Alternative treatments for muscle injury: massage, cryotherapy, and hyperbaric oxygen

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Abstract Current evidence suggests that popular alternative therapies such as massage, cryotherapy, and hyperbaric oxygen exposure as currently practiced on humans have little effect on recovery from minor muscle damage such as induced by exercise. While further research is still needed, hyperbaric oxygen exposure shows clear promise for potentially being a successful adjunct treatment for enhancing muscle repair and recovery from more severe crush or contusion injury in humans. Cryotherapy or icing, as currently practiced, will not likely be successful in cooling muscle sufficiently to have any significant influence on muscle repair regardless of the degree of injury. However, based on studies in animal models, it may be that if sufficient muscle cooling could be achieved in humans, it could actually delay recovery and increase muscle scarring following significant muscle damage. Conclusions about the effectiveness of massage on influencing muscle recovery from more severe injury cannot yet be made due to a lack of experimental evidence with a more significant muscle damage model.

Keywords Muscle damage · Massage · Cryotherapy · Hyperbaric oxygen · Muscle repair

Introduction

Muscle injuries are common in sports as well as recreational physical activity. There is a continuum of severity of muscle

disruption or injury ranging from mild to moderate exercise-induced damage through varying degrees of muscle strain and tearing up to significant contusion, laceration, and crush injury [1, 2]. The mechanisms of muscle repair and their manifestations also follow this continuum with responses that vary with the degree, extent, and localization of damage [2].

A variety of treatments have been suggested as having the potential to accelerate muscle repair with rest, limb elevation, and icing often being recommended as a typical conservative treatment for most mild to moderate muscle injuries [2, 3]. Other treatment alternatives that have been suggested to enhance muscle healing include various pharmacological therapies such as angiotensin II receptor blockers, platelet-rich plasma, non-steroidal anti-inflammatories (NSAIDs), glucocorticoids, fenoterol, insulin-like growth factor-1 (IGF-1), and decorin; nutraceutical therapies such as curcumin and suramin; and alternative therapies such as hyperbaric oxygen, massage, ultrasound, and cryotherapy [3, 4]. While there is some clear evidence for the potential for some of these interventions to enhance some aspects of muscle repair and recovery, others are less well supported and some have been shown to be essentially ineffective [1–4]. Additionally, while some of these treatments have demonstrated possible efficacy in animal models of muscle damage, they lack data from human studies [1, 2].

This review will critically examine current evidence regarding the potential for three high-profile or common alternative treatments (massage therapy, cryotherapy, and hyperbaric oxygen) for muscle injury to influence the course of muscle repair and its potential complications to determine if they could be recommended as primary or adjunct treatments for various types or degrees of muscle injury. Potential physiological mechanisms for their efficacy will also be discussed.

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Massage therapy

Massage therapy involves topical stroking, kneading, and/or striking of the skin and underlying musculature for periods of time such that pressure and muscle distension are produced. Massage is a widely used treatment for mild to moderate muscle injuries, for reduction of muscle soreness and for enhancement of post-exercise muscle recovery [3, 5, 6]. Despite its common usage as a potentially therapeutic intervention for enhancing muscle repair, its effectiveness and potential mechanisms of action are still controversial [6, 7]. Studies examining the effects of massage on indirect indicators of muscle damage and repair such as muscle soreness, force recovery, and swelling in humans have generally failed to demonstrate significant or consistent benefits [6–9].

Muscle force loss ranging from 15–60 % of pre-exercise values is a commonly seen following muscle damage induced by eccentric exercise [1]. This loss is followed by a delayed recovery of force which may typically take between 3–14 days to normalize depending on the degree of muscle damage. The rate of return of muscle force has been reported to be a reliable indirect indicator of the rate of muscle repair and has often been used to assess the effectiveness of various therapeutic modalities in influencing muscle repair processes [1, 4, 10]. The loss and recovery of muscle force following muscle damage has been variously attributed to direct muscle sarcomere damage and related muscle excitation-contraction uncoupling via disruption of muscle membranes and t-tubules leading to disruption of calcium channels [1].

A number of studies involving human subjects have examined the potential effectiveness of various forms, timing, and duration of massage therapy on eccentric exercise-induced muscle damage using muscle force recovery as an indicator of post-eccentric exercise muscle repair rates. In a review of a number of studies, Torres et al. [7] recently concluded that except for some possible minor benefits at 1 h post-exercise, massage therapy does not have any significant effect on the rate of muscle force recovery following eccentric exercise at any time point up to 72 h post-exercise. Other studies have also confirmed the above findings and extended the time points of no effect of massage on muscle force recovery to 96 h post-exercise [9, 11] and to findings of no effect on rate of recovery of functional movements such as one-legged long jump [12].

Muscle soreness and its amelioration have also been used as an indirect indicator of muscle damage and repair [1]. The soreness sensation is thought to be related to post-damage muscle inflammatory response when invading inflammatory white blood cells release bradykinins and prostaglandins or influence the production of other substances within muscle which may act on muscle nociceptors to induce soreness sensation [1]. Muscle inflammation is important in initiating muscle repair, but may also induce further muscle damage [1, 3, 13]. Therefore, amelioration of muscle soreness by massage

may indirectly indicate a reduction in inflammatory response and possibly a reduction in muscle damage. As with muscle force recovery, reviews of literature involving studies using various types, frequencies, and durations of post-eccentric exercise massage interventions have concluded that massage is of little consistent effect in mitigating muscle soreness sensation at any time point up to 96 h post-exercise [3, 14]. In this regard, a review by Tiidus [14] concluded that “if massage has any effect on muscle soreness, it is small, transitory and of lesser magnitude than the effect that can be brought about by light exercise of the affected muscles.”

Hence, the preponderance of research to date, using human subjects and indirect indicators of muscle damage and repair such as return of post-exercise muscle force or muscle soreness sensation, has not shown massage to have major positive effects on muscle damage and repair indices. Nevertheless, a few recent studies involving animal models of muscle damage and a human study looking at massage effects on other indicators of muscle inflammation and repair have shown some promise for massage-like interventions in speeding muscle recovery from exercise-induced disruption.

Recently, a series of studies from the Best laboratory used a rabbit model and “massage-like compressive loading” (MLL) which applied quantifiable and repeatable lengthwise strokes to muscle for 15 min for four consecutive days [15–18]. These studies reported significantly enhanced muscle force recovery following muscle damage induced by forced eccentric contractions in animals exposed to MLL relative to controls, particularly if the MLL was first administered immediately following the lengthening protocol [15, 16, 18]. Significant reductions in muscle inflammatory-related responses as exemplified by reduced edema and white blood cell (neutrophils and macrophages) infiltration were also noted in the MLL-treated animals. MLL has also been demonstrated to modulate passive stiffness of muscle via positive changes to its viscoelastic properties in the rabbit model [17].

While the muscle injury induced by this protocol (forced muscle lengthening against electrically induced contracture) is not identical to that seen with voluntary exercise in humans, the repeated findings from these studies do provide support a role for massage-like pressure in enhancing indicators of muscle recovery and modulation of immune-related responses in this animal model [15].

Another relatively recent study which supports possible positive effects of massage on muscle repair-related processes was reported in untrained humans [19]. This study applied 10 min of massage to the vastus muscles of one leg immediately following exhaustive cycling exercise while leaving the control leg unmassaged. Biopsies were taken from the vastus lateralis of both legs at 10 and 150 min following the massage. The study reported that inflammatory-related signalling and responses, specifically production of the inflammatory cytokine tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6)

as well as the phosphorylation of heat shock protein 27 (HSP27), were attenuated in the massaged leg relative to the control leg [19•]. Additionally, the upregulation of nuclear peroxisome proliferation-activated receptor- γ co-activator 1 α (PGC-1 α) in the massaged leg suggested enhanced signalling for mitochondrial biogenesis [19•].

As a number of mechano-transduction pathways in the massaged muscles were also activated, it was suggested that massage-induced muscle stretch and strain may induce the signalling which reduces muscle inflammatory signalling responses [19•]. The authors further suggested that reductions in some of the inflammatory signalling pathways may also influence pain and muscle soreness sensation [19•]. Historically, massage benefits have putatively been ascribed to its potential enhancing effects on muscle blood flow. However suggestions of the ability of massage to affect muscle blood flow have repeatedly been refuted by studies that show no effect, or even attenuating effects of massage on muscle arterial or venous blood flows [11, 20, 21].

While the findings of reduced inflammatory signalling in massaged muscles are very interesting and warrant further research, they have yet to be directly correlated to any positive findings for actual improved muscle repair, reduced direct measures of inflammation, or attenuated muscle soreness sensation in human subjects, all of which have not been reported to be significantly influenced by massage in previous studies [6, 8, 9]. It is apparent that further research using human subjects examining more specific indicators of muscle damage, inflammation, repair, and function combined with measures of muscle soreness sensation is needed to fully elucidate what, if any effects massage of various types, frequencies and durations may have on recovery from exercise-induced muscle damage.

The influence of massage on recovery from more severe muscle injuries or contusions has not been as well researched. While it has been suggested that massage may be able to reduce post-damage scar tissue formation or calcification, no studies have been conducted to verify such claims [6].

Cryotherapy

Cryotherapy involves the application of cooling via ice packs or similar methods to the skin surface above muscle in order to temporarily reduce muscle temperature, induce vasoconstriction, and inhibit pain sensation. The potential benefits of cryotherapy for healing of muscle following various trauma-induced damage are controversial. Animal studies have reported both potentially beneficial and detrimental effects of icing on various physiological aspects of muscle recovery [22, 23, 24••]. Human studies on application of cryotherapy in the form of icing to promote muscle healing exercise-induced or other types of muscle damage have generally shown little or no beneficial effects [22, 25, 26]. It has been suggested that human studies have typically failed to induce

the degree of muscle cooling seen in animal models (10 °C in animals vs 25 °C in human muscle cooling studies) and therefore may not have achieved the temperature changes necessary to induce any significant effects [22].

Animal studies have shown both positive and negative physiological influences of muscle cooling on indices of muscle inflammation and repair-related responses, suggesting that specific repair-related mechanisms may be either enhanced or inhibited by cryotherapy during the post-injury phase [22, 23, 24••]. For example, Schaster et al. [23] induced a closed muscle injury in the thigh muscles of rats via a controlled impact. The limb was then cooled for 6 h such that muscle surface cooling to 8 °C was achieved and compared to a control, uncooled injured limb. At 24 h post-injury, the muscle in the cooled limb, relative to the control injured muscle, exhibited significantly reduced intramuscular pressure, reduced adhering and invading granulocytes, and reduced tissue damage and myonecrosis (assessed histochemically). In addition, restoration of diminished functional capillary density was also improved in the cooled limb [23]. The authors concluded that the use of prolonged cryotherapy following closed muscle injury improved “nutritive perfusion” and reduced leukocyte-mediated post-injury muscle damage and potentially reduced the risk of compartment syndrome at 24 h following this type of injury [23]. Other studies have also reported reduced muscle necrosis and apoptosis consequent to cryotherapy in contusion-induced muscle injury in animal models [22].

A more recent study [24••] extended the examination of cryotherapy in crush-injured muscle of rats to up to 28 days of recovery to assess its effects on mechanisms of muscle repair, collagen deposition, and muscle recovery. Takagi et al. [24••] also cooled rat muscle to a surface temperature of 10 °C by applying ice packs for 20 min at 6 and 12 h and 1–7, 14 and 28 days post-injury. Their findings supported previous reports of possible beneficial effects of cryotherapy [e.g., 23] by also noting an early reduction in muscle degeneration and leukocyte infiltration in the cooled muscles and suggested that this may in part be due a temperature-induced reduction in calcium activation of calpain activity, which results in a reduction in calpain-induced muscle degeneration [24••].

More significantly, the cryotherapy-induced reduction in muscle leukocyte infiltration leads to an attenuation of muscle IGF-1 and TGF- β 1, which are signalling factors for muscle satellite cell activation [24••]. As a result, there were significant delays in satellite cell-induced repair and recovery from crush damage in muscles that were exposed to cryotherapy over 28 days, relative to muscles that were not treated with cooling. In addition, in the cryotherapy-treated muscles, collagen deposition or scarring was significantly more extensive at 14 and 28 days post-injury relative to the untreated muscles. These findings lead these researchers to conclude that regular post-injury cryotherapy delayed and impaired late-stage muscle regeneration and also resulted in thicker collagen

deposition and that cryotherapy was thus counterproductive to optimal muscle healing following crush injury in their rodent model [24••]. While earlier studies had interpreted evidence of reduced indices of muscle damage and leukocyte infiltration consequent to post-injury cryotherapy in the first days following injury as being beneficial [23], their longer-term effects seem to be to delay ultimate repair and augment collagen deposition-associated muscle scarring [24••].

Human studies have generally found little beneficial effect of icing on indices of muscle recovery or repair, following exercise-induced muscle damage [25, 26] and there is little experimental evidence from humans as to the effectiveness of cryotherapy on muscle recovery following contusion-type muscle injury [22]. It has been suggested that due to much larger limb size, adipose tissue insulation and muscle diameter in humans, relative to rodent models, the degree of cooling induced by external application of ice is such that it is difficult to induce muscle temperature reductions to much below 25 °C [22]. Based on animal studies, this limited reduction in muscle temperature may not be sufficient to induce any positive or negative effects of cryotherapy on muscle inflammation and repair mechanisms [22]. Hence, it is likely that the use of cryotherapy in humans as a therapeutic modality for post-damage muscle repair does not induce robust enough changes in muscle temperature to have significant effects on repair mechanisms. Additionally, if cryotherapy in humans were administered such that it cooled injured muscle to levels seen in animal studies, it may be that longer-term recovery from more severe injury would be delayed as reported in recent animal studies [24••].

Hyperbaric oxygen

Hyperbaric oxygen therapy “is the therapeutic administration of 100 % oxygen at environmental pressures greater than one atmosphere” [27]. It has been suggested that hyperbaric oxygen therapy can be an effective treatment for muscle crush injuries, muscle contusions, and sports-related injuries [28, 29]. The evidence for these benefits comes primarily from studies using animal models [30]. Hyperbaric oxygen therapy may work by reducing hypoxia and enhancing blood supply in damaged soft tissues, thereby helping preserve energy homeostasis and limiting edema and further leukocyte infiltration, attenuating oxidative damage and enhancing healing [27, 30, 31].

Human studies involving treatment of minor exercise-induced muscle damage or sports injuries have not typically demonstrated significant benefits from hyperbaric oxygen therapy in enhancing indices of muscle recovery or repair [27, 30]. For example, a study by Babul et al. [32] found no effect of exposure of human subjects, subsequent to eccentric exercise-induced muscle damage, to 100 % oxygen at 2 atm

for 1 h/day for 4 days, on muscle soreness, return of muscle force, muscle swelling or blood creatine kinase, or malondialdehyde levels.

However, a number of studies using animal models examining recovery from more extensive muscle crush injury or muscle toxin-induced degeneration have reported positive effects of hyperbaric oxygen exposure [30, 31, 33]. For example, a recent study by Horie et al. [33••] reported that hyperbaric oxygen treatment (100 % oxygen at 2.5 atm for 120 min, daily for 5 days post-injury) enhanced post-damage muscle satellite cell proliferation and myofiber maturation in a rat model. Recovery of post-damage muscle size and maximum force-producing capacity were also better in the animals exposed to hyperbaric oxygen. In particular, the hyperbaric oxygen exposure accelerated muscle regeneration relative to control animals by inducing earlier muscle satellite cell activation and proliferation, possibly by its enhanced stimulation of IGF-1 expression in the damaged muscles [33••]. Based on studies which demonstrated the regulatory effects of oxygen on satellite cells [34], the authors also suggested that by reducing post-damage muscle hypoxia, hyperbaric oxygen therapy may serve as a “developmental trigger” to induce muscle cell differentiation by enhancing oxygen availability and thereby inducing myoblasts to move out of their undifferentiated states [33••].

The difference between the positive findings of hyperbaric oxygen exposure on muscle repair seen in animal models relative to the general lack of effects seen in human studies may be related to the degree of muscle damage induced by the different experimental models. The human studies typically involved relatively minor damage induced by eccentric muscle contraction while the animal studies involved much more extensive muscle damage induced by administration of muscle toxins or crush injuries. It may be that the potential beneficial effects of hyperbaric oxygen may only be manifested in recovery from extensive muscle damage. Recently, it has again been proposed that hyperbaric oxygen therapy could be effective in treating more extensive muscle damage in humans such as that induced by crush injury [28]. In support of this suggestion, there also have been recent reports of reduced complications following muscle crush injury in humans who have been exposed to hyperbaric oxygen therapy [35]. While further research is needed to define the mechanisms and the range of potential benefits of hyperbaric oxygen therapy on healing following more severe muscle injuries in humans, it seems that there is growing evidence for its benefits in these situations.

Conclusions

Current evidence suggests that popular alternative therapies such as massage, cryotherapy, and hyperbaric oxygen

exposure, as currently practiced on humans, have little effect on recovery from minor muscle damage such as induced by exercise. While further research is still needed, hyperbaric oxygen exposure shows clear promise for potentially being a successful adjunct treatment for enhancing muscle repair and recovery from more severe crush or contusion injury in humans. Cryotherapy or icing, as currently practiced, will not likely be successful in cooling human muscle sufficiently to have any significant influence on muscle repair regardless of the degree of injury. However, based on studies in animal models, it may be that if sufficient muscle cooling could be achieved in humans, it could actually delay repair and increase muscle scarring following recovery from significant muscle damage. Conclusions about the effectiveness of massage on influencing muscle recovery from more severe injury cannot yet be made due to a lack of experimental evidence with a more significant muscle damage model.

Compliance with Ethics Guidelines

Conflict of Interest Peter M. Tiidus declares that he has no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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