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REVIEW

Cryotherapy – A Review

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ABSTRACT

Technical advances in recent years have made the application of controlled low temperatures a feasible proposition in many branches of surgery. In the last decade there has been a proliferation of reports on the uses of cryotherapy; nevertheless, many of the applications are still experimental, or await the test of time. Cryotherapy is the deliberate destruction of tissue by application of extreme cold. The mouth is reasonably accessible to cryotherapy apparatus. The warm moist surface of the oral mucosa is well suited to the application of a freezing probe. Recent advances in cryotherapy equipment have brought treatment by this means within the range of the dentist.

Key Words: Cryotherapy; cryogens; ice pack; oral lesions; intraoral surgery

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Introduction

Cryotherapy is the use of cold, applied locally or generally through various methods, to lower the temperature of the skin and subcutaneous tissues. It has been used in oral medicine and pathology for over 30 years. Reports of tissue destruction by freezing date back to the British physician, Arnott in 1851. Initially, its use was limited to the treatment of cancer of the lip and oral cavity. At present its applications in the head and neck region are broad [1]. Also cryotherapy can be recommended after physical injuries and various surgical procedures.

Modes of cold application include ice pack, gel pack, ice chips, melted ice water, ice massage, prepackaged chemical ice pack and ice in a washcloth [2].

Cryogens

The commonly used cryogens include liquid nitrogen (-196^0 C), nitrous oxide (-89^0 C), solidified CO2 (-78^0 C) (dry ice CO2 snow), chlorodifluromethane (-41^0 C), dimethyl ether and propane (-24^{0}C, -42^{0}C)[3].

Principles Of Cryotherapy:

The basic technique of cryotherapy stresses rapid cooling, slow thawing and repetition of the freezing process to maximize tissue destruction. The two methods recognized are;

1) A closed system with use of probes and nitrous oxide

2) An open system with use of a liquid nitrogen spray or a cotton tip.

The probe system follows the principles of Joule-Thompson expansion which enable substances to undergo a drop in temperature when moved from a high pressure area to a low pressure area. For instance, when nitrous oxide is released from the high pressure inside the cryoprobe to the lower pressure cryotip, the drop in temperature allows freezing of the tissues to occur[1],[4],[5].

Modern cryoprobes may also be fitted with tip temperature monitors allowing for time selection and increased control. This allows clinicians to observe the effects at a certain probe temperature and use this as a basis for future treatment [1],[6].

Liquid nitrogen sprays and cotton swabs are more accessible to clinicians but not suitable for use in the oral cavity. Their disadvantage is a lack of control over the temperature achieved within cells and the area of freezing, which makes them hazardous to use intra-orally. Also, rapid evaporation of liquid nitrogen from cotton swabs requires numerous applications on the lesion. Due to direct contact between the cryogen and tissues, a more controlled and profound depth of freezing can be achieved with a nitrous oxide cryoprobe [1].

Cryotherapy Of Oral Lesions [1]

Cryotherapy is used for the treatment of keratotic, hyperplastic, granulomatous, vascular, pigmented lesions, and salivary gland lesions as well as for gingival

Stages of cryotherapy (Hocutt et al 1982) [2]
Stage 1: sensation of cold 1-3 min
Stage 2: aching or burning 2-7 min
Stage 3: local numbness 5-12 min
Stage 4: deep dilation >12 min
It has been suggested that after an injury >12 min should be used to attain stage 3.

Cryolesion Dimensions

Cryolesion dimensions are dependent upon three variables; the temperature of the cryotip, the period of contact and the area of contact between the tip and tissue. The temperature of the probe tip contributes to the size of the freeze-ball as well as determining the velocity of freezing within cells. Since lethal effects are observed with rapid freezing, a high velocity of freezing is desired. Growth patterns of the cryolesion in vitro suggest that the duration of freezing is proportional to the lesion size in the first 1-7 minutes.[1] After this time no further increase in size is observed and no added benefit is gained by continuous exposure. In addition, since it is difficult to freeze tissue ,2-3 cm away from the probe, multiple freeze sites in large lesions may be warranted. This is especially true when freezing bony tissue but freezing times are in the order of 20-30 seconds when dealing with most oral soft tissue lesions. The area of contact of the probe can be varied by tip diameter. Larger tip diameters correspond to an increasing size in the freeze-ball. However, diameter size also compromises the efficiency of the cryoprobe. Another factor to consider is that moisture in the vicinity of the lesion may enhance the area of contact, thus creating a larger freeze-ball [1].

Current protocols suggest that for most benign mucosal lesions a 1-2 min freeze/thaw cycle using a cryoprobe is sufficient. Premalignant/malignant lesions are recommended to undergo three 2 min freeze/thaw cycles. For smaller lesions, shorter freeze cycles (20-30 seconds) are adequate. In cases where hyperplastic tissue exists, freezing of the mass and then removing the bulk of tissue, followed by further freezing of the tissue base results in higher success rates [1].

Mechanisms Of Tissue Damage In The Cryolesion

At present, the optimal temperature of cell death is unclear, however, it has been determined that most tissues freeze at -2.2^{o}c and that the temperature must fall below -20^{o}c for cell death to occur. On this basis, dermatological guidelines suggest that temperatures of -30^{o}c may be effective for small cancers. The treatment of more aggressive cancers in the oral cavity may require repetitive freeze cycles at temperatures of at least -50^{o}c or more for tissue necrosis to occur [1],[7].

Tissue destruction following cryotherapy is believed to be a multifactoral process. Accumulation of damage occurs as the lesion undergoes repetitive freeze and thaw cycles. Immediately following treatment, cryolesions are indistinguishable from original tissue. However, latent damage is produced which progresses to severe damage and subsequent necrosis of the tissues in the following days [1],[7].

During the freeze cycle as the temperature drops, it is believed that extracellular water undergoes crystallization. In addition, membrane lipids harden at low temperatures decreasing cell resistance to shrinkage. As extracellular stores of water diminish, the electrolyte concentration increases. In order to counteract this concentration gradient, intracellular water moves out of the cell, and this water becomes involved in the crystallization process. Also, the intracellular ice formed remains trapped within the cellular membrane. As a result of these processes, intracellular electrolytes reach toxic levels, which become lethal to the cell. During a slow thaw cycle, cells at the periphery of the cryolesion will take up excess electrolytes. To equalize this gradient, water enters the cell and this can lead to swelling and lysis. Further re-crystallization may contribute to cellular damage; however, this phenomenon may be avoided if cells are thawed rapidly [1],[7].

Cold Therapy After Intraoral Surgical Procedures

The therapeutic use of cold is applied locally or generally through various methods, to lower the temperature of the skin and subcutaneous tissues [2].Clinicians often recommend that patients apply ice for therapeutic purposes after physical injuries and various surgical procedures [2],[8]. THE Physiological and clinical effects of cryotherapy have been widely studied but there is still dearth of scientific information with respect to the best mode of application, optimal time interval for therapy (time on and off), and total duration of cryotherapy. To establish a basis for discussion the basic physiological responses to cold subsequent to oral surgery was reviewed [2].

Benefits Of Cold Application On Inflammatory Response

Historically, five cardinal signs of inflammation were identified: pain, swelling, heat, redness and loss of function. However, signs of inflammation are not inflammatory response. The inflammatory reaction consists of overlapping stages that can impair tissue function or structure [8]. The r reason for applying cold therapy (e.g., ice) after an injury is to cool tissues to accomplish the following physiological objectives: decrease inflammation, inhibit swelling (edema), diminish blood supply (vasoconstriction), decrease hemorrhage, inhibit temperature elevation, reduce metabolic alterations (cold decreases the metabolic rate, thereby lessening secondary injuries due to lack of oxygen), assuage pain (cold decreases nerve conduction speed), and, ultimately, speed up the recovery of the patient to resume normal functions [1],[10].

Physiological Effects

Temperature Changes

Cold or ice packs work on the **Principle of conduction.** Heat is transferred between molecules from warmer to cooler areas. Thus, cryotherapy does not convey cold to tissues because cold is not transferable. In contrast, tissues lose heat because they warm the cold agent. Following the same principle, deeper structures lose heat to more superficial tissues that were cooled. The amount of temperature change in treated areas depends on various factors: differences in temperature, size & shape of pack, duration, tissue thickness, anatomic location and mode of therapy. The temperature declines gradually until skin warmth plateaus a few degrees above the temperature of the applied cold agent [1],[11]. Ebrall et al (1992) used wet ice pack of 37ºC to 7.6ºC in 5 min and to 5ºC within 10 min and found no change in skin warmth 1 cm proximal or medial to ice pack.[2] After cessation of cold therapy, Bugaj (1975) noted the skin readjusted at 1.9ºC per minute. The target temperatures that need to be reached to accomplish the desired physiological endpoint remained unsolved. In conclusion, temperatures to inhibit signs of inflammatory response range between 10ºC and 15ºC. Ice and cold packs reduced skin temperature by 10ºC to 15ºC within 15 minutes [2].

Hemodynamics (Blood Flow)

Studies indicated that cold application initially resulted in vasoconstriction of blood vessels. After an injury, this reduced the hemorrhage and perfusion of fluids, and ultimately resulted in decreased edema. Subsequent to vasoconstriction, there may be vasodilatation, despite continued use of cold. This is believed to occur as a result of reactive hyperthermia. The vasodilatation is referred to as a "**hunting**

response" and represents the flow of blood through arteriovenous anastomoses. This may be a compensatory mechanism that prevents injury caused by extreme cold temperatures. The hunting response was reported to occur after 20-30 minutes [2] which is refuted completely by Knight who called it a measurement artifact. However, the controversy has not yet been resolved [2].

Edema

Swelling can be caused by hemorrhage and/or edema. After an injury, bleeding usually stops within 5 minutes because of clotting; therefore, swelling is usually caused by edema. Decreased temperature also reduces tissue metabolism and permeability. Depressed metabolism results in less tissue debris, a diminished amount of free protein and subsequently, less osmotic pressure for fluid to exit cells. In addition, reduced cell death because of tissue hypoxia results in fewer mediators (e.g., bradykinin) being released; therefore, there is less vascular permeability and edema. Cold could help prevent swelling from occurring, but it does not decrease edema that is already present [2].

Pain Reduction

Decreased pain was caused by cold-induced diminished nerve conduction velocity. Alterations of nerve transmission were due to thermal effects on nerve fibre membranes. Superficial nerves demonstrated the greatest nerve velocity reduction, and cold temperature blocked sensory fibres before motor fibres. Cold affected the small myelinated fibres first, then the large myelinated fibres and finally, the small unmyelinated fibres. The critical temperature at which alterations of nerve velocity commenced were 27ºC, while analgesia began after skin temperature decreased to 13.6ºC (pin-prick test) [2].

Metabolic Processes

Reducing tissue temperature suppresses the injured tissue's metabolic rate and enzymatic processes. But some studies demonstrated that cooling diminished the demand for ATP and the need for oxygen; therefore, tissues survived well during hypoxia induced by injury. To diminish skin metabolic rates, the temperature needed to be around 10ºC for a period of about 15 min [2].

The physical changes noted were that; the collagen became stiffer and was not able to stretch, motion was decreased temporarily, and the tissue became pallid [2],[12].

Psychological benefits can be achieved by giving patients a task which will distract them from focusing on their discomfort, causing a placebo effect [2],[12].

Contraindications include a history of frost bite or arteriosclerosis, hypertension, local limb ischemia, paroxysmal cold hemoglobulinuria, Raynaud's disease, rheumatoid arthritis and cryoglobulinemia [2],[3].

Advantages

The merits of cold therapy include relative lack of discomfort and pain (decreases nerve conduction speed), the absence of bleeding(vasoconstriction), minimal to no scarring, ease of application, preservation of inorganic structures of bone, very low incidence of infection(decreases the metabolic rate, thereby lessening secondary injuries due to lack of oxygen), no permanent side effects and being more localized in action . Perhaps its greatest advantage is its usefulness in candidates for whom surgery is contraindicated [1],[2],[7].

Disadvantages

But cold therapy has its own limitations. These include the unpredictable degree of swelling, lack of precision with depth and area of freezing and its high dependence on operator skill and experience [1],[2],[7].

Length Of Therapeutic Intervals & Duration Of Ice Application

Therapeutic intervals are prescribed for the time cold is applied and the subsequent rest periods. Duration of therapy denotes the overall time (cycles of cold therapy and rest periods) that treatment is continued. In many of the studies related to oral surgical procedures, there has been a great deal of variation with respect to the length of intervals and durations of time recommended for cold therapy. LaVelle & Synder (1985) limited therapy time to 10 min intervals instead of 20 min as it may achieve the same skin temperature but with less hunting response. But Knight (1995) proposed a protocol for cooling and rewarming tissues at a 1:2 ratio. Accordingly ice was applied for 30-45 min at 1-2 hr intervals for the first 12-24 hrs after injury. Another investigator suggested that cold should be applied post-surgically until response to trauma is stabilized, which could be between 24 to 72 hours.

But, there are no clear clinical guidelines based on dental or physiotherapy literature for the optimal time that ice should be applied to achieve specific clinical objectives [2].

Intermittent V/S Continuous Application

The efficacy of intermittent versus continuous cold therapy has not been resolved. Intra orally investigators recommend continuous ice therapy. Many studies recommend continuous therapy for 2 – 24 hours but fail to provide significant benefits compared to no cold therapy. No clinical trials have compared these two parameters after intraoral surgical procedures [2],[14].

Conclusion

Currently, cryotherapy is an effective treatment method for intraoral surgeries. By reviewing various physiological responses to cold application it is expected that ice therapy would provide several benefits. However clinical trials are required to provide a strong evidence to prove the therapeutic efficacy of cryotherapy.

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