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Article

Cold water immersion and anti-inflammatory response: a systematic review

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Abstract: Cold water immersion (CWI) and other post-exercise techniques have become increasingly popular with goals of reducing inflammation and increasing mitochondrial capacity in skeletal muscle following exercise. CWI is the process of submerging the majority of the body in cold temperature water for a certain period. The thought behind this is to hasten the recovery process and reduce signs of fatigue in skeletal muscle. Proposed mechanisms of CWI are to decrease nerve conduction, resulting in reduced perception of pain, as well as a change in the pressure and temperature of skeletal muscle blood flow [16]. The decrease in temperature and metabolism of muscle tissue is thought to limit hypoxic stress and generation of reactive oxygen species, which can cascade inflammatory pathways [17]. CWI has been used in many modalities including high school, and elite athlete recovery protocols. Some practices include switching from cold to hot temperature water immersion; this is utilized more with injury protocols and will not be focused on [13]. More of the proposed benefits for CWI are mental clarity, antidepressant properties, weight loss, and anti-inflammatory effects. The focus of this paper is to review the literature of CWI in relation to its proposed anti-inflammatory effects.

Keywords: Cold Water Immersion, Mitochondrial Capacity, Skeletal Muscle, Fatigue, Cellular Stress, Anti-inflammatory, Nerve Conduction, Hypoxic Stress, Reactive Oxygen Species.

1. Introduction

Inflammation has been shown to occur after aerobic exercise [1]. This is a necessary process the body initiates for muscle to repair and grow. The recovery process is a interaction of inflammatory cells, satellite cells, fibroblasts, and endothelial cells [2,10]. It has been shown that reducing inflammation after exercise can reduce muscle repair [9]. Specifically in one study, CWI was shown to reduce gains in muscle mass following 3 months of resistance training [11]. However, when inflammation is present in the body for prolonged periods, this is referred to as chronic inflammation. Chronic inflammation has been shown to have adverse effects on the body as it can lead to stressed skeletal muscle tissue [3]. The goal of CWI and other recovery techniques is to decrease localized inflammation at the muscle site. This is thought to happen via two pathways. First being vasoconstriction of muscle blood vessels, reducing circulation of inflammatory cells. Second being reduction of myokines and cytokines, which are involved in mediating inflammatory pathways [4]. What is unknown about CWI in the literature is if the mitochondrial capacity increases or the inflammation response to exercise decreases. As stated before, this review article will discern from the science if the promised effects happen from exposure to cold water. The difference in this review from others is that this looks at the most recent literature published having a focus on both athletic and general population's response to treatment. There is a lack of research on CWI on general population use and as said before, it is becoming increasingly popular for daily intervention. For this use, the literature is scarce in showing the many proposed benefits. Another difference of this review between others is that this takes a look at the most recent literature published, and it focuses on the role that the PGC-1 alpha, cytokines, MAPK, and JNK pathways play in inflammation following CWI.

2. Methods

Materials used for this review are research studies published in the last 20 years. These studies were analyzed for findings and implications on the field of CWI, explaining found benefits and statistically significant hypotheses for the same proposed benefits. Article searches conducted from Microsoft EndNote in January, February, March, and April 2019 were reviewed for the purpose of this paper. Keywords in the search process include cold water immersion, human, inflammation, and exercise, MAPK, PGC-1 alpha, p53 protein, resistance training, aerobic training, skeletal muscle, JNK, AMPK, pathway, marker, and mechanism. Studies with experimental groups including animal subjects were not included in this review.

3. Markers of Inflammation

Three inflammatory markers will be examined in depth for the purpose of this review. Mitogen activated protein kinase (MAPK), c-Jun N-terminal Kinase (JNK), and Peroxisome proliferated- activated receptor y coactivator 1α (PGC-1 alpha). MAPK is a family of proteins consisting of Extracellular signal-regulated kinases (ERK) and 1 and 2, p38 MAPK, JNK, and ERK5 or big MAPK [37]. PGC-1 alpha is a transcriptional coactivator that is known to influence a wide variety of metabolic effects. PGC-1 alpha has been identified in mitochondrial rich tissues including skeletal muscle, heart, kidney, liver, and brain. Stress in skeletal muscle during exercise is one of the few mechanisms in which these markers will be enacted [2-5, 7-11].

4. Mitogen activated protein kinase (MAPK)

Inflammation activity is noted following exercise with cytokines, neutrophils, and other inflammatory markers increasing in the blood samples [2,5,8]. Specifically MAPK and NF-kB signaling in skeletal muscle increases post exercise. Both MAPK and NF-kB are involved in regulating inflammation pathways, which is beneficial for hypertrophy. [21-24]. Interestingly, in certain amounts, MAPK and NF-kB extend insulin resistance and protein catabolism. This could be potentially looked at in regards to diabetes or sarcopenia intervention [20]. As for short intense exercise, P38 protein and MAPK are shown to be increased in muscle tissue [25].

5. c-Jun N-terminal Kinase (JNK)

JNK is involved in hypertrophy of muscle tissue, as shown when it is present; it causes muscle fibers to grow via the transcription factor SMAD2, which inhibits myostatin [36]. In human skeletal muscle, this pathway is activated through resistance training and has not been shown to be active during endurance training. As said, JNK coincides with the SMAD2 a known regulator of muscle remodeling via inflammation [29,30]. It has hypothesized by Lessard and colleagues that JNK activation during aerobic exercise inhibits endurance adaptation in the muscle [36]. Inflammation activity was noted following exercise with cytokines, neutrophils, and other inflammatory markers increasing in the blood [2,5,8,36]. It is still unclear how CWI affects JNK regulation as no studies involving JNK measurements in direct correlation with CWI could be found.

6. Peroxisome proliferated- activated receptor y coactivator 1α (PGC-1 alpha)

PGC-1alpha is a key factor for endurance exercise adaptation in skeletal muscle. In addition, this is also shown by PGC-1alpha initializing oxidative metabolism in muscle and other organs [32]. High amounts of PGC-1alpha in the muscle will trigger a shift from a glycolytic muscle fiber dominant environment, to an oxidative dominant environment [31]. PGC-1alpha is elevated post-exercise, which is correlated with tissue macrophage activity. Elevated PGC-1 alpha also inhibits activity of NF-kB, the main pro-inflammatory genetic expression [32]. However, when being exposed to inflammatory stimuli, immune cells will be present in the localized area affecting the expression of pro and anti-inflammatory genes [33,34]. PGC-1 alpha was shown by Kong et al. to play a protective role against skeletal muscle atrophy [38]. Interestingly, PGC-1 alpha MRNA was increased twofold 2 hours after exercise, whereas PGC-1 alpha protein content was unchanged [25]. It is still unclear how PGC-1alpha reduces muscle damage. This is extremely important as the volume of this potential pathway could be beneficial or detrimental through post exercise protocols such as CWI.

7. Cold Water Immersion Effect on Adaptation from Specific Training Modalities

7.1. Aerobic

There were increases in cardiovascular endurance in all of the studies involving CWI as a recovery protocol following exercise [5,8,10,11,18,27,39-41]. Exercise was determined to be the main factor of an increase in cardiovascular endurance from these studies. Mitochondrial capacity did not increase with CWI introduction post-exercise nor were anti-inflammatory pathways affected as shown by no effects on PGC-1alpha or p53 protein content [5]. Regular post exercise CWI had no effect on phosphorylated (p-) AMPK, p-p38 MAPK, and PGC-1alpha [5]. PGC-1alpha was increased with water immersion following exercise along with other mitochondrial proteins. This indicates that mitochondrial biogenesis may be enhanced from water immersion, but not specifically CWI [40]. The main derivative to produce mitochondrial proteins post-exercise found in the study by Ihsan and colleagues was by cooling the temperature of the legs. One hypothesis for later research is at what specific cooling temperatures are most beneficial [40]. On the other hand, a general consensus of studies reviewed showed heart rate increase with the introduction of CWI, but no aerobic benefits occurred [5,39]. This was also shown by no change in mitochondrial biogenesis markers following CWI [5].

7.2. Resistance Training

Resistance Training (RT) is defined as lifting a load that requires use of skeletal muscle [1,4,8,10,11,19]. Training with an external or body weight load can imply vibrations and contractions in the muscle tissue [27,28]. This can have damaging effects, leading to inflammation, fatigue, or delayed onset muscle soreness (DOMS) [26]. CWI was shown to increase submaximal workload of skeletal muscle compared to an active recovery protocol [41]. The proposed benefit is to allow the athlete to complete more work short term, which could be extrapolated to help in the long term if the goal is hypertrophy. In the literature, studies show the introduction of CWI had minimal to no effect on benefitting maximal strength recovery after eccentric exercise [42,43]. It has also been shown that inflammation is not affected and the reduction of myokines and cytokines does not occur with CWI [4,8].

7.3. Sport Specific

CWI as a therapy for post exercise recovery is a modality that is common to be in use with sports teams [44-49]. As Crowther et al. outlines, a total of 331 athletes were surveyed on recovery techniques utilized after competition at a state, national and international level. Figure 1 is adapted from the research and shows feedback from athletes on their choice of post exercise recovery. The athletes were all from different sports.

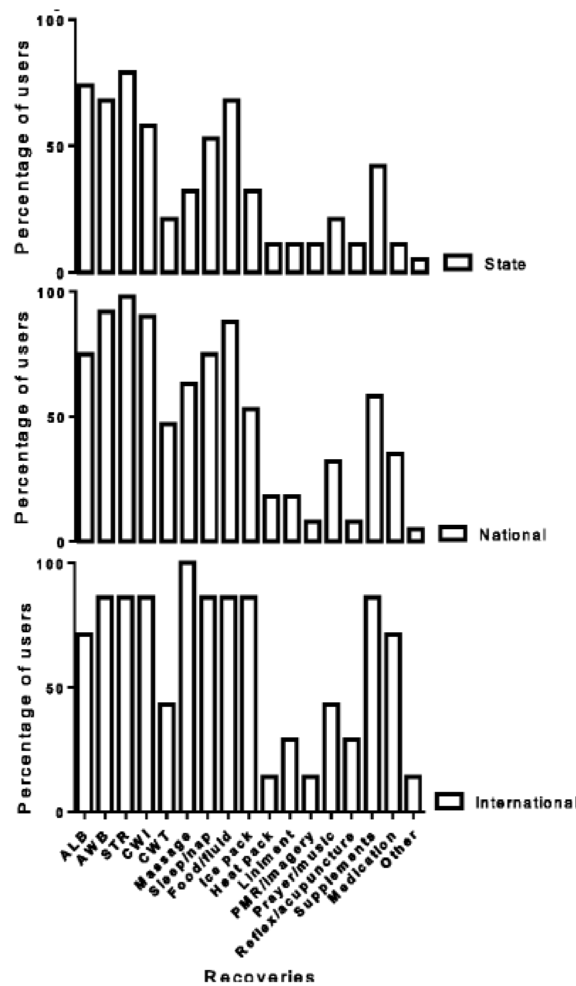

Figure 1. Active land-based recovery (ALB), Active, water based recovery (AWB), Stretching (STR), Contrast water therapy (CWT), Progressive muscle relaxation (PMR), Reflexology (Reflex).

As shown in **Figure 1**, CWI had a high usage rate in all 3 athletic populations. Other techniques used by athletes are included. Reported findings from CWI are decreased pain perception and fatigue [35,49]. For sprinters, CWI for 10 minutes following High intensity 120 meter sprints did not significantly reduce plasma concentration of inflammatory markers. CWI in both 10 degrees celsius and 20 degrees celsius for 30 minutes actually increased inflammatory markers [18]. Exercise that induces weight loss has been shown to decrease markers of inflammation including C-reactive protein (CRP) as shown by Church et al [1]. This is relevant to sports that require weight gain or weight loss at a constant change of body composition for competition such as wrestling or mixed martial arts.

8.0 Summary and Practical Applications

Some key findings from the literature includes, thermoregulation of the body during CWI is in an increased state as evidenced by a flow of hormones and anti-inflammatories throughout the body. Anti-inflammatory pathways are turned on by increasing PGC-1 alpha protein and are mediated by cytokines, myokines, and p53 protein. CWI neither slowing down nor speeding up mediation of these pathways in the subjects is interesting due to metabolic rates in the body increasing by 350% following CWI at 14 degrees Celsius [6]. CWI was also shown to have minimal or a negative effect on muscle recovery for the goal of hypertrophy. As for submaximal strength increase, this is a promising subject and requires more research.

Key limitations in the literature seem to be that the adaptations of CWI are focused mainly on performance in an athletic population. Another is that most studies examine systemic inflammation markers in the blood rather than biopsy samples. This may not be transferable to how it could potentially benefit health. On average, the hypothesis regarding benefits of CWI seem to be slight and ambivalent. One unique finding is the hypothesis that in any water immersion, the hydrostatic pressure of the water has been shown to increase cardiac output as high as 102%. This potentially makes sense due to vascular pressure increasing from the immersion. The human cardiorespiratory would increase the stroke volume, heart rate, and cardiac preload. The increase in heart rate would not be the goal, but in comparison to active recovery, similar physiological processes occur without any additional energy expenditure [13-15]. There is some science to say that CWI mediates gene expression involving mitochondrial biogenesis and angiogenesis after high intensity exercise [19]. This promising technique needs more review. In conclusion, not much is yet known about the anti-inflammatory effects of CWI, if any. Most of the literature focuses on performance outcomes and the information on anti-inflammatory response is vague. This is a promising subject in the field as more science is released. CWI could also be a great tool to use for alleviating chronic inflammation, which has been proven detrimental on the body [3]. There is a need to redefine a study focus as information is released on how CWI could potentially benefit athletes of different sports based on specificity or involving general population. Many questions still reside for the technique such as, timing of the day during therapy, sport and goal specific, and adaptation response from CWI. Depending on the goal of the adaptation for both an athletic or general population, CWI may be either useful or unnecessary. For athletes who may compete day-to-day in bouts of exercise, this is extremely important regarding potential performance in certain sports. When in repeated bouts of exercise with short-term rest over multiple days, CWI may be useful for its analgesic effect. As more science is released on the subject, the use of the technique and rationale behind it will become clearer.

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