Dynamic Chiropractic

VITAMINS / SUPPLEMENTS

Managing Autoimmune Diseases With Nutrition and Supplementation, Part 1

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In many cases of autoimmune disease, especially those affecting the joints (e.g., rheumatoid arthritis), the patient is seldom provided with evidence-based nutrition and supplementation practices from their medical practitioner. Studies show, however, that specific dietary and supplementation measures can play a significant role in long-term management of these conditions with respect to preserving joint integrity, reducing pain and inflammation, improving quality of life and extending years of functional living.

Clinical and preclinical studies have identified three main biological targets that can be favorably influenced using nutrition and supplementation-based interventions: 1) suppressing inflammatory eicosanoids; 2) inhibiting inflammatory and hyperproliferative cytokines and transcription factors; and 3) immune modulation (bioregulation of immune system).

Eicosanoid Synthesis and Inflammation

The inflammatory process involves the synthesis of prostaglandin series-2 (PG-2) eicosanoids. PG-2 eicosanoids are derived exclusively from the polyunsaturated fat known as arachidonic acid, which is found at appreciable levels in many domestic meat products. The over-ingestion of linoleic acid (from corn, sunflower, safflower and mixed vegetable oils, for example) also encourages the conversion of linoleic acid to arachidonic acid via desaturation and elongation biochemical pathways. Thus, reducing intake of high-animal-fat products and using oils that are higher in monounsaturated fats (e.g., olive oil) in place of linoleic acid-rich vegetable oils help to reduce the synthesis of PG-2 eicosanoids.

It is also well-documented that omega-3 fats and supplementation with gamma-linolenic acid (GLA) produces anti-inflammatory effects via their conversion to prostaglandin series-3 (PG-3) and prostaglandin series-1 (PG-1) hormones, respectively. PG-3 and PG-1 are known to have anti-inflammatory effects. The precursor to prostaglandin series-3 eicosanoids is eicosapentaenoic acid (EPA), an omega-3 fat found in cold-water fish and fish oil. However, docosahexaenoic acid (DHA) can be converted to EPA within the body. DHA is also found in fish and fish oil. Alpha-linolenic acid can also be converted to EPA via desaturation and elongation enzymes. Alpha-linolenic acid is an omega-3 fat found at high levels (58 percent) in flaxseed oil.

To increase synthesis of PG-1, many patients supplement with borage seed oil, black currant oil and/or evening primrose oil. The GLA in these oils can be converted into dihomo gamma linolenic acid, which can then be converted into anti-inflammatory PG-1 eicosanoids.

As such, studies support a second step in controlling the production of inflammatory eicosanoids, which involves daily supplementation with essential fatty acids (EFA's), as explained above.[1-6] Based on the available data, I personally feel that a supplement combining 400 mg each of fish oil, flaxseed oil and borage oil is the ultimate EFA supplement for autoimmune patients and those with other inflammatory conditions. This combination is also a very cost-effective formula and makes

EFA supplementation practical for long-term patient compliance. I recommend 3-6 capsules per day, depending on the severity of inflammation. (I also recommend 2-3 capsules per day for general prevention of cancer, heart disease, Alzheimer's disease, general well-being, and to promote healthy skin texture.)

Studies also suggest that certain antioxidants (vitamin C, vitamin E, selenium, beta-carotene etc), as well as certain B vitamins (e.g., vitamin B_6) and magnesium, act as co-factors and co-enzymes to hasten the synthesis of anti-inflammatory PG-1 and PG-3 eicosanoids from their precursor polyunsaturated fatty acids. Various clinical studies have shown important anti-inflammatory outcomes and improved patient management of various autoimmune and other inflammatory conditions, using supplementation with meaningful dosages of antioxidants, B vitamins and/or magnesium.

Vitamin B6 and antioxidants may also inhibit the inflammatory effects of tumor necrosis factor alpha, a cytokine that is known to perpetuate the inflammatory and hyperproliferative processes in many autoimmune diseases.[7-17] (We will examine these cytokines, as well as nuclear transcription factors, in the next section.)

A third way in which patients can suppress the synthesis of inflammation-promoting PG-2 is via supplementation with herbs that directly inhibit cyclo-oxygenase and lipoxygenase enzymes. These enzymes are responsible for the conversion of arachidonic acid into PG-2. Certain herbal agents including curcumin, white willow extract, ginger, boswellia and others have shown significant effects on reducing various inflammatory conditions, including autoimmune diseases, in clinical trials. Thus, I also recommend a supplement containing curcumin, white willow extract, ginger and boswellia, which delivers therapeutic dosages of their active constituents. Patients usually require 1-3 capsules, three times per day, to achieve control of their inflammatory condition. These natural agents work in a similar way as aspirin, ibuprofen, COX-2 inhibitors and some other nonsteroidal anti-inflammatory drugs, but without the risk of gastrointestinal bleeding or liver and kidney toxicity.[18-36]

Inflammatory Cytokines and Nuclear Transcription Factors: Hallmark Features of Autoimmune Disease

In recent years it has been identified that in many autoimmune diseases, macrophages (and some other immune cells, to a lesser degree) secrete disproportionately high levels of a cytokine known as tumor necrosis factor alpha (TNF-alpha). In turn, TNF-alpha encourages other immune cells (and some non-immune cells, such as endothelial cells) to increase the translocation of nuclear factor kappa beta (a cytoplasm-based protein) to the nuclear DNA of the cell.

Acting as a transcription factor, nuclear factor kappa beta up-regulates genes that code for the synthesis of inflammatory and hyperproliferative cytokines, such as interleukin [1,6,8]. Thus, in autoimmune diseases, the oversecretion of TNF-alpha (primarily for activated macrophages) activates the downstream effects of nuclear factor kappa beta on specific genes that promote the release of inflammatory and hyperproliferative cytokines. These events are a hallmark feature of many autoimmune diseases.

Pharmaceutical companies have introduced drugs that inhibit the action of TNF-alpha. These drugs demonstrate anti-inflammatory effects, but are associated with a myriad of untoward and undesirable side effects, including lymphoma, infections, congestive heart failure, demyelinating disease, a lupus-like syndrome, induction of auto-antibodies, injection site reactions, systemic side effects and opportunistic infections.

The reason for this is that under certain situations, the release of TNF-alpha is desirable to help fight infections and encourage programmed cell death (apoptosis) of emerging cancer cells. Thus, drugs that impose a complete blockade to the effects of TNF-alpha are associated with many adverse side effects, as described previously.

Editor's note: Part 2 of this article appears in the July 29 issue and explores other nutritional considerations in managing autoimmune diseases.

References

1. DeCaterina R, Basta G. N-3 fatty acids and the inflammatory response – biological background. *European Heart Journal Supplements, 2001;*3(Suppl D):D42-D49.
2. Funk CD. Prostaglandins and leukotrienes: advances in eicosanoid biology. *Science,* 2001;294(5548):1871-1875.
3. Kinsella JE, Lokesh B, Stone RA. Dietary n-3 polyunsaturated fatty acids and amelioration of cardiovascular disease: possible mechanisms. *Am J Clin Nutr*, 1990;52:521-28.
4. Calder PC. N-3 polyunsaturated fatty acids and inflammation: from molecular biology to the clinic. *Lipids*, 2003;4:343-52.
5. Fan YY, Chapkin RS. Importance of dietary gamma -linolenic acid in human health and nutrition. *Journal of Nutrition*, 1998;128 (9):1411-1414.
6. Prescott S. The effect of eicosapentaenoic acid on leukotriene B production by human neutrophils. *J Biol Chem*, 1984;259(12):7615-21.
7. Murray M, Pizzorno J. *Encyclopedia of Natural Medicine, 2nd Edition.* Prima Publishing, 1998:770-1.
8. Borenstein O. "Osteoarthritis Clinical Update." American College of Rheumatology, 1999; Annual Scientific Meeting. Medscape, 1999.
9. McAdam P. "Chicken Cartilage Assessed in Rheumatoid Arthritis." *Medical Tribune*, November 1993.
10. Wittenborg A, et al. Effectiveness of vitamin E in comparison with diclofenac sodium in treatment of patients with chronic polyarthritis. *Z Rheumatol*, Aug 1998;57(4):215-21.
11. Edmonds SE, et al. Putative analgesic activity of repeated oral doses of vitamin E in the treatment of rheumatoid arthritis. Results of a prospective placebo controlled double blind trial. *Ann Rheum Dis*, Nov 1997;56(11):649-55.
12. Heinle AK. Selenium concentration in erythrocytes of patients with RA. Clinical and laboratory chemistry infection markers during administration of selenium. *Med-Klin,* 1997;92(suppl 3):29-31.
13. Situnayake RD. Chain breaking antioxidant status in rheumatoid arthritis: clinical and laboratory correlates. *Ann Rheum Dis*, Feb 1991;50(2):81-6.
14. Kose K, et al. Plasma selenium levels in rheumatoid arthritis. *Biol Trace Elem Res*, 1996;53(1-3):51-6.
15. Tarp U, et al. Low selenium level in severe rheumatoid arthritis. *Scand J Rheumatol*, 1985;14(2):97-101.
16. Yanaka N, Koyama TA, Komatsu S, Nakamura E, Kanda M, Kato N. Vitamin B6 suppresses NF-kappaB activation in LPS-stimulated mouse macrophages. *Int J Mol Med.* 2005;16(6):1071-5.
17. "Magnesium Supplements Could Reduce Inflammation." Nutraingredients-usa.com, July 27, 2006.
18. Deadhar, et al. Preliminary studies on anti rheumatic activity of curcumin. *Ind J Med Res*, 1980;71:632-34.
19. Satoskar RR, et al. Evaluation of anti-inflammatory property of curcumin in patients with post-operative inflammation. *Int J Clin Pharmacol Ther Toxicol,* 1986;24:651-54.
20. Murray MT. *The Healing Power of Herbs*. Prima Publishing, Rocklin, CA, 1995:327-35.
21. Arora RB, et al. Anti-inflammatory studies on curcuma longa (turmeric). *Ind J Med Res*, 1971;50:1289-95.

22. Heck A, et al. Potential interactions between alternative therapies and warfarin. *Am J Health – Syst Phar*, 2000;57(13):1221-1227.
23. Schweizer S, et al. Workup-dependent formation of 5-lipoxygenase inhibitory boswellic acids analogues. *J Nat Prod*, Aug 2000;63(8):1058-1061.
24. Etzel R. Special extract of boswellia serrata (H15) in the treatment of rheumatoid arthritis. *Phytomed*, 1996;3:91-94.
25. Bradley PR, et al. *British Herbal Compendium, Volume 1*. Bournemouth, Dorset, UK: British Herbal Med Assoc., 1992:224-26.
26. Mills SY, et al. Effects of a proprietary herbal medicine on the relief of chronic arthritic pain: a double-blind study. *Br J Rheum*, 1996;35:874-78.
27. Chrubasik S, et al. Treatment of low back pain exacerbations with willow bark extract: a randomized double-blind study. *Am J Med*, Jul 2000;109(1):9-14.
28. Srivastava KC, et al. Ginger in rheumatism and musculoskeletal disorders. *Medical Hypotheses*, 1992;39:342-8.
29. Bliddal H, et al. A randomized placebo-controlled, cross-over study of ginger extracts and ibuprofen in osteoarthritis. *Osteoarthritis Cartilage*, Jan 2000;8(1):9-12.
30. Klein G, et al. Short-term treatment of painful osteoarthritis of the knee with oral enzymes. *Clin Drug Invest*, 2000;19(1):15-23.
31. Cohen A, et al. Bromelain therapy in rheumatoid arthritis. *Pennsyl Med J*, June 1964;67:627-30.
32. Seligman B. Bromelain: an anti-inflammatory agent. *Angiology*, 1962;13:508-510.
33. Ferrandiz JL, et al. Anti-inflammatory activity and inhibition of arachidonic acid metabolism by flavonoids. *Agents Action,* 1991;32:283-287.
34. Tarayre JP, et al. Advantages of a combination of proteolytic enzymes, flavonoids and ascorbic acid in comparison with nonsteroidal anti-inflammatory agents. *Arzneium Forsch*, 1977;27:1144-1149.
35. Yoshimoto T, et al. Flavonoids and potent inhibitors of arachidonate 5–lipoxygenase. *Biochem Biophys Res Comm*, 1983;116:612-18.
36. Weiss RF. *Herbal Medicine*. Beaconsfield, 1988:362.