SUPPLEMENTS FOR PAIN

HOW IS PAIN NORMALLY TREATED?

Chronic Pain is a major treatment challenge. It is incredibly common and difficult to treat. Pain is a subjective experience that has many influences. Even in localized pain there are often multiple physiologic sources of pain. Pain is influenced by multiple factors, including:

- Peripheral structures such as muscles and ligaments
- The central nervous system
- Psychological and emotional states

Because of these multiple influences, treatment approaches that are too narrow are likely to fail.

Conventional medical treatments for pain include medications, interventional pain procedures (i.e., epidural injections, radiofrequency ablation), surgical interventions, and physical therapy. Which specific medications and procedures are recommended varies depending on the specific diagnosis and individual needs, but overall, these options have many limitations, not to mention many associated risks especially when it comes to treating chronic pain. Patients often become frustrated with conventional treatment choices and turn to complementary therapies for pain more than any other diagnosis.[1]

WHAT ARE THE RISKS OF TRADITIONAL MEDICATIONS USED TO TREAT CHRONIC PAIN?

Medication recommendations normally begin with acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs). These are generally regarded as the safest medications, but they are certainly not without risk. Acetaminophen carries the risk of hepatotoxicity, and NSAIDs cause gastrointestinal bleeding, interfere with platelet aggregation, can worsen renal function, and may increase risk of cardiovascular events.[2] Tricyclic antidepressant medications are recommended as adjunctive treatments for both nociceptive and neuropathic pain.[2] These may cause sedation and are on the Beers list for cautious use in the elderly.[3] Opioid medications are under increasing scrutiny due to their multiple adverse effects, their potential for causing addiction, and their failure to demonstrate functional improvement when compared to non-opioid analgesics.[4]

WHY SHOULD WE CONSIDER DIETARY SUPPLEMENTS IN THE TREATMENT OF PAIN?

With medication options often being limited due to lack of effectiveness, increased risks, or adverse effects, there is a need for safe therapeutic options that reduce pain and augment the effects of other treatment modalities. Supplements can fill that void in some patients, reducing their pain so that they can pursue other active modalities. When discussing

supplements with patients, it is recommended that supplements be discussed as part of an overall holistic treatment approach, as opposed to a quick fix or magic bullet.

IF SUPPLEMENTS ARE EFFECTIVE FOR ONE TYPE OF PAIN, ARE THEY EFFECTIVE FOR OTHER PAIN CONDITIONS AS WELL?

Not necessarily. This make sit daunting to choose from among different supplement options. Products effective for chronic low back pain are not necessarily good choices for fibromyalgia, headache pain, or neuropathic pain. The differing causes and sources of pain in each of these conditions, not to mention the different mechanisms of action of various supplements, make it difficult to make generalizations. There are many supplements with proposed benefits in individual pain conditions. When evaluating research on a supplement, consider the condition being studied in addition to the benefits and limitations of the study.

To help guide choosing appropriate supplements for specific pain conditions, the remainder of this clinical tool is split into two sections. The first section will simply list supplements to consider for several common pain conditions. The second section will provide a more detailed look at these individual supplements, including research related to efficacy, dosing, and potential side effects.

SUPPLEMENTS TO CONSIDER FOR INDIVIDUAL PAIN CONDITIONS

Note: *Please refer to the Passport to Whole Health, Chapter 15 on Dietary Supplements for more information about how to determine whether or not a specific supplement is appropriate for a given individual. Supplements are not regulated with the same degree of oversight as medications, and it is important that clinicians keep this in mind. Products vary greatly in terms of accuracy of labeling, presence of adulterants, and the legitimacy of claims made by the manufacturer.*

CHRONIC HEADACHE

- Magnesium
- Vitamin B2
- Butterbur
- Feverfew

CHRONIC LOW BACK PAIN

- Willow bark
- Devils claw
- Vitamin D
- Capsaicin topical cream

FIBROMYALGIA

- Vitamin D
- Magnesium
- Sleep-related supplements
- Energy-related supplements

NEUROPATHIC PAIN

- Alpha lipoic acid
- Vitamin B12 (important to test, and replace if deficiency exists)

OSTEOARTHRITIS

- Omega-3 supplements
- S-Adenosylmethionine (SAMe)
- Glucosamine and chondroitin
- Devils claw
- Willow bark

RHEUMATOID ARTHRITIS

- Omega-3 supplements
- Gamma linoleic acid
- Devils claw
- Willow bark

INDIVIDUAL SUPPLEMENT DETAILS

ALPHA LIPOIC ACID

Alpha lipoic acid (ALA) is a chemical that the body produces itself. It has been found to increase blood flow to the nerves, reduce oxidative stress, and improve distal nerve conduction. It has also been found to improve glucose uptake and enhance insulin sensitivity. It has long been approved in Germany for the treatment of diabetic and alcoholic neuropathy. A meta-analysis in 2004 concluded that treatment with ALA for 3 weeks is safe and provides a 24% overall improvement in total symptoms score versus placebo.[5] The dose for prevention of peripheral neuropathy is 100 milligrams, one to two times daily. For active treatment, the dose is 600 milligrams daily or twice daily. Increasing to even higher doses has not been found beneficial. The most common side effects are GI-related, including upset stomach and nausea.

CAPSAICIN TOPICAL CREAM

Capsaicin is widely available as a cream in various doses. It is useful as a short-term analgesic, and a review has shown it to be superior to placebo for acute episodes of chronic low back pain.[6] It is widely available in most drug stores.

DEVILS CLAW (*HARPAGOPHYTUM* PROCUMBENS)

Despite the amusing name, this is an herbal supplement with good evidence of effectiveness in pain conditions. A 2007 review of the evidence found five systematic reviews on devils claw with strong evidence of effectiveness for low back pain and osteoarthritis pain of the knee and hip.[7] This effect was not inferior to NSAIDs. The review concluded by stating since there is strong evidence for devils claw, the possible place in the treatment schedule before NSAIDs should be considered.[7] Doses should be at least 50 milligrams of the harpagoside constituents, which equates to 2.6 grams/day of the root. Effects are dose dependent. It is generally well tolerated.

ENERGY-RELATED SUPPLEMENTS

In some patients, it may be useful to actively try to boost energy levels. This may be useful in helping patients to exercise. A general class of herbal medications with this property is known as the adaptogens. There is no data on these supplements specifically in terms of their effects on fibromyalgia or chronic pain. Energy-boosting beverages, which typically contain high doses of caffeine or other stimulant compounds, are not likely to be beneficial. For more information on adaptogens, see the Adaptogens tool.

GAMMA LINOLEIC ACID

Gamma linoleic acid (GLA) is an omega-6 fatty acid found primarily in vegetable oils. Specifically, it is found in evening primrose oil, borage seed oil, and black currant seed oil. A Cochrane review found moderate evidence for effectiveness of GLA in rheumatoid arthritis.[8] Specifically, GLA was found to decrease pain, improve disability scores, and improve overall well-being compared with placebo oils. Doses of GLA varied significantly in these studies, ranging from 500 milligrams to 2,800 milligrams daily. Evening primrose oil is preferred over borage seed oil because borage seed oil contains some chemicals (pyrrolizidine alkaloids) that are toxic to the liver. Side effects include headaches, nausea, and diarrhea.

GLUCOSAMINE AND CHONDROITIN

These are compounds found in the joint cartilage, synovial fluid, and connective tissue. Both may prevent cartilage destruction, and as such, they have been popular supplements for osteoarthritis (OA). Evidence of effectiveness has been mixed and controversial. A

Cochrane review found efficacy for glucosamine *sulfate*, but this was specific to the Rotta brand, and not noted when findings were pooled together with research on other brands.[9] Improvement in knee OA was in both pain and function. Glucosamine *hydrochloride* supplements have not shown efficacy in OA. Glucosamine sulfate has also been tested in chronic low back pain and showed no evidence of efficacy.[10] At this point there is some evidence for the use of glucosamine and chondroitin in the treatment of knee OA, but not for other painful conditions. For patients with knee OA, it may be worth a trial of therapy, keeping in mind the effects may not be seen for 3 months. Dosing for both glucosamine and chondroitin is in the range of 500 milligrams three times daily.

MAGNESIUM

Magnesium deficiency appears to be more common in patients with fibromyalgia, and deficiency is correlated with the presence of fibromyalgia symptoms. Supplementation with magnesium citrate has been shown to reduce the intensity of fibromyalgia symptoms.[11] Magnesium supplements can be calming for some patients, so it can be useful to take them before bed. A dose of 400-800 milligrams of supplement is often recommended. Magnesium oxide should be avoided as a supplement due to its laxative effects. Dietary sources of magnesium includes whole grains, spinach, almonds, soybeans, and avocados.

OMEGA-3 SUPPLEMENTATION

Supplementation with omega-3 fatty acids has been found in meta-analyses to improve joint tenderness and morning stiffness in patients with rheumatoid arthritis.[12] While efficacy is more established in inflammatory conditions such as rheumatoid arthritis, it is unknown what effect omega-3 supplementation has on pain with less of an inflammatory component.[13] Doses should be standardized based on the amount of EPA and DHA present in the supplement, and should exceed 2 grams per day of EPA and DHA to get the desired benefit. Omega-3 supplements are quite safe and may improve other aspects of health, such as lipid profiles. Cost varies significantly depending on the brand. Consumer Labs provides information on individual brands and their overall content. These supplements are normally well tolerated. They can have a fishy aftertaste and cause dyspepsia in some people; this improves if the supplement is kept refrigerated.

S-ADENOSYLMETHIONINE (SAME)

This is a supplement with indications for both depression and osteoarthritis, which makes it an intriguing option for chronic pain. SAMe is a coenzyme present in nearly all the body's tissues and is involved in dozens of reactions. It ahs several potential mechanisms of action, including having anti-tumor necrosis factor (TNF) effects, improving glutathione uptake, and demonstrating anti-inflammatory properties. However, exactly how it helps depression and OA is not clear. Research has generally been positive with regards to efficacy, but many studies have been limited by size and quality. A 2009 Cochrane review of

its use in OA, which included four studies, showed a very small beneficial effect in terms of pain and functional improvement. However, the review was limited by poor quality of the studies and was judged inconclusive.[14] A previous 2002 meta-analysis of 11 studies compared SAMe to placebo and NSAIDs. SAMe had an effect comparable to NSAIDs with fewer adverse effects. Again, the analysis was limited due to methodological problems with the included studies.[15] Currently there is not any evidence for its use specific to fibromyalgia.

Given the high coexistence of pain and depression, and given its overall good safety profile, SAMe is a supplement to consider for patients with pain. The major drawback is cost, as it is quite expensive. Cost can be $2-$4 per day. Dosages for depression are typically 400 milligrams, three or four times daily. The dosage for OA is 200 milligrams, three times a day.

SLEEP-RELATED SUPPLEMENTS

Sleep is important to address in fibromyalgia and chronic pain and, as discussed, is often dysfunctional. There are many aspects to addressing healthy sleep, but some dietary supplements may be beneficial. For more information, see the Recharge overview.

VITAMIN D

The relationship between vitamin D deficiency and chronic pain is intriguing, but not yet clear. Epidemiologic studies have correlated low vitamin D levels and chronic musculoskeletal pain, with prevalence in one study exceeding 90%.[16,17]. Vitamin D deficiency is known to cause osteomalacia and a resultant dull, achy pain, which can be either localized or widespread.[18] Despite the high correlation and a plausible mechanism of contributing to pain states, a recent Cochrane review found poor evidence to support vitamin D supplementation in chronic pain.[19] This finding was based on four studies, three of which were deemed of low quality. A similar study published since the Cochrane review on vitamin D supplementation in Veterans showed that it improved pain, sleep, and quality of life.[20] Clearly, more research is needed in this area to guide future recommendations. At this time it seems reasonable to test vitamin D levels in patients with chronic pain and institute a trial of supplementation with low levels, given the safety of supplementation and the potential to have a positive impact on health in other areas in addition to pain.

WILLOW BARK (*SALIX* ALBA)

Willow bark contains salicin, which is related to aspirin. It has been used for centuries to relieve pain.[21] The mechanism of action is thought to be COX-2 inhibition, similar to aspirin, but without the effects on prostaglandins or coagulation.[22] There is evidence of efficacy in chronic low back similar to that seen for rofecoxib 12.5 milligrams.[21] Evidence

in osteoarthritis is mixed.[21] The effect is dose dependent, and the willow bark dosage used in studies was standardized to 240 milligrams of salicin.

OTHER HERBAL ANTI-INFLAMMATORIES

Other herbal medicines have known anti-inflammatory properties, most notably turmeric and ginger. Both of these supplements have some preliminary evidence to support their use, but overall evidence is not strong at this point. Ginger has shown some effectiveness for osteoarthritis of the knee and turmeric for rheumatoid arthritis.[7] Both are considered safe and are good additions to an anti-inflammatory diet, but clear recommendations cannot be made this time for chronic pain patients.[13]

RESOURCE LINKS

- Adaptogens. https://www.va.gov/WHOLEHEALTHLIBRARY/docs/Adaptogens.pdf
- Consumer Labs. https://www.consumerlab.com
- Passport to Whole Health, Chapter 15. https://www.va.gov/WHOLEHEALTHLIBRARY/passport/chapter-15.asp
- Recharge. https://www.va.gov/WHOLEHEALTHLIBRARY/overviews/Recharge.asp

AUTHORS

"Supplements for Pain" was written by Russell Lemon, DO (2014).

This Whole Health tool was made possible through a collaborative effort between the University of Wisconsin Integrative Health Program, VA Office of Patient Centered Care and Cultural Transformation, and Pacific Institute for Research and Evaluation.

REFERENCES

1. A New Portrait of CAM Use in the United States. NCCAM. 2004;XI. Issue 3.
2. Rosenquist E. Overview of the treatment of chronic pain. *UptoDate*. 2013. Accessed 12/1/2013.
3. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2012;60(4):616-631.
4. Turk DC, Wilson HD, Cahana A. Treatment of chronic non-cancer pain. *Lancet*. 2011;377(9784):2226-2235.
5. Ziegler D, Nowak H, Kempler P, Vargha P, Low PA. Treatment of symptomatic diabetic polyneuropathy with the antioxidant alpha-lipoic acid: a meta-analysis. *Diabet Med*. 2004;21(2):114-121.
6. Gagnier JJ. Evidence-informed management of chronic low back pain with herbal, vitamin, mineral, and homeopathic supplements. *Spine J*. 2008;8(1):70-79.
7. Chrubasik JE, Roufogalis BD, Chrubasik S. Evidence of effectiveness of herbal anti-inflammatory drugs in the treatment of painful osteoarthritis and chronic low back pain. *Phytother Res*. 2007;21(7):675-683.

8. Cameron M, Gagnier JJ, Chrubasik S. Herbal therapy for treating rheumatoid arthritis. *Cochrane Database Syst Rev*. 2011(2):CD002948.
9. Towheed TE, Maxwell L, Anastassiades TP, et al. Glucosamine therapy for treating osteoarthritis. *Cochrane Database Syst Rev*. 2005(2):CD002946.
10. Wilkens P, Scheel IB, Grundnes O, Hellum C, Storheim K. Effect of glucosamine on pain-related disability in patients with chronic low back pain and degenerative lumbar osteoarthritis: A randomized controlled trial. *JAMA*. 2010;304(1):45-42.
11. Bagis S, Karabiber M, As I, Tamer L, Erdogan C, Atalay A. Is magnesium citrate treatment effective on pain, clinical parameters and functional status in patients with fibromyalgia?. *Rheumatol Int*. 2013;33(1):167-172.
12. Goldberg RJ, Katz J. A met-analysis of the analgesic effects of omega-3 polyunsaturated fatty acid supplementation for inflammatory joint pain. *Pain*. 2007;129(1-2):210-223.
13. Teets RY, Dahmer S, Scott E. Integrative medicine approach to chronic pain. *Prim care*. 2010;37(2):407-421.
14. Rutjes AW, Nuesch E, Reichenbach S, Juni P. S-Adenosylmethionine for osteoarthritis of the knee or hip. *Cochrane Database Syst Rev*. 2009(4):CD007321.
15. Soeken KL, Lee WL, Bausell RB, Agelli M, Berman BM. Safety and efficacy of S-adenosylmethionine (SAMe) for osteoarthritis. *J Fam Pract*. 2002;51(5):425-430.
16. Macfarlane GJ, Palmer B, Roy D, Afzal C, Silman AJ, O'Neill T. An excess of widespread pain among South Asians: are low levels of vitamin D implicated?. *Ann Rheum Dis*. 2005;64(8):1217-1219.
17. Plotnikoff GA, Quigley JM. Prevalence of severe hypovitaminosis D in patients with persistent, nonspecific musculoskeletal pain. *Mayo Clin Proc*. 2003;78(12):1463-1470.
18. Holick MF. Vitamin D deficiency: what a pain it is. *Mayo Clin Proc*. 2003;78(12):1457-1459.
19. Straube S, Derry S, Straube C, Moore RA. Vitamin D for the treatment of chronic painful conditions in adults. *Cochrane Database Syst Rev*. 2015(5):CD007771.
20. Huang W, Shah S, Long Q, Crankshaw AK, Tangpricha V. Improvement of pain, sleep, and quality of life in chronic pain patients with vitamin D supplementation. *Clin J Pain*. 2013;29(4):341-347.
21. Vlachojannis JE, Cameron M, Chrubasik S. A systematic review on the effectiveness of willow bark for musculoskeletal pain. *Phytother Res*. 2009;23(7):897-900.
22. Vlachojannis J, Magora F, Chrubasik S. Willow species and aspirin: different mechanism of actions. *Phytother Res*. 2011;25(7):1102-1104.