drjamesdunning February 8, 2021 Osteopractor

Chronic Low-Grade Inflammation, Metabolic Syndrome & Dietary Recommendations: Implications for Physical Therapists

Inflammation is necessary for regeneration, proliferation and healing,[1] especially in the acute phase of healing post-injury or surgery.[2] Numerous cells within the body release inflammatory mediators, which propagate pain in joints, tendons, discs, muscles, ligaments fascia and epineurium so as to signal an immune response. Macrophages and monocytes remove tissue debris and release cytokines, chemokines and growth factors, which propagate inflammation.[3, 4] In doing so, tissue remodeling is facilitated by removing apoptotic neutrophils.[4] Thus, inflammation drives both a vascular and cellular immune response so as to protect and repair compromised tissue.[5]

However, inflammation becomes problematic when anti-inflammatory mediators (e.g., lipoxins, aspirin-triggered lipoxins, PGE_2,PGD_2, glucocorticoids, resolvins, protectins, annexin-1, cyclopentenone prostaglandins)[6] are not released appropriately to break the cycle. As a result, inflammatory markers (e.g., c-reactive protein, histamine, cytokines, free radicals, eicosanoids, tumor necrosis growth factor, bradykinins and interleukin-6) remain elevated, both locally and systemically, causing low-grade chronic inflammation, which is present in many degenerative conditions such as osteoarthritis, rheumatoid arthritis and various other neuromusculoskeletal pain syndromes.[3, 7-12] While many patients attempt to control and break the cycle of chronic inflammation with synthetic inflammatory agents, many of these oral medicines are known to have adverse effects with long-term use.[4]

Chronic low-grade inflammation often accompanies metabolic syndrome and is thought to be a primary causative factor of the condition and its associated consequences.[13] Metabolic syndrome describes a number of metabolic disturbances such as glucose intolerance, central obesity, hypertension and dyslipidemia and has been linked to cardiovascular disease, type-2 diabetes, stroke and cancer.[14] Individuals with metabolic syndrome are also more likely to have musculoskeletal pain and tendinopathies.[3, 15] For example, researchers have found a link between increased

waist circumference and insulin resistance with rotator cuff tendinitis[16] and Achilles tendinopathy.[15]

While overuse can be a causative factor for tendon related pathologies, nearly one third of tendon injuries affect sedentary, overweight individuals and have been associated with dyslipidemia, insulin resistance, hypertension and obesity.[15] Insulin resistance has also been linked to fat deposits and inflammation in muscle, resulting in less force production and increased atrophy.[15-18] Additionally, patients with metabolic syndrome have a higher prevalence of painful neuropathy, allodynia, and hyperalgsia.[9]Given the relationship between food consumption and chronic, low-grade inflammation,[19] diet may be an important consideration for physical therapists attempting to optimize therapeutic outcomes.

DIET & INFLAMMATION

According to Ann Wigmore, "The foods you eat can be either the safest and most powerful form of medicine or the slowest form of poison."[20] Moreover, 60% of the American diet comes from starches, sugars, flour and foods with a high glycemic index,[21] which stimulates postprandial free radicals and nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kB), both of which mediate inflammation.[3, 16]

Additionally, 30% of the American diet consists of meat and dairy products rich in omega-6 fatty acids (also referred to as linoleic acid or arachidonic acid), which significantly contributes to the membrane phospholipids of cells involved in inflammation and mediates two potent pro-inflammatory eicosanoids, prostaglandin and leukotrienes.[22] Arachidonic acid, accumulates in joints due to excessive consumption,[3] and has been shown to be elevated in the cartilage and synovial fluid of patients with osteoarthritis.[23, 24] Although omega-3 fatty acids found in lean meats, fish, eggs, and nuts have significant anti-inflammatory benefits, the ratio of consumption of omega-6 to omega-3 fatty acids ranges between 15:1 and 20:1.[25]

Notably, only 10% of the American diet is comprised of fruits and vegetables, which aid in anti-inflammation.[21]The majority of experimental studies included in a recent systematic review found that fruits and vegetables led to increased anti-inflammatory biomarkers including high-sensitivity C-reactive protein (hs-CRP), tumor necrosis factor alpha (TNF-α), interleukin 6 (IL-6), and E-selectin along with stronger immune system activity.[26] Moreover, one cohort[27] and 5 cross-sectional studies[28-32] reported an inverse association between fruit and vegetable intake and circulating factors of inflammation.[26] Additionally, fruits and vegetables also contain antioxidants, which neutralize free radicals and limit inflammatory arachidonic acid and cytokines.[33]

DIET & REHABILITATION

While many post-injury nutrition strategies aim to reduce and/or abolish inflammation, it is an important aspect of wound healing, and nutritional interventions meant to drastically reduce inflammation should be avoided.[34] However, small dietary changes designed to control inflammation (as described above) may facilitate recovery[35] and reduce the risk for chronic dysfunction and pain.[36] In addition, the following dietary recommendations may be considered during the rehabilitation of muscle, bone and connective tissue:

DIET AND MUSCLE TISSUE REPAIR

Individuals that have suffered a muscle injury should be careful not to significantly reduce their carbohydrate intake, as the healing process has been shown to result in a substantial increase in energy expenditure.[37] Furthermore, additional protein is recommended to limit muscle atrophy and promote repair.[38] However, the most frequently studied micronutrients to promote skeletal muscle repair are vitamin D, polyphenols, vitamin C, vitamin E, and creatine monohydrate.[38, 39]

Vitamin D deficiencies have been shown to impair muscle regeneration, and for individuals with limited sun exposure, 2000 to 4000 IU D3 is recommended per day.[40] While polyphenols have been found to attenuate muscle damage caused by inflammation and promote free radical production, recent studies have reported limited ability for Vitamins C and E to promote repair.[41] In contrast, creatine monohydrate has been found to attenuate upper arm muscle mass and lower leg muscle hypertrophy during immobilization.[42] Therefore, 20g/day for 5 days followed by 5g/day thereafter is recommended to facilitate muscle healing.[42]

DIET AND BONE REPAIR

For bones, consumption of dairy, fruit and green, leafy vegetables are recommended, as these foods contain calcium, protein, magnesium, phosphorus, vitamin D, potassium and fluoride to support bone formation and manganese, copper, boron, iron, zinc, vitamin A, vitamin K, vitamin C and vitamin B for bone health.[38, 43] Notably, a number of studies have specifically linked stress fractures to deficiencies in vitamin D, calcium and carbohydrate intake.[44] While protein intake has been debated for bone strength and repair secondary to acidic load,[45] recent systematic reviews[46] and meta-analyses[47] do still recommend a high-protein intake during recovery.[38]

DIET & CONNECTIVE TISSUE REPAIR

For ligament and tendon injuries, a combination of load and nutritional interventions has been recommended to maximize healing.[48] Vitamin C and copper regulate prolyl hydroxylase and lysyl oxidase activity, respectively,[49, 50] which are required for collagen cross-linking and export from the endoplasmic reticulum. Supplementing high-dose vitamin C every two days has been shown to improve Achilles tendon

healing due to angiogenesis and increased collagen synthesis.[51] Moreover, following histological evaluations of rat Achilles tendons, a combination of high-dose vitamin C and hyaluronic acid has shown significant therapeutic effects compared to controls, particularly in the later stages of tendon healing.[52]

Glycine, is an amino acid, a building block for protein, and allows collagen to form a tight triple helix, which facilitates strength. Previous studies that gave rats a 5% glycine diet reported increased collagen, glycosaminoglycan, and mechanical strength 21 days after Achilles tendon injury.[53] Gelatin or hydrolyzed collagen may also increase collagen synthesis and promote repair.[38] Previous double-blind, placebo-controlled randomized controlled trials found that consuming 10g of hydrolyzed collagen led to improved knee pain in athletes,[54] and consuming 15g resulted in double the collagen synthesis.[55]

Improved collagen synthesis of engineered ligaments was recently found when vitamin C induced gelatin was incorporated into an intermittent exercise program.[55] Notably, Gatorade now recommends ingesting both vitamin C and gelatin to prevent connective tissue injuries and accelerate recovery following injury.[56] While turmeric curcumin, taurine, arginine, bromelain and boswellic acid have all been linked to tendon and ligament health due to their ability to reduce inflammation, the role of inflammation in tendinopathy continues to be a topic of debate in the literature.[38] Supplements that protect and promote connective tissue biosynthesis continue to be heavily researched by pharmaceutical powerhouses such as Ortho Molecular and Vital Proteins.[57, 58]

CONCLUSIONS

While inflammation is an important aspect of tissue protection and repair following injury, chronic low-grade inflammation is a causative or contributing factor in a number of musculoskeletal disorders, degenerative diseases, and metabolic syndrome comorbidities. Given the close relationship between food consumption, inflammation and repair rates for various tissue types (i.e., muscle, bone, tendon, ligament), physical therapists should consider diet education as part of their treatment strategy.

AUTHORS

Raymond Butts, PhD, DPT, MSc, Dip. Osteopractic
Senior Instructor, American Academy of Manipulative Therapy
Coordinator, AAMT Fellowship in Orthopaedic Manual Physical Therapy
Louisville, KY

Benjamin England, DPT, Dip. Osteopractic, Cert. SMT, Cert. DN
Physical Therapist, Mallers & Swoverland Orthopaedic Physical Therapy

Fellow-in-Training, AAMT Fellowship in Orthopaedic Manual Physical Therapy
Fort Wayne, IN

Robin Bewley, DPT, OTR/L, OCS, Dip. Osteopractic
Fellow-in-Training, AAMT Fellowship in Orthopaedic Manual Physical Therapy
Physical Therapist & Clinic Director, Physio Whitefish
Whitefish, MT

James Dunning, PhD, DPT, MSc, FAAOMPT, Dip. Osteopractic
Director, AAMT Fellowship in Orthopaedic Manual Physical Therapy
Owner, Montgomery Osteopractic Physiotherapy & Acupuncture Clinic
Montgomery, AL

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