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## **Antioxidant Supplementation in the Treatment of Rheumatoid Arthritis**

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Rheumatoid arthritis (RA) is a chronic condition that causes joint pain and loss of mobility. An estimated 3 percent of the population is affected, with women outnumbering men by approximately 3-1. In more severe cases, RA can lead to eye inflammation; neurological problems; inflamed blood vessels; disorders of the lymph system; and cardiac complications. The scientific community views it as an autoimmune disease, whereby the body's immune system attacks its own tissues as if it were a foreign invader.<sup>1</sup>

The normal white blood cell count in synovial fluid is less than 100 per milliliter, on average. In patients afflicted with osteoarthritis, this figure rises to approximately 800 per milliliter; in those with rheumatoid arthritis, it is significantly higher. White blood cells are known to contribute to pain and inflammation via several mechanisms, one of which involves the conversion of arachidonic acid to inflammatory leukotrienes (LTB-s4). This reaction is catalyzed by the 5-lipoxygenase enzyme within leukocytes. Evidence suggests that free radicals generated by white blood cells within the synovial fluid serve to increase the rate of synthesis of certain inflammatory mediators (e.g., LTB-4, PG-2, interleukin-1, tissue necrosis factor-alpha).<sup>2</sup> As such, investigators have recently explored the use of antioxidant vitamins and minerals as a possible means to reduce the pain and inflammatory events associated with rheumatoid arthritis.

Several important clinical trials support the use of antioxidant vitamin and mineral supplementation, at specific doses, as a complementary intervention to help manage this condition. In many cases, the need for anti-inflammatory drugs can be significantly reduced, and sometimes eliminated, when antioxidant supplementation is co-administered.<sup>3,4,5,6</sup> As long-term use of anti-inflammatory drugs is associated with many adverse and life-threatening side-effects, any safe and effective treatment shown to reduce reliance on these medications should be considered.<sup>4</sup> Therefore, health practitioners should be aware of the research status pertaining to the use of antioxidant vitamins and minerals in the global management of patients with rheumatoid arthritis.

## **Vitamin E**

With other antioxidants, vitamin E has been shown to modulate the activity of the cyclooxygenase and lipoxygenase enzymes. These enzymes are involved in the conversion of arachidonic acid to pro-inflammatory prostaglandins and leukotrienes, respectively. Experimental evidence demonstrates that vitamin E and other antioxidants reduce the synthesis of pro-inflammatory prostaglandins (e.g. PG-2) and leukotrienes (LTB-4).<sup>3,4,5</sup>

One randomized, double-blind clinical study tested vitamin E supplementation against the anti-inflammatory drug diclofenac sodium in hospitalized rheumatoid arthritis patients. Patients were given 400 mg of natural vitamin E, three times daily, or the standard anti-inflammatory dosage of diclofenac sodium. After three weeks of treatment, both groups showed the same significant degree of improvement with respect to joint stiffness, improved grip strength and pain reduction. Duration of morning stiffness was reduced in the vitamin E group from 90 to 68 minutes, compared with 68 to 30 minutes in the diclofenac group. Physicians and patients considered both interventions similarly effective, and indicated that the use of vitamin E in these cases could help reduce the incidence of serious side-effects associated with the use of anti-inflammatory drugs.<sup>4</sup>

Other clinical studies using vitamin E as a treatment for rheumatoid arthritis have shown more modest improvement; however, even these researchers concluded that vitamin E's small, but significant, pain-relieving effect justifies using this vitamin as a complement to standard anti-inflammatory treatment.<sup>5</sup>

## **Vitamin C**

With regards to vitamin C and rheumatoid arthritis, several studies show that RA patients tend to have low blood levels and white blood cell levels of vitamin C. It is known that white blood cells use vitamin C at a faster rate when fighting an infection, and that vitamin C modulates the activity of cyclooxygenase and lipoxygenase enzymes within white blood cells, in a similar manner as vitamin E. Animal studies show that vitamin C reduces inflammation and swelling, and demonstrates greater pain tolerance in animals with arthritis.<sup>7</sup>

## **Selenium**

Selenium also participates as an antioxidant by activating the enzyme glutathione peroxidase. In this role, selenium serves as the prosthetic group, attaching to four different sites on the glutathione peroxidase enzyme, thereby activating its antioxidant capabilities. Patients with rheumatoid arthritis have been shown to have lower blood levels of selenium.<sup>8,9</sup> In an important double-blind clinical trial, patients administered 200 micrograms of selenium daily for three months showed fewer tender and swollen joints, and less morning stiffness. They also required lower doses of anti-inflammatory medication than patients in the control group.<sup>6</sup>

In conclusion, administration of the antioxidant vitamins E and C, and the mineral selenium, to patients suffering from rheumatoid arthritis, represents a scientifically sound complementary intervention that has been shown to enhance the reduction of joint pain, swelling and tenderness in clinical and experimental studies. Some of the biological mechanisms through which these antioxidants act to reduce the synthesis of inflammatory mediators within the joint synovial tissues have been documented. It is important to note that the doses of these micronutrients associated with reduction of RA signs and symptoms are at levels well beyond what an individual can derive from food alone. Thus, supplementation is required to achieve the desired results in RA cases.

As a precautionary note, vitamin E intake above 400 IU per day may potentiate the effects of anticoagulant drugs (Coumadin, warfarin, Plavix, aspirin), and possibly lead to a bleeding disorder. Therefore, patients on these medications should not exceed daily vitamin E intake of 400 IU from supplement sources.<sup>10</sup> Aside from these potential adverse side-effects, there are few other instances in which antioxidant supplementation (at the above-noted dosages) is contraindicated.

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