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Connecting the Dots: Exploring the Interplay of Calcium, Delayed Onset Muscle Soreness, and the Myofascial System

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Abstract

Introduction

This study aimed to elucidate calcium's role in muscle fiber inflammation, delayed onset muscle soreness (DOMS), and myofascial remodeling following exercise. The objective was to clarify the etiologies of DOMS in relation to calcium physiology to allow clinicians to modulate its presentation and tissue adaptation more effectively.

Methods

A review was performed of the current literature regarding the role of calcium in myofascial damage after strenuous exercise. A database search was conducted via PubMed. The types of studies included were randomized controlled trials, crossover studies, double blind studies, retrospective studies, and meta-analysis.

Results

This study discovered the largest contributor to DOMS is deep fascia damage, which had a higher concentration of nociceptors compared to muscle fibers. Fibroblastic remodulation of connective tissue was preceded by the cell signaling actions of calcium. Techniques including massage therapy and pneumatic compression devices work through a similar mechanism by providing an external force resulting in increased regional blood circulation and decreasing the inflammation that is the pathophysiological hallmark of DOMS. Treatment modalities such as cold-water immersion and therapeutic ultrasound have demonstrated mixed results on the efficacy in alleviating the symptoms of DOMS.

Conclusion

In unraveling the intricate interplay of calcium dynamics, DOMS, and myofascial remodeling, this study has shed light on crucial mechanisms influencing post-exercise tissue adaptation. Calcium emerges as a multifaceted player, intricately involved in the inflammatory cascade at the myofibrillar level, as well as within the fascial and myofibroblast domains. Significantly, deep fascia damage, characterized by heightened nociceptor concentration, emerged as a primary instigator of DOMS following eccentric exercise. Understanding the pivotal role of calcium in fibroblastic remodulation emphasizes its relevance as a therapeutic target for modulating DOMS. Armed with this knowledge, clinicians can make informed decisions to optimize recovery strategies, ultimately enhancing patient outcomes and performance longevity.

1. Introduction

Delayed onset muscle soreness (DOMS) is a common ailment that many people experience, whether it is athletes preparing for a competition or the average person performing an exercise or movement their muscles are not yet accustomed to. DOMS can be defined as muscle stiffness, pain, and tenderness occurring 12-24 hours post exercise, often peaking at 48 hours and can take several days to over a week to subside [1]. Current literature shows there are several hypotheses to the mechanism of DOMS; inflammation, enzyme efflux, micro- muscle damage, lactic acid, muscle spasm, connective tissue [2]. The pathophysiological process of DOMS is likely to be a combination of these theories. However, there have been few studies on how one of the key elements in muscle function can impact the development of DOMS, calcium.

The physiological role of calcium (Ca^{2+}) in excitation-contraction coupling of skeletal muscle has been well understood for over 70 years [3]. This bridge connecting electrical stimulation with the somatic nervous system is crucial for skeletal muscle contraction. The process begins with a nerve impulse that excites the muscle cell membrane (sarcolemma) by releasing acetylcholine at the motor end plate [4]. Membrane depolarization travels the length of the muscle down the T-tubules and causes a conformational change in the voltage-sensing channels in the sarcolemma [5]. The voltage sensing dihydropyridine (CaV1.1) and the coupled ryanodine receptor release Ca^{2+} from the sarcoplasmic reticulum into the cytoplasm of the cell [5,6]. The influx of Ca^{2+} into the intracellular space induces the binding of Ca^{2+} to troponin, allowing the interaction of myosin and actin known as the "crossbridge." The actin filaments slide atop the myosin filaments shortening the sarcomere and releasing ADP after the contraction [7,8]. Afterwards, calcium ions are sequestered by the sarcoplasmic reticulum Ca^{2+} ATPase (SERCA) allowing muscle relaxation [9]. Therefore, more contractions increase the activity of the Ca^{2+} ATPase and rate of Ca^{+} sequestration.

Rapid changes in cellular calcium levels during eccentric exercise can induce the activity of calcium-dependent proteases, most notably calpain. Due to calpain's various cellular process roles it has been shown to be a main contributor to muscle damage once triggered by high levels of cytoplasmic calcium [10]. Calpains are capable of sarcomere degradation by cleaving structural proteins including titin, desmin, alpha-actin, filamin. Dystrophin [11]. In addition, calpains can trigger inflammatory responses. Calpains mediate the activity of cytokines, most notably IL-1, IL-6, and TNF-α. This cytokine release recruits inflammatory cells including neutrophils, lymphocytes, and macrophages [12]. This synergistic effect of muscle damage and inflammation caused by calpains is a large contributor to DOMS.

While most of the focus is on muscle parenchyma, there are other structures that are essential in muscular contraction, including fascia. The fascia is dense connective tissue that surrounds, separates, and provides structure to the muscles together making up the myofascial system [13]. Approximately 30% of force expressed in movement is due to lateral compression of the deep fascia [14]. The damage that occurs at the myofascial system requires fibroblastic activity to repair the collagen-rich connective tissue. Ca^{2+} is an essential component of the cell signaling pathway that occurs in fibroblasts within the fascia [15]. Another uncomfortable condition that many people encounter during or immediately after exercise is muscle cramping, or exercise-associated muscle cramps (EAMC). Defined as painful, sporadic involuntary muscle contractions during or immediately after exercise [16]. The cause of EAMC has been proposed by multiple theories. The most common being the dehydration- electrolyte imbalance. Large amounts of sweat loss during intense exercise decreases the amount of electrolytes like calcium, potassium, sodium, and chloride which alters the motor nerve signaling and muscle function potentially resulting in cramping [17]. The next most postulated theory is the altered neuromuscular control theory, which is when a fatigued muscle is a disconnect between the inhibitory (Golgi tendon organ) and excitatory (muscle spindle) activity [18]. One theory does not always take precedence over the other, the can occur simultaneously which is known as the multifactorial theory. This study aims to investigate how the well-known roles of Ca^{2+} in muscle contraction and cell signaling alter muscle structure at the myofibril layer and myofascial system and how this leads to DOMS. In addition to discovering the most effective ways to enhance performance and recovery in those who participate in strenuous eccentric exercise.

2. Methods

2.1. Overview

A review of current literature was employed to explore Ca^{2+} role in muscle and myofascial damage after strenuous exercise and how it played a role in DOMs. A database search was conducted via PubMed.

2.2. Search Term Strategy

Studies were identified using keywords such as "exercise OR delayed onset muscle soreness" AND "myofascial damage OR skeletal muscle" AND "recovery OR inflammatory markers" AND "calcium cell signaling OR calcium influx OR efflux"

2.3. Inclusion and Exclusion Criteria

Inclusion criteria included studies that measured various markers before and after strenuous exercise; calcium levels, myofibril damage, myofascial damage, inflammatory reactions, and protease activity. As well as studies that aimed to best reduce those markers post exercise including massage, compression, cold water immersion, rollers, and hydration.

2.4. Types of Studies

Numerous types of research studies were used to complete this narrative review. This included randomized controlled trials, crossover studies, double blind studies, retrospective studies, meta-analysis, and systemic reviews.

2.5. Types of Outcome Measures
Calcium cell signaling, protease activity, inflammatory markers, myofibril damage, myofascial damage after specific types of exercise. Recovery modalities that decrease delayed onset muscle soreness and these various markers were also measured.

2.6. Data Extraction
The range of time in the studies analyzed was from 1952 to 2022. Study design, sample size, demographics, and the qualitative analysis of results pertaining to this study were extracted.

2.7. Data Analysis
The extracted data was analyzed descriptively. The analysis was included in the results section of the study to offer better understanding of calcium and the myofascial system's role in delayed onset muscle soreness and ways to reduce it for better performance.

3. Results
3.1. Myofibril Damage
It's well known that the demand for Ca2+ increases as muscle contractions increase, activating calcium-dependent proteases like calpains that damage muscle as previously mentioned. Raastad et al measured the activity of calpain and its effect on muscle structure and function. Muscle biopsies were taken from the vastus lateralis muscle before and after 11 healthy males performed 300 eccentric knee extensors. Results showed that calpain activity increased three times as much in the exercised leg compared to the control left after 30 minutes of the knee extensor exercise. This study also revealed that myofibrillar destruction was congruent with calpain activity. Though it was not proportional, there were still significant disruptions in the myofibril structure with 36 +- 6% of all fibers in the exercised muscle and only 2 +- 1% in the control muscle [10]. Next, Vissing et al examined how calpain transcription activity levels changed during concentric and eccentric exercise activity. Muscle biopsies were taken from the vastus lateralis muscle before and after repeated bouts of bench stepping up (concentric) and stepping down (eccentric). It was concluded that mRNA regulation of calpain-calpastatin expression was only increased to the damaged muscles in the eccentric exercise group and not the concentric. Calpain transcription was upregulated 42% and 62% in the first and second bout of eccentric exercise, respectively ($p<0.05$) [19]. No changes were observed in the concentric exercise group. Calapin's role in mediating cytokines like IL-1, IL-6, and TNF-α to recruit major inflammatory cells like macrophages, neutrophils, and lymphocytes are evident in several other inflammation associated diseases ranging from microbial infections to neurodegenerative diseases like Parkinson's [12].

A study conducted by Feasson et al showed that IL-6 to be the main activator in proteolysis and most of its production occurred in contracting skeletal muscle [20]. Injected IL-6 into mice gastrocnemius showed to produce muscular hyperalgesia in the muscle as well as the dorsal root ganglion [21]. Inflammatory markers such as IL-6 activate nociceptors and generate action potentials. The action potentials travel along the sensory nerves to the spinal cord, to second-order neurons which eventually relay these pain sensations to the brain. Specifically, it is the N-methyl-D-aspartate (NMDA) receptors that are found in deep tissues and have been proven to play an important role in pain [22]. Once Ca2+ enters through these receptors, multiple intracellular cascades enhance the nociceptive neuronal excitability.

Studies have found that certain dietary interventions can decrease DOMS by altering the central nervous system response. Specifically, a cross over study found that a sustained caffeine ingestion (5 mg*kg-1 body weight) for 3 days after decreased DOMS. Caffeine is known to be an adenosine receptor antagonist, which increases the sympathetic nervous system response which thus reduces the sensation of soreness, pain, or fatigue [23]. Omega-3 fatty acid supplementation was also shown to decrease DOMS due to its anti-inflammatory properties. Jouris et al conducted a study of participants on a strict no omega-3 fatty acid diet and the other group took 2,000 mg of eicosatetraenoic acid (EPA) and 1,000mg of docosahexaenoic acid (DHA).

Post-eccentric exercise swelling did not change between the groups, but soreness did decrease in the omega-3 fatty acid group. Which was measured by the degree of elbow extension ($p<0.004$), weighted ($p<0.02$), and palpation ($p=.11$) on the VAS 48 hours post hoc [24]. Da Silva et al discovered that a 50mg of taurine supplementation for 14 days prior to exercise and 7 days following resulted in decreased DOMS, oxidative stress markers, lactate dehydrogenase, creatine kinase activity but had no chance in inflammatory marker levels (IL-1B, IL-10) [25]. Another study measured DOMS with a combination supplement of branched chain amino acids (BCAA) and taurine for 3 times a day for 2 weeks prior to and 3 days after eccentric exercise. The group with the combination of 3.2g of BCAA and 2.0g taurine had a significantly lowered DOMS compared to the placebo group as well the BCAA or taurine only groups. Subjectively, the combination group had significantly lowered VAS scores on Day 2, while the other groups were peaking. Objectively, the aldolase, creatine kinase activity, and lactate dehydrogenase were all significantly decreased in the combination group. Therefore, taurine with BCAAs is more effective at reducing DOMS compared to supplements alone [26].

3.2. Myofascial Damage
However, other studies provided evidence that DOMs occur in the absence of muscle fibers destruction. Mizumura et al study measured muscle damage and DOMs using a Randall-Selitto apparatus in mice and compared it to human pain thresholds. The study demonstrated that observed muscle damage did not correlate with the timing of DOMs. In addition, they reported that there was muscle damage in regular- exercising individuals that did not report DOMs [27]. In addition, Lau et al found that fascia is more sensitive to pain than fascia after eccentric exercise. Ten young men performed 2 bouts of eccentric elbow flexor exercises, and

after each session the biceps brachii fascia and the biceps brachii muscle pain threshold was measured using a pulse alogmeter. The needle was inserted into each layer and started at a frequency of zero then increased at a constant rate, the participant would hit a button when they felt pain and that current level was recorded. It was concluded that the electrical pain threshold was significantly lower in the fascia compared to the muscle 1- and 2-days post-exercise but no significant difference on days 3 and 4 [28].

A review of 16 studies examined the prevalence of connection tissue damage in muscle strain injuries and found that 32.1% of injuries were observed to have myofascial lesions [29]. A 2022 Wilke et al study measured how deep fascia was altered and the degree of DOMS participants experienced after eccentric exercise. In the 19 healthy male adults (age 27 +- 4 years), it was found that it was not not muscle stiffness that led to DOMS but rather the deep fascia. The stiffness of the fascia was measured using ultrasound-based technique and discovered that 24 hours post exercise the deep fascia stiffness increased from 18 kPa to 21.12 kPa (p=0.017). While muscle stiffness was unchanged. The DOMs were measured after eccentric exercise using soft tissue pressure pain of 100 mm visual analogue (VAS). There was a correlation between facial stiffness and reported pain, peak pain was 48 hours post hoc at 19 mm [30].

Agten et al also conducted a study that quantified DOMs with MRI. This study also included the comparison of men to women who participated in unilateral eccentric exercise of the brachialis muscle. MRI results show that muscle edema peaked 3 days after exercise in men and 1-3 days after in women. The cross-sectional area (CSA) of men increased the most after 3 days, by 8.9% from the average size of 2045.60 mm^2. This was the same for women, an 11.49% increase from the average 1175.20 mm^2. Both men and women reported the highest degree of soreness using the pain scale (3.0 for men and 4.0 women) at 2 days post hoc. The fractional anisotropy level was inversely related to the amount of pain all participants experienced [31].

3.3. Ca2+ Role in Myofibroblast Activity

A study by Arora et al showed that the extent of how much stretch the myofascial system experiences correlates with the concentration of intracellular Ca2+ and fibroblastic activity. Mechanically stretched human gingival fibroblasts in culture showed that at 1% stretch there was no calcium response, but at a 2.8% stretch there was an intracellular concentration of Ca2+ increase oscillations of up to 2,000 sec. [32]. Godbout et al conducted a study that isolated subcutaneous myofibroblasts (SCMF) of mice and seeded them on silicone substrates and collagen gels of different elasticities. The different elastic modulus (E-modulus) were soft/ normal (5kPa), under repair (15kPa) or fibrotic/stiff (50kPA) and fluorescent Ca2+ indicators were added to each sample. It was discovered that oscillation frequencies of intracellular Ca2+ increased with the increasing substrate of E-modulus [33].

Ca2+ likely increases when there is stress or tension on the myofascial system due to its ability to aid in the tissue repair. One way that it does this is by regulating cell-cell adhesion in fibroblasts, a vital step in the remodulation of the myofascial. 34 Ko et al conducted a study that visualized Ca2+ using fluorescence and found that the intracellular concentration of Ca2+ rises in the early stages of contact formation. Cell-cell adhesion was also measured in the presence of calcium channel blocker, which showed a roughly 60% decrease in cell-cell adhesion [34].

3.4. Exercise Associated Muscle Cramps

As mentioned, EAMCs is currently best explained by the multifactorial theory which is a combination of the dehydration and neuromuscular control theories. But neither explain exactly how Ca2+ interferes. With repetitive muscle skeletal contraction, the sarcolemma eventually fatigues and reduces the amount of Ca2+ being released due to the decreased excitability and decreased force of each muscle contraction. However, an acidic environment is created by the influx of protons and lactic acid within the cell and the extracellular fluid. This alters the sarcolemmal Vmax, forcing more muscle contractions leading to cramping [35]. The dehydration theory postulates that key electrolytes involved in motor nerve signaling and muscle function like calcium, potassium, sodium, and chloride are lost through perspiration from intense exercise [17].

A study based out of the University of Alabama, looked at the influence of hydration and electrolyte supplementation in college-aged males with a history of EAMCs, and found that the replenishment of lost electrolytes using a carbohydrate-electrolyte rich beverage aids more in the delaying of EAMCs, but not in the complete reduction of them. The experimental group was given a carbohydrate-electrolyte rich beverage which was composed of carbohydrate (sucrose, glucose, fructose), sodium, potassium, and chloride, all at concentrations that have been researched as the replenishment of average losses through sweat. The results from this study support the multifactorial theory behind EAMCs, because although electrolyte imbalances were rectified 69% of subjects in the experimental group still developed EAMCs. The neuromuscular control theory states that there is a disconnect between the inhibitory (Golgi tendon organ) and excitatory (muscle spindle) activity [18].

It has been theorized that static stretching could reduce the frequency of EAMCs. A crossover study performed on 17 college-aged students aimed to determine if static stretching, specifically of the flexor hallucis brevis, would lead to an increased cramp threshold frequency (CTF), which in turn would lower the risk of EAMCs. The results of this study found that although static stretching did result in an increased CTF, there was not a significant difference, since the control group without static stretching also was found to have an increased CTF. The lack of significant data leads to the conclusion that static stretching is an ineffective modality to decrease EAMCs [36].

3.5. DOMS Recovery

Recovery methods such as massage, foam rollers, compression devices, and cold-water immersion have been studied in the reduction of DOMS. Zainuddin et al. performed a study that involved 10 minutes of massage after 3 hours of eccentric exercise on one arm, while the contralateral arm did not receive any treatment. They found that DOMS was significantly less in the experimental group, specifically upon palpation of the brachioradialis (P=0.01) compared to control. They also found that there was a non-significant, but substantial decrease in soreness while flexing the elbow and upon palpation of the brachialis (P < 0.06). Although it was discussed that a placebo effect could be in play due to their study design, it was concluded that the massage resulted in up to a 40% reduction in severity of muscle soreness compared to the control group without massage [37].

A meta-analysis performed on the effect of different post-exercise recovery techniques and their effect on inflammatory markers demonstrated that a 20–30-minute massage that is performed up to 2 hours following exercise has been shown to reduce DOMS for 24 to 96 hours after exercise [38,39]. Massage recovery techniques have been shown to result in reduced concentrations of creatinine kinase (CK) and IL-6, both which have been proposed to result in DOMS [40]. In addition to the reduction of circulating CK and IL-6, massage therapy has been demonstrated to result in a decrease in neutrophils from injured muscle areas, leading to the prevention of muscle fiber breakdown and in turn the signs and symptoms of DOMS [37]. Another post-recovery technique that has been cited in several literature sources to result in a decrease of DOMS, is the use of compression devices.

The positive effect on DOMS that is a result of compression devices such as compressive arm sleeves or pneumatic compression devices (PCDs) specifically on the lower limbs, has been hypothesized to be due to a decrease in space that could lead to swelling and edema and a resultant decrease in migration of the inflammatory modulators seen in the pathophysiology of DOMS [41]. A study specifically looking at the effects of compressive arm sleeves for 24 hours following eccentric exercises and their effect on DOMS demonstrated a different hypothesis, since their study did not result in a statistically significant reduction in levels of CK, TNF-a, or IL-6 [42]. Kim et al. concluded that use of a compressive arm sleeve may support the findings of another similar study which stated the beneficial effect on DOMS is due to reduced muscle oscillation leading to decreased muscle stretch and resultant damage [43].

Pneumatic compression devices (PCDs) are another form of compression device that have been shown to reduce negative performance effects associated with DOMS. A study looking at the effects of PCDs compared to a continuously worn compression device on DOMS demonstrated that the PCD-treatment group showed increased range of motion, specifically elbow flexion and extension, in addition to lower subjective pain ratings compared to the continuous compression device treatment group [44]. The mechanism of action of PCDs as a form of compression therapy is like that of a sequential compression device used in the prophylaxis of deep vein thrombosis. Compression therapy utilizing PCDs typically lasts between 20-30 minutes and is initiated up to 1 hour after workout completion. PCDs work via the sequential inflation and partial deflation of 4 chambers up to 80 mmHg beginning distally and moving proximally, with the whole process taking 30 to 40 seconds, before starting again [45]. A randomized controlled trial on the effects of pneumatic compression devices in ultramarathon runners demonstrated statistically significant muscle pain and soreness rating ($p < 0.001$) compared to control groups [46].

Alongside compression garments, studies on the effects of cold-water immersion (CWI) as a post-exercise recovery modality to reduce DOMS have demonstrated similar findings. The postulated mechanism that outlines the beneficial effects of CWI in regard to DOMS follows that of compression devices. CWI at a temperature of around 11-15oC (52-59oF) for a period of 10-15 minutes has been demonstrated as the most effective exposure to achieve optimal results in reducing DOMS (Machado,2016). The vasoconstriction that results from the CWI is believed to reduce migration of inflammatory molecules and also decrease muscle fiber breakdown [39].

One of the most heavily utilized post-exercise recovery modalities utilized by all types of athletes; from the novice to the professional ranks, are foam rollers. Foam rollers can be utilized as a warm-up tool (i.e., pre-rolling) or as a recovery tool (i.e.,post-rolling), and both modalities have been extensively studied in the literature on their efficacy in either the prevention or treatment of DOMS. Similar to the proposed mechanism of massage leading to the positive effects in regard to DOMS, post-rolling is believed to reduce DOMS mainly through mediating biochemical effects. Foam rolling, specifically post-rolling, has been shown to lead to increased levels of circulating neutrophils and plasma creatine kinase, as well as transcription of mechano-sensory receptors; COX7B and ND1, which signify the formation of new mitochondria. The formation of new mitochondria in muscle cells allows for increased muscle healing, which can be the mitigating factor in the reduction of DOMS [48].

4. Discussion

Calcium's role in muscle damage at the myofibril level has been shown to lead to DOMs. The increase in protease activity, inflammatory cells, and the levels of bradykinin, leukotrienes, and prostaglandins leading to the sensation of pain and soreness days following strenuous exercise [40]. Nutritional intervention is an effective way to alleviate most of these factors. Caffeine was shown to enhance the sympathetic nervous system and thus decrease the sensation of pain and soreness [23]. Omega-3 fatty acid supplementation was shown to reduce those inflammatory markers and thus decreased DOMS. Taurine supplementation

decreased DOMS but was found to be more effective with the combination of BCAAs.

This study also discovered that DOMS is a multifactorial symptom that can be experienced from many different etiologies. This review discovered that in addition to muscle inflammation and degradation leading to DOMS, fascia is also deeply involved with the development of DOMS. The myofascial system was shown to have more nociceptors and sensitivity to pain compared to muscle fibers. The implications of calcium on the myofascial system; specifically, in regards to sport and exercise have been cited in the literature and can be utilized to maximize performance from novice to elite level athletes. The theory that has been widely accepted to result in the DOMS phenomenon begins with high mechanical forces which act on the muscle resulting in muscle tissue damage and consequently an inflammatory response consistent with increasing circulating neutrophils, mast cells, and macrophages [2]. DOMS has been demonstrated to negatively impact athletic performance in a variety of ways including perceived functional impairment, decreased joint mobility (ankle dorsiflexion and plantarflexion), and significant reductions in strength and power. Contrary to the conventional understanding that DOMs is directly linked to myofibril damage, Mizumura et al's findings challenge this notion. The lack of correlation between observed muscle damage and the timing of DOMS, coupled with the presence of muscle damage in regular-exercising individuals who did not report DOMS, raises the question about the direct relationship between myofibril damage and DOMS [27]. Lau et al's study on fascial sensitivity further adds complexity to the discussion by highlighting the importance of fascia in pain perception after eccentric exercise. The lower pain threshold in fascia compared to muscle suggests that fascial elements contribute significantly to the experience of DOMS [28].

Wilke et al's exploration of deep fascia stiffness and its correlation with DOMS provides novel insights into the role of fascia in the post-exercise experience. The increased stiffness of deep fascia, opposed to muscle stiffness, is implicated in the development of DOMS. This challenges the traditional focus on muscle stiffness and underscores the importance of considering fascial elements in understanding post-exercise sensations [30]. The role of Ca2+ in myofibroblast activity, as elucidated by Arora et al and Godbout et al, adds another dimension to the discussion. The correlation between mechanical stretch, intracellular Ca2+ concentration, and fibroblastic activity suggests a link between Ca2+ signaling and tissue repair mechanisms [32,33]. The multifactorial theory of EAMCs has been a subject of extensive research. Lindinger's explanation of how an acidic environment and altered sarcolemma Vmax contribute to cramping provides a mechanistic understanding of the role of Ca2+ in EAMCs [35]. However, there were no significant changes in EAMCs with acute replenishment of all the key ions.

Limitations in this literature review the various study designs in the results, which could potentially lead to heterogeneity in the data. Also, the topic of DOMS has been well studied for many years, therefore there were dated studies used in this review, but the most recent advancements or changes were sure to be included. Future research should aim for a more standardization in outcome measures, such as criteria for defining and measuring DOMS, muscle damage, and recovery. This would enhance the comparability of results across studies. Also, future interventional studies are necessary to make further advancements. Interventions as intargeting calcium-related pathways directly, either through exploring potential pharmaceutical or nutritional interventions that could modulate calcium levels and alleviate DOMS. Investigating the dose-response relationships of calcium-related interventions to understand the optimal dosage or duration is needed for meaningful effects of DOMS and recovery.

5. Conclusion

The pathophysiology of DOMS, specifically the role that Ca2+ plays in its development as a result of muscle and myofascial damage, has been extensively studied in the literature. Research has also been dedicated to the various prevention and treatment modalities of DOMS, which has resulted in mixed outcomes throughout the current literature. It has been demonstrated that techniques which work by decreasing the migration of pro-inflammatory cytokines and the neutrophils that follow result in the most positive impacts on DOMS recovery. These techniques include massage therapy, pneumatic compression devices, and foam rollers; all which work through a similar mechanism by providing an external force resulting in increased regional blood circulation and decreasing the inflammation that is the pathophysiological hallmark of DOMS. The lack of standardization in the current treatment modalities for DOMS is seen in the variability of results and consequently the conclusions that could be drawn from those results. Treatment modalities such as cold-water immersion, therapeutic ultrasound, and electrical stimulation have also been studied and demonstrated mixed results on the efficacy in alleviating the symptoms of DOMS. The most effective treatment regimen may be a combination of the modalities in order to receive the optimal results in the reduction of DOMS related symptoms. Future research on the topic should aim to include randomized controlled trials, in hopes of providing more standardization of the current treatments in the literature.

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