



Is it time to put traditional cold therapy in rehabilitation of soft-tissue injuries out to pasture?

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Abstract

Cold therapy has been used regularly as an immediate treatment to induce analgesia following acute soft-tissue injuries, however, a prolonged ice application has proved to delay the start of the healing and lengthen the recovery process. Hyperbaric gaseous cryotherapy, also known as neurocryostimulation, has shown the ability to overcome most of the limitations of traditional cold therapy, and meanwhile promotes the analgesic and anti-inflammatory effects well, but the current existing studies have shown conflicting results on its effects. Traditional cold therapy still has beneficial effect especially when injuries are severe and swelling is the limiting factor for recovery after soft-tissue injuries, and therefore no need to be entirely put out to pasture in the rehabilitation practice. Strong randomized controlled trials with good methodological quality are still needed in the future to evaluate the effects of different cryotherapy modalities.

Key Words: Cryotherapy; Hyperbaric gaseous cryotherapy; Neurocryostimulation; Cold therapy; Soft tissue injury

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Core Tip: Traditional cold therapy (e.g., topically icing the injured area) may not be helpful but rather act as a barrier to recovery process. A prolonged period of cold on the skin was reported to lead to a reduction of the blood flow, resulting in tissue death or even permanent nerve damage. Hyperbaric gaseous cryotherapy, also known as neurocryostimulation, has shown the ability to induce greater analgesic, anti-inflammatory, vasomotor, and muscle relaxing effects than other traditional cold application, thus quickening recovery and heal following soft tissue injuries. More high quality level evidence is still needed to confirm the efficacy of hyperbaric gaseous cryotherapy about its clinical effects for soft-tissue injuries in the future, in order to find the optimal

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INTRODUCTION

The use of cold/ice therapy has been an extremely controversial topic in sports medicine and acute injury rehabilitation (such as soft tissue injuries). This therapy is used regularly as an immediate treatment to induce analgesia following acute soft-tissue injuries. For injured athletes or ordinary patients under specific conditions, the use of cold therapy has been generally accepted as a therapeutic modality based on the numerous physiological benefits that it offers.

It is well documented that cold therapy is generally to diminish the inflammatory reaction to trauma, reduce edema, reduce hematoma formation and pain, reduce muscle spasm, decrease tissue metabolism, and reduce enzymatic activity[1-5]. There is an anti-nociceptive effect on the gate control system, reduced nerve conduction velocity, and reduced vascular permeability and vasoconstriction[6,7]. Ice appears to be an ingrained part of the acute injury management process, but does its use align with the latest research?

COLD THERAPY FOR DIFFERENT SOFT-TISSUE TYPES

There are a variety of soft-tissue types in the human body, and each of which heals at a different rate after injuries and responds differently to various treatments. The tendon, which can be seen as bands of fibrous tissue that connect muscles to bones, could help our muscles initiate and control different movement in joints. When the tendon is suddenly overstretched or torn, strains could happen. Immediate treatment including icing the injured area for about 20 min is always recommended to reduce the pain and swelling after the acute traumatic injuries. Evidence[8] supports that the ability of cold treatment to reduce pain for acute tendon injuries may be attributable to its ability to decrease the levels of prostaglandin E₂ production in tendons, which is a highly active inflammatory molecule that causes pain and induces vasodilatation and hyperalgesia. For muscle, while cryotherapy works by reducing blood flow to a particular injured area, it could reduce the muscle spasms and muscle soreness, and ease its pain. The general range of time frame for muscle healing is around 2-4 wk, which is relatively shorter because of its rich blood supply. It is therefore important to activate its circulatory system to encourage healing after injuries and promote regeneration of the damaged muscle fibers. Therefore, the cold application on acute muscle fiber injuries should not last long and need to be controlled precisely to avoid harming the neuromuscular muscle function. Being similar to tendons, ligaments are also fibrous bands of connective tissue, and generally play roles in stabilizing the skeleton and allowing controllable and sage movement. When a sprain occurs, the ligament around the joint (such as knees, wrists, or ankles) would tear. Sprains in ligament are classified by several grades, and for the minor level of symptom, cold therapy could have the ability to reduce swelling and pain in a short time, but if the ligament tears completely, a simple cold therapy may not be useful and a surgery is needed. A general range of time frame for tendon healing is around 10-12 wk, which is longer than that of the muscle and tendon. A previous study[9] shows that cold treatment may decrease the flexibility of anterior and posterior cruciate ligaments in the knee, and could increase the force necessary to passively move through range of motion, therefore, how to effectively apply cryotherapy still needs to be carefully judged.

ACUTE SOFT-TISSUE INJURY MANAGEMENT OVER THE YEARS

Let's review the historical progress of acute injury management: ICE (ice, compression, and elevation) was initially used before 1978, however, the origin of its use was unknown and it was coined without any sound scientific evidence. The earliest documentation of cold/ice therapy as part of the acute injury management guideline dates back to 1978 when the term RICE (rest, ice, compression, and elevation) was proposed by Dr. Mirkin *et al*[10] in their book "Sports Medicine". Their intent was to use topical cooling to reduce the inflammatory response after acute injury to accelerate healing the vascular function. This initial guideline became deeply rooted in our therapeutic applications for almost 20 years. However, 14 years later, it became a myth when "protection" was included in the protocol (PRICE). Another 14 years later, POLICE (protection, optimal loading, ice, compression, and elevation) replaced PRICE [11], and has become a relatively well-known guideline when long-term rest proved to be detrimental to recovery. In 2019, the latest and most comprehensive acronym: PEACE & LOVE (protection, elevation, avoid anti-inflammatory drugs, compression, and education & load, optimism, vascularization, and exercise)[12] appeared. Since then, ice has been finally removed from the treatment guideline.

RE-THINKING THE USE OF TRADITIONAL COLD THERAPY

Most injured patients report that cold therapy makes them "feel less painful". However, this subjective impression of symptomatic pain reliefs is only experienced in the short-term, and the actual impact of immediate icing on the mid-to-long-term healing process may not remain the same. Moreover, although cold therapy has been widely and empirically used in practice, the way we clinically treat those injuries must continually change based on the most up-to-date and evidence-based research. However, the evidence for the use of cryotherapy is relatively low. There is significant heterogeneity between studies, making it difficult to compare them, and the number of controlled randomized controlled trials (RCTs) remains low[13-16].

We have to keep in mind that anything that reduces inflammation also delays healing since the process of inflammation is an essential aspect of recovery itself. Although cold therapy typically slows the soft tissue swelling to some extent, it does not hasten the recovery process. Ice could be a useful option when our treatment goal is to limit the extent of the oedema[17], since too much or prolonged swelling has been proved to impede the healing process during the recovery period[18], which is typically seen in severe joint sprains. However, when the edema level is not severe (e.g., muscle tear), cold therapy may not be helpful but rather act as a barrier to recovery.

MECHANISMS OF COLD APPLICATION AND PHYSIOLOGICAL RESPONSES

By decreasing the number of leucocytes and granulocytes as well as reducing macrophage infiltration following soft tissue injury, cryotherapy has been proved to reduce inflammation in different body parts[19]. Nevertheless, although applying cold on the surface of the injured site may be effective in pain management or swelling, it could lengthen the recovery process. This is because, when we are injured, our body sends signals to our inflammatory cells (macrophages), which release the hormone-insulin-like growth factor (IGF-1). These factors initiate healing by killing damaged tissue. However, when ice is applied topically, the cold will act as a vasoconstrictor and impede the transport of those inflammatory chemicals and cells to the injured site [20,21]. We may prevent the body's natural release of IGF-1 and, therefore, delay the start of the healing and recovery process. A prolonged period of cold on the skin will lead to a reduction of the blood flow, resulting in tissue death or even permanent nerve damage[22].

SHOULD WE STILL BE USING THE COLD THERAPY?

Therefore, with all of the evidence on the negatives of topically icing injuries, it may reshape our thoughts and raise a doubt: 'If ice delays healing, should we still be using

it?' The answer may not be entirely negative. Although merely applying cold packs or ice on the injured area will reduce inflammation and delay healing, cold therapy does not need to be entirely forbidden since it still has the ability to numb the pain and reduce swelling to some extent. That being the case, we need to know if there is a way to minimize the drawbacks of traditional cold therapy methods and, in the meantime, maintain our ultimate goal to promote tissue healing.

Before addressing that question, we need a basic understanding of the categories of cryotherapy. Generally, cryotherapy consists of two parts based on the way we apply it: local cryotherapy and whole-body cryotherapy. Local cryotherapy is the local application of ice, cold packs, or cold gases, while whole-body cryotherapy primarily includes gaseous application and cryostimulation[23,24]. Conventional cold therapy always leads to a prolonged application of cold temperatures, which may cause serious side effects such as nerve injuries, healing process restriction, or neuromuscular impairments. Then what about the others?

HYPERBARIC GASEOUS CRYOTHERAPY

It is now the time to highlight a more sophisticated application: Hyperbaric gaseous cryotherapy. It is an analgesic process first developed by Cryonic company in 1993 by spraying microcrystals of CO₂ at -78°C under high pressure (50 bars) on the painful site. This treatment technique, also referred as neurocryostimulation (NCS)[25], has shown the ability to reduce skin temperature to a greater extent than a simple ice bag by using a medical gun projecting compressed gas at high speed. This technique induces a more pronounced physiological response called "thermal shock", which triggers a swift systemic response by cutaneous vasoconstriction in our human body. The effects of thermal shock are always beneficial, since it has proved to induce greater analgesic, anti-inflammatory, vasomotor, muscle relaxing, anti-oedematous, and other beneficial effects than conventional cold therapy[25-27]. Gaseous cryotherapy triggers a swift systemic response through cutaneous vasoconstriction, and this response could cause severe vasoconstriction followed by vasodilation, called "hunting reaction", through sympathoadrenal nervous system involvement, endogenous norepinephrine, and cortisol secretions[27]. These effects have been proved to hasten the recovery and healing process following soft tissue injuries[28]. Moreover, NCS could be used not only for the treatment of acute soft-tissue injuries (*e.g.*, ligament and tendon injuries and muscle injuries), but also benefit older patients with acute pain significantly.

It is generally accepted that cryotherapy techniques providing more rapid cooling and reducing temperature may be more effective than slower cooling techniques like traditional ice or cold pack[3,27-29], and that is one of the reasons why hyperbaric gaseous cryotherapy could trigger more systemic vasoconstriction and is less likely to cause secondary injury than traditional cold therapy. Evidence[30] also indicates that skin temperature must reach 14.4 °C for analgesia and 13.8 °C to reduce local blood flow and obtain therapeutic benefits from the cold application. However, the surface temperature only decreases to 1-10 °C when ice is applied topically for the cooling of tissues from the baseline skin temperature[31-33]. Therefore, using an ice pack is always hard to achieve the particular low skin temperature to induce analgesia, while hyperbaric gaseous cryotherapy has the ability to shorten cooling time drastically and drop the skin temperature to about 4 °C through the sublimation of gas on the skin under high pressure.

Thus, we could say that this innovative cold treatment overcomes most of the limitations of traditional cold therapy, meanwhile effectively promoting the analgesic and anti-inflammatory effects. It further enhances the vasodilation activity to reach the required level for treatment. Therefore, we must acknowledge that there has been a significant evolution in injury rehabilitation from traditional cold therapy (topically cooling) to hyperbaric gaseous cryotherapy. Table 1 describes a detailed comparison in various aspects between traditional cold therapy and hyperbaric gaseous cryotherapy.

The question remains, could we say that hyperbaric gaseous cryotherapy represents the gold standard in treatment that we have been seeking? Unfortunately, it is still too early to draw conclusions based on the relatively poor and speculative evidence that we have now. Here, we offer some examples of hyperbaric gaseous cryotherapy in some common clinical cases, illustrating its controversial efficacy.

When studying the effect of NCS in individuals with acute lateral ankle sprains, Tittley *et al*[34] suggested that NCS is no more effective than traditional ice application in improving functional recovery, pain, edema, and ankle dorsiflexion range of motion during the first 6 wk of physiotherapy treatments. Similar results were reported in

Table 1 Comparison between application of gaseous cryotherapy and traditional cold therapy

| | Hyperbaric gaseous cryotherapy | Traditional cold therapy |
|--|--|--|
| Cooling modality | Projection of CO ₂ microcrystals under high pressure (75 bar) and low temperature (78 °C) | Simply locate ice or a cold gel pack on the top of injured skin |
| Lowest temperature can be reached | Below 2 °C[27] | Hard to drop below 13.6 °C[21,27] |
| Time to achieve enough low temperatures to produce local analgesia | 20-45 s[27,34-35] | 15-30 min[27,34] |
| Time to recover the normal skin temperature | 5 min[27] | 60 min[3-5] |
| Amount of heat absorption | Greater and more rapid[34] | Lesser and more slowly[34] |
| Cutaneous vasoconstriction area | Systemic[27] | Localized only to the cooled area[27] |
| Physiological response after application | Thermal shock - a swift systemic response resulting in cutaneous vasoconstriction[27,34-36]; profound vasomotor effects[34]; modulates inflammation and release cytokines; sooner metabolic rate[27,34-35] | Prolonged application may happen, which would cause neuromuscular impairments, frostbite and nerve injuries [19,27]; prevent the release of IGF-1[5,6]; slower metabolic rate[34-35] |
| Clinical treatment effect of application | Controversial results[34-36] across different studies when comparing the two | |

IGF: Insulin-like growth factor.

RCT research by Demoulin *et al*[35], who concluded that gaseous cryotherapy was no more beneficial than routinely used strategies(cold pack and cryo-cuff) following total knee arthroplasty. However, the authors discussed that they might have underestimated its benefits because of the time effects, and other limitations observed in their trial (*e.g.*, cooling to a warmer temperature than the target value). In contrast, a prospective study conducted by Chatap *et al*[36] reported that hyperbaric CO₂ cryotherapy is an innovative tool to achieve acute and chronic pain relief in older patients. However, the result may not be valid since there is no control or comparison group. Therefore, the existing studies may have shown conflicting results on recovery using cryotherapy compared to traditional ice application.

Confirmation of whether hyperbaric gaseous cryotherapy is superior to traditional cold therapy modalities still needs to be evaluated. The number of studies using a good methodological experimental design in a larger population is still inadequate. In addition, gaseous cryotherapy is more expensive and requires specific training; therefore, it may not be readily available to a more general population. Thus, when we choose the type of cryotherapy, we need to take specific advantages and drawbacks of each, including the context of the therapy into account.

CONCLUSION

In summary, when considering a cryotherapy protocol for treating soft-tissue injuries, variables such as its forms, local or whole-body, physical agents, cooling temperature, and time duration must be well-designed and controlled. The existing knowledge gaps have contributed to the persistent difficulty in clarifying the clinical usefulness of cold therapy in clinical healthcare. Hopefully, this will be addressed in future studies. Effective randomized controlled clinical trials with demonstrated methodological quality are needed to better evaluate potential utility and superiority of hyperbaric gaseous cryotherapy. That effectiveness can be demonstrated by considering different target populations, injuries, and treatment protocols. Continuing education and applying quality research should remain a focus for clinicians to develop better treatment outcomes for patients.

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