a temperature range of -196°C (-321°F) will be sprayed onto the diseased tissue, circulating through a cryoprobe duct, or patted on with a cotton or foam swab. These extreme temperatures are adequate to destroy damaged tissues [37,38,50].

2.9.2. Carbon Dioxide

Available as Carbon dioxide "snow" spray is delivered to the site to treat a wide range of benign lesions. Carbon dioxide is mixed with acetone to form a slush applied to the target area [38.39,40].

2.9.3. Argon

Argon gas is another cryotherapeutic agent used to freeze tissues. This gas gives physicians superior control over ice usage and reduces the complications associated with cryo needles [34].

2.9.4. Freeze Sprays

A blend of dimethyl ether and propane is supplied in some "freeze spray" preparations. When dispensed, the blend is preserved in an aerosol spray-type vessel at room temperature and dips to -41°C (-42°F). Similar products may use tetra fluoro-ethane or other substances [32,50].

2.9.5. Cryotherapy and Endodontics

The initial contributions to the field of cryotherapy were attempted by Vera et al. 41, who used a final rinse of 2.5 degrees Celcius cold saline solution coupled with an Endovac irrigation device for 5 minutes. Based upon this study, they concluded that a significant reduction in the temperatures of external root surfaces of teeth up to 10 degrees Celcius which lasted for about 4 minutes, was seen. Based on this speculation, an assumption was made that to exert a local anti-inflammatory and analgesic action on periapical tissues, such therapy would provide promising results. A slightly variant recent study based on the above results applied the knowledge clinically to reduce postoperative pain succeeding root canal treatment. It was thus the first attempt to successfully introduce this concept into the field of Endodontics. An exact application of the protocol recommended by Vera et al. was used in their study, also with a few modifications. While negative pressure was utilized in the former for irrigation, the latter utilized a side-vented, positive-pressure 31-G NaviTip needle instead to evaluate its additional effect on reducing postoperative pain. This needle tip controlled the amount of cryogen delivered at the tooth root apex, thereby preventing its apical extrusion. The study claimed a major decrease in post-operative pain among participants in the Cryotherapy group when associated with the control group. However, they lacked in differentiating between symptomatic and asymptomatic pulpitis. The inability to non-categorize, not differentiate, and analyze a diverse pool of results affects the results. Also, the degree and nature of preoperative pain influence the manifestation of post-operative pain too. Similar studies following these footsteps affirmed that using chilled normal saline solution and following the same protocols presented a reduction in postoperative pain levels following single-visit root canal treatment in teeth having vital pulps [42,43,48]. The procedure of super-chilled Saline application procedure is shown in "Figure 2".

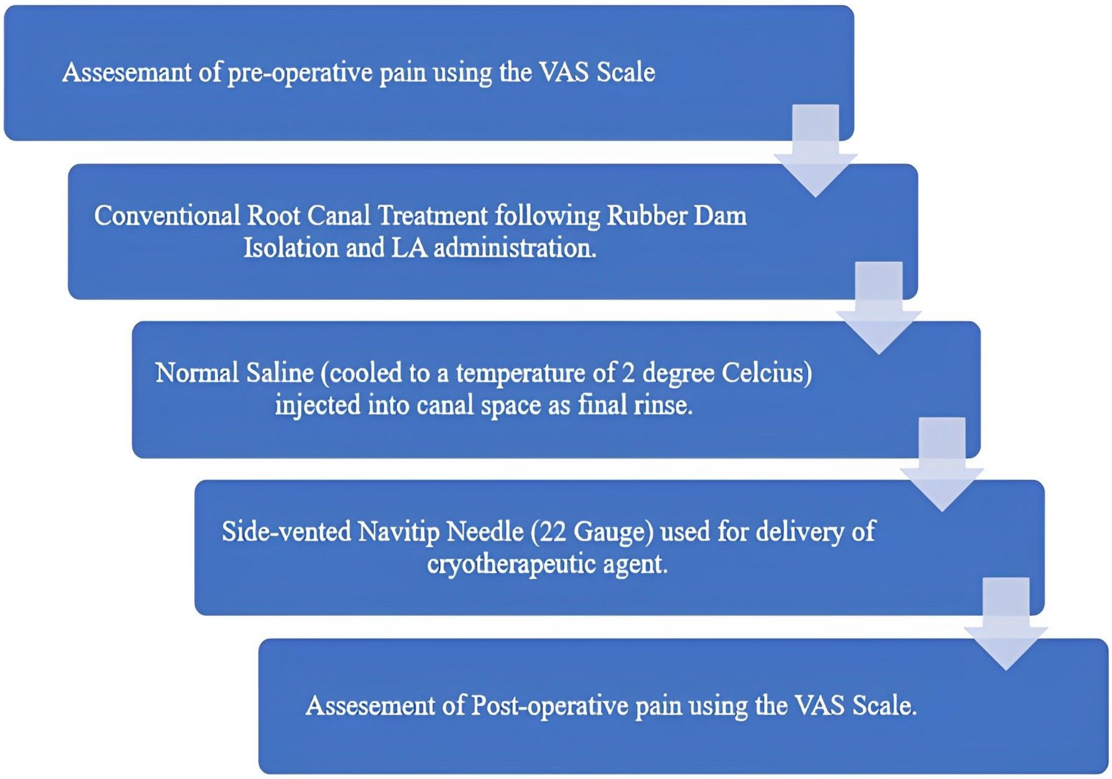

Fig 2: A Flowchart depicting the procedure of application of Intracanal Cryotherapeutic Agent into the root canal System

Cold saline was dispensed as a last washout with the help of a 27-G side vented needle. A major limitation of cryotherapy is its application only in scenarios limited to the resolution of apical periodontitis. It does not hold a significant difference in minimizing post-operative pain levels in cases of irreversible pulpitis [44]. Recently, in endodontics, its spectrum of application has been escalating in vital pulp management, where it has been effectively applied in cases of direct pulp capping where there was obvious pulp exposure. Studies reveal that when sterile shavings of water ice (0 degrees Celcius) were applied openly to exposed pulp tissue, the entire tooth surface for the duration of 1 minute, the entire tooth became asymptomatic, vital, and functional for a period of 2 weeks and remained functional for a follow-up tenure of 12-18 months [45]. Although sufficient studies have only been made recently in the branch of Oral Surgery, it has been shown that intraoral cryotherapy application increased the success of Inferior Alveolar Nerve block [46,47]. However, additional anesthesia practices may still be mandatory for deep pulpal anesthesia. Cryotherapy also claims to improve the surface hardness of stainless steel files during manufacturing. The cryogenic treatment allows the metal to return to room temperature slowly. This procedure has, however, claimed to increase microhardness, but improvement in cutting efficiency has yet to be demonstrated.

3. CONCLUSION

Cryotherapy originated in human medicine long back in the 18th Century, and until today, it has been evolving as a new treatment modality in various fields of medicine. Currently, by demonstrating promising results in reducing postoperative pain, discomfort, and inflammation associated with vital pulp tissue management, cryotherapy is a promising treatment options clinicians can implement in routine endodontic practices. Furthermore, although the long-term prognosis of cryotherapy in vital pulp therapy is recommended, it alludes to bringing down or diminishing the tissue temperatures for therapeutic purposes. Thus, cryo-treatment is expanding widely in endodontics as a modality that is simple, cost-effective, quick, less invasive, and safe to use. It is, therefore, a pleasing adjunct for both patients and caregivers.

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5. AUTHORS CONTRIBUTION STATEMENT

Dr. Manoj Chandak conceptualized the data concerning this work. Then, Dr. Anuja Ikhar analyzed these data and provided the necessary inputs for designing this article. Finally, all authors discussed and compiled the data to contribute to this final manuscript.

6. CONFLICT OF INTEREST

Conflict of interest declared none.

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