

A review of nutritional intervention on delayed onset muscle soreness. Part I

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This review is focused on the effect of nutritional intervention on delayed onset muscle soreness (DOMS) that occurs after exercise. In general, high force eccentric contractions and/or unaccustomed exercise result in DOMS attributed to reduction in performance such as muscle strength and range of motion (ROM) for both athletes and non-athletes. Nutritional intervention is one of the preventive or therapeutic ways to reduce DOMS. Previous research studies have suggested the following nutrition intervention: caffeine, omega-3 fatty acids, taurine, polyphenols, and so on. Nutritional intervention with these nutrients before and after exercise was reported to be effective in reducing DOMS. These nutritional interventions have also been reported to

affect inflammatory responses and oxidative stress leading to DOMS reduction. However, other studies have reported that these nutritional interventions have no effect on DOMS. It is suggested that intake of proper nutrition intervention can effectively reduce DOMS after exercise and quickly help an athlete return to exercise or training program. In addition, nutritional intervention may help both athletes and non-athletes who engage in physical therapy or rehabilitative programs after surgery or any injurious events.

Keywords: Delayed onset muscle soreness, Nutritional intervention, Inflammatory response, Oxidative stress, Eccentric exercise

INTRODUCTION

It is commonly accepted that delayed onset muscle soreness (DOMS) occurs when a person is repeatedly exposed to high eccentric muscle contractions or unaccustomed exercise (Clarkson and Hubal, 2002). In general, DOMS continues to increase after exercise and peaks between 24 and 48 h after exercise (Armstrong, 1990; Connolly et al., 2003). Even though the exact cause of DOMS remains unclear, several studies have suggested that DOMS is triggered by a sequence of various biochemical changes after muscle damage rather than a single event of damage (Armstrong et al., 1984; Close et al., 2005; Smith et al., 1991).

DOMS is the main cause of reduced exercise performance including muscle strength and range of motion for both athletes and non-athletes, and it also brings continual psychological discomfort (Chen et al., 2007; McKune et al., 2012; Serinken et al., 2013). Therefore, there is a need to distribute information on how to reduce DOMS. Ways to reduce DOMS have been studied extensive-

ly, and many studies have reported on nutrition interventions to reduce DOMS. Commonly known nutritional interventions include caffeine, omega-3 fatty acids, taurine, and polyphenols (da Silva et al., 2014; Hurley et al., 2013; Tartibian et al., 2009; Trombold et al., 2011). The purpose of this review is to provide guidelines and information about DOMS to the public, athletes, and coaches in the practical field so that they can carefully select nutritional intervention.

ETIOLOGY OF DOMS

The reasons behind DOMS have been a steady interest for many sports scientists for a long time. Although several factors including lactic acid, connective tissue damage surrounding muscles, muscle temperature, muscle spasm, inflammatory responses, free radicals, and nitric oxides have been suggested for causing DOMS, there is no clear explanation (Close et al., 2005; Radak et al., 2012). Previous literatures have speculated that the cause of DOMS is

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due to structural muscle damages and perturbation of calcium homeostasis or acute inflammatory responses to exercise (Armstrong et al., 1984; Smith et al., 1991). Thus, DOMS may occur with numerous complex factors combined after exercise-induced muscle damage. By gathering the results from previous studies, DOMS is found to be caused by exercise-induced muscle damage. Inflammatory responses will occur after morphological damage caused by eccentric contractions (Clarkson and Hubal, 2002). Chemokines (signaling proteins) are released in the damaged muscle, making inflammatory cells such as neutrophil and macrophages more active (Tidball, 2011). Due to the accumulation of inflammatory cells in the damaged site, the levels of bradykinin, leukotrienes and prostaglandins are concomitantly increased (Connolly et al., 2003). When bradykinin reacts with B2 receptor, it can activate phospholipase. This change isolates calcium ions in the cell and abnormally increases calcium levels in the cell membrane by opening ion channels, leading to secretion of neurotransmitters such as substance P, which stimulates the production of arachidonic acids (Murase et al., 2010; Taguchi et al., 2005). Due to arachidonic acids, the levels of prostaglandins and leukotrienes are also increased. Prostaglandins and bradykinin are known to be potential substrates of DOMS by direct interaction with type III & IV afferent nerve fibers through pain receptors (nociceptor). On the other hand, leukotrienes increases vascular permeability resulting in adhesion of neutrophils to endothelial cells in the damaged site. Increased neutrophils undergo phagocytosis by respiratory burst activity releasing free radicals which may induce further damage of

the cell membrane (Connolly et al., 2003). By the time inflammatory cells are activated in the damaged muscle, muscle swelling is occurred by various exudates resulting in increased intramuscular pressure and sensitivity of type III & IV afferent fibers. When these stimuli reach medulla and cerebral cortex through spinal cord, muscle soreness is perceived (Cheung et al., 2003). A possible mechanism of DOMS is shown in Fig. 1.

DOMS has recently been associated with nerve growth factor (NGF). NGF is known to increase pain responses (Nie et al., 2009), and NGF secreted by inflammatory responses can stimulate nociceptors (Lewin et al., 1993; Turrini et al., 2002). In an animal model, lengthening muscle resulted in increased mRNA levels of NGF (Murase et al., 2010). Similarly, in a human study, when NGF was injected into trapezius muscle, muscle soreness was higher in NGF injection compared to saline injection following eccentric contractions (Nie et al., 2009).

DOMS AND NUTRITIONAL INTERVENTION

Caffeine

In general, caffeine is known to have glycogen sparing effect during endurance events by promoting fat oxidation (Graham, 2001). A recent study reported that caffeine has an effective nutritional agent for reducing DOMS after exercise (Hurley et al., 2013). A mechanism proposed for caffeine to reduce DOMS is closely related to adenosine receptor. Caffeine can block adenosine receptor because it acts as an adenosine antagonist. The blocking

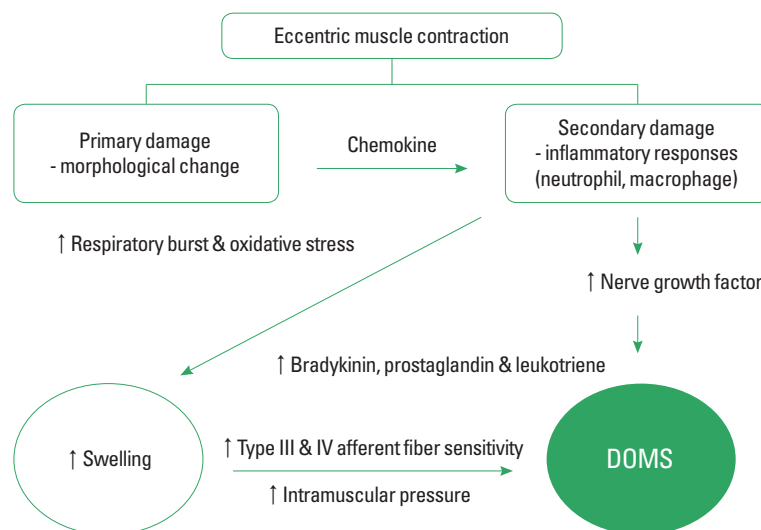


Fig. 1. A possible mechanism of DOMS.

effect on adenosine receptor may reduce DOMS by deactivating the central nervous system (CNS, Hurley et al., 2013; Maridakis et al., 2007).

A recent study demonstrated the effect of caffeine on DOMS. In this experiment, healthy males ($n=9$), who performed a bout of biceps brachii exercise on a preacher curl bench, ingested 5 mg per body weight of caffeine 1 h before and 24 h after exercise for 4 days. As a result, DOMS was significantly reduced between 2 and 3 days after exercise in caffeine ingested group compared to the placebo group (Hurley et al., 2013). Other study reported positive effect of caffeine on DOMS reduction in healthy females ($n=9$) who performed 64 eccentric contractions of quadriceps muscle and ingested 5 mg per body weight of caffeine 24 and 48 h after exercise (Maridakis et al., 2007). It is suggested that caffeine intake with 5 mg per body weight would reduce DOMS after exercise.

Omega-3 fatty acid

Omega-3 fatty acid is one of the essential fatty acids rich in fish oils containing eicosanoids such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Eicosanoids have been reported to regulate inflammatory response (Jouris et al., 2011). Ingestion of omega-3 fatty acid can increase EPA and DHA levels which in turn decreased synthesis of other eicosanoids including thromboxane, leukotriene, and prostaglandin associated with inflammatory response. Phillips et al. (2003) reported that nutritional intervention with DHA reduced exercise-induced inflammatory response. Therefore, it is assumed that intake of omega-3 fatty acid results in anti-inflammatory response to exercise which may reduce DOMS (Jouris et al., 2011; Tartibian et al., 2009).

Several studies reported positive effect of omega-3 fatty acid on DOMS. Tartibian et al. (2011) demonstrated that 1.8 g of omega-3 fatty acid ingestion by healthy males ($n=45$) reduced pro-inflammatory factors such as interleukin-6 (IL-6), prostaglandin E2 (PGE2), and tumor necrosis factor- α (TNF- α) following eccentric exercise. Lembke et al. (2014) reported that 2.7 g of omega-3 fatty acid ingestion for 30 days could reduce DOMS and C-reactive protein (CRP) following eccentric contractions compared to sunflower oil ingestion. Similar studies also showed that intake of omega-3 fatty acid was effective on DOMS. A study with 1.8 g of omega-3 fatty acid ingestion among 27 males demonstrated reduced DOMS following eccentric exercise (Tartibian et al., 2009). In addition, 3 males and 8 females ingested 3 g of omega-3 fatty acid for 7 days and DOMS was significantly reduced following eccentric exercise (Jouris et al., 2011). Therefore, 1.8-3 g of omega-3 fatty acid ingestion may be effective on reducing DOMS after exercise.

Although several studies measured oxidative stress markers to elucidate the cause of reducing DOMS by omega-3 fatty acid, the results from those studies are still controversial. Lenn et al. (2002) reported that 1.8 g of omega-3 fatty acid ingestion for 30 days among 22 subjects did not significantly reduce DOMS and malondialdehyde (MDA) level after exercise. In contrast, Gray et al. (2014) reported that 3 g of omega-3 fatty acid ingestion for 6 weeks significantly reduced thiobarbituric acid-reactive substance (TBARS), a marker for lipid peroxidation, compared to the placebo group, but there was no difference in DOMS between the groups. Therefore, it is suggested that intake of omega-3 fatty acid is associated more with inflammatory response than oxidative stress for reducing DOMS.

Taurine

Taurine is an organic acid found in skeletal muscle and has many biological functions such as membrane stabilization, antioxidant capacity, osmoregulation and calcium homeostasis regulation (Schaffer et al., 2010). Several studies recently demonstrated the effect of taurine on DOMS although the exact mechanism is not elucidated (da Silva et al., 2014; Ra et al., 2013).

da Silva et al. (2014) reported that 50 mg of taurine ingestion by healthy males ($n=21$) for 21 days (14 days before and 7 days after eccentric exercise) showed significant reduction in DOMS and oxidative stress markers after exercise, yet no effect on inflammatory response. Another study examined the combined ingestion with taurine (2.0 g) and branched-chain amino acid (BCAA, 3.2 g) three times a day for 18 days by 36 healthy males; it resulted in significant reduction in DOMS and oxidative stress marker compared to the control group (Ra et al., 2013). Therefore, both taurine only ingestion and combined intake of taurine and BCAA are suggested to reduce DOMS following high force eccentric exercise. A possible explanation for reducing DOMS by taurine may be related to the attenuated oxidative stress shown in both studies. The evidence was ascertained by an animal model in which 300 mg per body weight of taurine for 15 days significantly reduced superoxide radical production after exercise (Silva et al., 2011).

Polyphenol

Polyphenol is a component of phytochemicals found in many plants (Malaguti et al., 2013). The major biological functions of polyphenol are antioxidant capacity and anti-inflammation. Specific components of polyphenol such as anthocyanins and flavonoids are known to serve antioxidant and anti-inflammatory activities (Kuehl et al., 2010). According to the previous studies, a

potential mechanism for reducing DOMS by ingestion with polyphenol is its action on membrane stability and reduced lipid peroxidation by inhibiting peroxy radical activation (Jówko et al., 2011). In addition, both animal and human studies demonstrated the anti-inflammatory effect of polyphenol in exercise-induced muscle damage model (Davis et al., 2009; Howatson et al., 2010). Among many nutritional interventions rich in polyphenol, pomegranate, cherries, and blueberries have been examined in the following studies (Connolly et al., 2006; McLeay et al., 2012; Trombold et al., 2010, 2011)

Trombold et al. (2010) reported that intake of 500 mL of ellagi-

tannins extracted from pomegranate two times a day for 9 days showed significant reduction in DOMS compared to the placebo group 2 h after eccentric exercise; however, there was no significant difference between the groups from 24 to 96 h after exercise. In contrast, the same investigators compared 250 mL of pomegranate juice ingestion two times a day for 15 days between arm and leg eccentric exercise. As a result, DOMS was significantly reduced after arm exercise in pomegranate juice supplement group compared to the placebo group, but there was no difference in DOMS after leg exercise between the groups (Trombold et al., 2011).

Ingestion of cherry juice has been effective on reducing DOMS.

Table 1. Effect of caffeine, omega-3 fatty acids, taurine, and polyphenol on DOMS

Supplement	Researcher	Subject	Exercise	Intervention	Main outcome
Caffeine	Maridakis et al., (2007)	College-aged females (n=9)	64 repetitions of eccentric quadriceps exercise	5 mg/kg/day, 24 and 48 h after exercise	↓ DOMS=MVC
	Hurley et al., (2013)	Healthy, trained males (n=9)	4 sets, 10 repetitions of eccentric biceps curls	5 mg/kg/day, 1 h before and 4 days after exercise	↓ DOMS=CK ↑ Total repetitions
Omega-3 fatty acids	Lenn et al., (2002)	Healthy males (n=13) and females (n=9)	50 repetitions of eccentric biceps curls	1.8 g/kg/day, 30 days before exercise	= DOMS=Strength=RANG = Circumference=CK=Cortisol = MDA=IL-6=TNF-α=Iron
	Tartibian et al., (2009)	Healthy males (n=27)	40 min of bench stepping	1.8 g/day, 30 days before and during 48 h after exercise	↓ DOMS ↑ ROM ↑ Thigh circumference
	Tartibian et al., (2011)	Untrained males (n=45)	40 min of bench stepping	1.8 g/day, 30 days before and during 48 h after exercise	↓ CK ↓ Mb ↓ LDH ↓ PGE2 ↓ IL-6 ↓ TNF-α
	Jouris et al., (2011)	Healthy males (n=3) and females (n=8)	2 sets, until fatigue of eccentric biceps curls	3 g/day, 7 days before exercise	↓ DOMS ↓ Arm circumference = Arm volume=Skin temperature
	Lembke et al., (2014)	Healthy males and females (n=69)	2 sets, 30 repetitions of eccentric biceps curls	2.7 g/day, 30 days before exercise	↓ DOMS=CK ↓ CRP ↓ Lactate = Extension=Torque ↑ QOL ↑ POMS
Taurine	Gray et al., (2014)	Healthy males (n=20)	200 repetitions of eccentric knee exercise	3 g/day, 6 week before exercise	= DOMS=MVC=CK=Protein carbonyl = DNA damage ↓ TBARS
	Ra et al., (2013)	Untrained male (n=36)	6 sets, 5 repetitions of eccentric biceps curls	2.0 g (taurine) + 3.2 g (BCAA), 3 times/day, 2 weeks before and 4 days after exercise	↓ DOMS ↓ Arm circumference = CK ↓ LDH ↓ aldolase ↓ 8-OHdG
	da Silva et al., (2014)	Healthy males (n=21)	3 sets, until exhaustion of eccentric biceps curls	50 mg/kg/day, 14 days before and 7 days after exercise	↓ DOMS ↑ MVC ↓ LDH ↓ CK ↓ Xylenol ↓ Protein carbonyl=SOD=catalase = GPx=IL-1β=IL-10=TNF-α
Polyphenol (cherry juice)	Connolly et al., (2006)	Male college students (n=14)	2 sets, 20 repetitions of eccentric biceps curls	355 mL, twice/day, 4 days before and 4 days after exercise	↓ DOMS ↑ MVC = Muscle tenderness=RANG
Polyphenol (ellagitannins)	Trombold et al., (2010)	Recreationally active males (n=16)	2 sets, 20 repetitions of eccentric biceps curls	500 mL, twice/day, 4 days before and 5 days after exercise	↓ DOMS (only 2 h after exercise) ↑ MVC=CK= Mb=IL-6=CRP
Polyphenol (pomegranate juice)	Trombold et al., (2011)	Physically active males (n=17)	3 sets, 20 repetitions of eccentric biceps curls and 6 sets, 10 reps of knee eccentric exercise	250 mL, twice/day, 7 days before and 8 days after exercise	↓ DOMS (arm)=DOMS (leg) ↑ MVC (arm)=MVC (leg)
Polyphenol (blueberry)	McLeay et al., (2012)	Healthy females (n=10)	3 sets, 100 repetitions of knee eccentric exercise	200 g/day, 5 and 10 h prior to and then immediately, 12 and 36 h after exercise	= DOMS ↑ Peak isometric tension = ROS-generating potential = Protein carbonyl ↑ Antioxidant capacity=IL-6=CK

Equal sign, no significant difference; ↓, significantly decreased responses; ↑, significantly increased responses; IL-1β, interleukin-1β; IL-6, interleukin-6; IL-10, interleukin-10; TNF-α, tumor necrosis factor-α; PGE2, prostaglandin E2; CRP, C-reactive protein; GPx, glutathione peroxidase; 8-OHdG, 8-hydroxydeoxyguanosine; TBARS, thiobarbituric acid-reactive substances; DOMS, delayed onset muscle soreness; SOD, superoxide dismutase; MDA, malonyldialdehyde; QOL, quality of life; POMS, profile of mood states questionnaire; Other muscle damage markers; MVC, maximal isometric voluntary contraction; CK, creatine kinase; LDH, lactate dehydrogenase; Mb, myoglobin, ROM, range of motion, RANG, relaxed arm angle.

Connolly et al. (2006) reported that intake of 355 mL of cherry juice twice a day for 8 days could significantly reduce DOMS after eccentric contractions of the elbow flexor muscle. However, another study with blueberry consumption did not demonstrate the reducing effect on DOMS. McLeay et al. (2012) reported that intake of 200 g of blueberry smoothie at 5 and 10 h before and immediately after exercise, and 12 and 36 h after exercise did not produce any difference in DOMS between blueberry consumption and placebo groups after leg eccentric exercise. Therefore, the different effect of polyphenol on DOMS shown in the previous studies may be attributed to the specific exercise (arm vs leg), dose used, and/or ingestion periods. Effect of caffeine, omega-3 fatty acids, taurine, and polyphenol on DOMS is listed in Table 1.

Other nutritional interventions

There are several nutritional interventions to be examined including alicin, glutamine, panax ginseng, and lyprinol. It is well known that alicin rich in garlic has anti-inflammatory and antioxidant capacities. Alicin can inhibit the expression of adhesion molecule-1 which is known to play a critical role in inflammatory cell activation, and down-regulate several proteins related to inflammatory response or T-cells (Sela et al., 2004; Son et al., 2006). Also, alicin has an antioxidant capacity by preventing lipid peroxidation and scavenging hydroxyl radicals (Xiao & Parkin, 2002). Su et al. (2008) reported that 80 mg of alicin capsule ingestion daily from 2 weeks before exercise to 2 days after exercise significantly reduced

DOMS as well as IL-6 levels compared to the placebo group.

Glutamine is one of the non-essential amino acids that may play a role in modulating immune cell activity (Rahmani Nia et al., 2013). The results from studies are still controversial. Street et al. (2011) reported that 0.3 g per body weight of glutamine ingestion for 4 days after eccentric exercise significantly reduced DOMS compared to the placebo group. However, in the study, although the authors concluded that reduced inflammatory response may influence DOMS, they did not measure any inflammatory markers to confirm the hypothesis. In contrast, Rahmani-Nia et al. (2013) reported that 0.1 g per body weight of glutamine ingestion three times a week for 4 weeks did not show any difference in DOMS between groups.

Panax ginseng has been a candidate to reduce DOMS although the exact mechanisms are not identified. Pumpa et al. (2013) reported that 4 g of panax ginseng capsule ingestion 1 h before and 4 days after downhill running among trained males (n=20) reduced DOMS at 96 h after exercise compared to the placebo group, but the difference was not pronounced as in other nutritional intervention. Rather panax ginseng supplement group had a higher IL-6 and TNF- α levels at 24 h after exercise than the placebo group, and there was no difference in CRP levels between the groups. Several studies suggested that ingestion of ginseng may reduce inflammatory response, but these were not reported with exercise (Jhun et al., 2014; Wei et al., 2014).

Another candidate nutritional intervention for reducing DOMS

Table 2. Effect of other nutritional intervention on DOMS

Supplement	Researcher	Subject	Exercise	Intervention	Main outcome
Alicin	Su et al., (2008)	Well-trained athletes (n=16, male=8, female=8)	Downhill treadmill running, -10%, until exhaustion	80 mg/day, 2 weeks before and 2 days after exercise	↓ DOMS ↓ CK ↓ CK-MM ↓ LDH ↓ IL-6 = SOD ↑ TAC
Glutamine	Street et al., (2011)	Physically active males (n=15)	100 drop jump	0.3 g/kg, 4 days after exercise	↓ DOMS ↑ Peak torque = CK
	Rahmani Nia et al., (2013)	Healthy males (n=17)	6 sets, exhaustion leg eccentric exercise	0.1 g/kg, 3 times/week for 4 weeks	= DOMS = EMG activity = ROM
Panax notoginseng	Pumpa et al., (2013)	Well-trained males (n=20)	Downhill treadmill running, -10%, 5 bouts of 8 min	4 g/day, 1 h before and 4 days after exercise	↓ DOMS (minimal effect) ↑ Squat jump = CK = Mb = IL-1 ↓ IL-6 ↓ TNF- α = CRP
Lyprinol	Pumpa et al., (2011)	Well-trained males (n=20)	Downhill treadmill running, -10%, 5 bouts of 8 min	200 mg/day, 8 weeks before and 5 days after exercise	= DOMS = Counter movement jump = Squat jump = CK = Mb = IL-1 = IL-6 = IL-10 = TNF- α = CRP

Equal sign, no significant difference; ↓, significantly decreased responses; ↑, significantly increased responses; IL-1, interleukin-1; IL-6, interleukin-6; IL-10, interleukin-10; TNF- α , tumor necrosis factor- α ; CRP, C-reactive protein; DOMS, delayed onset muscle soreness; SOD, superoxide dismutase; TAC, total antioxidative capacity; Other muscle damage markers; MVC, maximal isometric voluntary contraction, CK, creatine kinase, CK-MM, muscle-specific creatine kinase, LDH, lactate dehydrogenase; Mb, myoglobin; ROM, range of motion.

is lyprinol, extracted from New Zealand green-lipped mussel (Sinclair et al., 2000). Similar to omega-3 fatty acid, lyprinol is abundant in EPA and DHA. Additionally, it down-regulates lipooxygenase and cyclooxygenase-2 which are responsible for subsequent synthesis of leukotrienes and prostaglandins, facilitating factors for inflammation and thus serves as anti-inflammatory action (Halpern, 2000). However, a study conducted by Pumpa et al. (2011) did not show any reducing effect on DOMS with 200 mg of lyprinol ingestion daily from 8 weeks before to 96 h after downhill running. Effect of other nutritional intervention on DOMS is listed Table 2.

CONCLUSIONS

Delayed-onset muscle soreness that occurs after exercise-induced muscle damage contributes to the reduction in exercise performance as well as psychological complaints. In this review, several nutritional interventions were discussed to prevent or treat DOMS. Many studies have examined the effect of caffeine, omega-3 fatty acid, taurine, and polyphenol on DOMS, while minor interventions with allicin, glutamine, panax ginseng, and lyprinol did not report consistent data. Most of the nutritional interventions are closely related to inflammatory response and antioxidant capacity for reducing DOMS, but this needs to be verified further. Many factors including study design, dose used, ingestion period, and markers to be measured to identify the hypotheses may affect the results.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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