

*Review Article*

**NEWER NUTRITIONAL BASIS IN THE MANAGEMENT OF  
RHEUMATOID ARTHRITIS**

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**Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disorder culminating in joint destruction with functional impairment & deformities. This disease is associated with poor nutritional status in relation to various nutrients due to not only because of increased requirements & reduction in their absorption but also due to disease modifying anti-rheumatoid drugs (DMARD's), Non-steroidal Anti-inflammatory Drugs (NSAID's) & corticosteroids prescribed to alleviate symptoms of this disease. This results in associated side effects like gastrointestinal bleeding & bone loss (osteoporosis). Supplementation with long chain n-3 polyunsaturated fatty acids (PUFA) has constantly demonstrated an improvement in symptoms & reduction in dosages of NSAID's. Such a supplementation can be provided with the use of fish oils which have an anti-inflammatory potential. Vitamin C (ascorbic acid) use has been found to augment the anti-oxidant defenses, so also the use of Vitamin E (tocopherol) which has got anti-inflammatory action. Beneficial effects of Vitamin B6 (pyridoxal 5-phosphate) used in conjunction with folate & Vitamin B12 have been documented in those group of RA patients with high homocysteine metabolism, there by reducing the cardiovascular risk in these patients. In addition role of Selenium, Iron, Zinc, Calcium, and Vitamin D has**

been discussed in this review article. Besides adding certain nutrients in food, elimination of certain foods like red meat, dairy products, cereals & wheat gluten have shown improvement in progression of this disease. This article emphasizes the need for dietary supervision in the hands of expert dietician, of the Rheumatoid arthritis patients. **Electronic Physician 2010; Vol 2, Pages 33-38**

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## INTRODUCTION

Rheumatoid Arthritis (RA) is a chronic inflammatory autoimmune disease resulting in joint inflammation that is manifested by swelling, pain, functional impairment and muscle wasting. It is characterized by both local & systemic inflammation with elevated plasma concentration of pro-inflammatory cytokines, such as interleukins -6 (IL-6), interleukin 1b (IL-1b), tumor necrosis factor – alfa (TNF-a), and acute phase proteins. Genetic susceptibility with disease manifesting in response to an environmental factor has also been postulated as the cause of the disease. Rheumatoid disease is a debilitating disease & is associated with increased risk of cardiovascular disease & osteoporosis.

## DISCUSSION

Poor nutritional status in Rheumatoid arthritis patients has been reported & some drug therapies such as Nonsteroidal Anti-Inflammatory Drugs (NSAID's), prescribed to alleviate rheumatoid arthritis symptoms, may increase the requirements for some nutrients and reduce their absorption. Poor nutritional status in diagnosed RA patients has been reported in observational studies, with reduced energy intake from carbohydrates, high therapies with consumption of saturated fat and poor intake of micronutrients relative to unaffected controls (1, 2). Supplementation with long chain n-3 polyunsaturated fatty acids

(PUFA) consistently demonstrates an improvement in symptoms & reduction in NSAID's usage.

Conventional treatments for RA, including NSAID's, slow acting anti-rheumatic drugs (DMARD's) and corticosteroids, aim to reduce the patients pain and joint inflammation, minimize loss of function and decrease the progression of joint damage. However, such treatments are rarely totally effective and some pharmacological therapies have the potential to cause side effects, such as gastrointestinal bleeding & bone loss (3). As a result many RA sufferers turn to alternative (self-prescribed) therapies including dietary supplements. Studies have suggested that diet may play a role in the management of RA, particularly in alleviating the symptoms of the disease and reducing the risk of complications (4, 5). This review article provides an overview of the scientific evidence for the role of many different aspects of diet & of nutrient supplementation in the management of RA, by alleviating symptoms, decreasing the progression of disease or by reducing the reliance thereon, and combating the side effects of concomitant medication.

Dietary n-6 & n-3 PUFA are modulators of the lipid content of cellular membrane phospholipids, where they are able to affect cell function, and precursor for eicosanoids production. Eicosanoids mediate inflammation, cytokine synthesis & cell mediated immunity (6). Metabolism of n-6 PUFA produces arachidonic acid (AA),

leading to the production of leukotrienes, prostaglandins & thromboxanes where as the metabolism of n-3 PUFA produces docosahexanoic acid (DHA) and eicosapentanoic acid (EPA). The major source of n-3 & n-6 PUFA are linoleic acid and alpha-linolenic acid (ALNA) respectively. DHA & EPA which are found in fish oils, are able to decrease the production of AA-derived eicosanoids and decrease the production of pro-inflammatory cytokines TNF-a, IL-b & IL-6, decrease lymphocyte proliferation and damaging reactive oxygen species(7). In a review of fish oil supplementation studies, it was concluded that after 3-4 months of supplementation patients may be able to reduce their NSAID's dose under the supervision of the physician(8). Clinical trials of fish oil supplementation have been predominantly of short duration and more studies are required to investigate the safety of long term supplementation. There is also need for studies to further examine the minimum doses and duration required to bring clinical improvement(7), particularly as suppression of cell mediated immunity has been observed with high doses of fish oil in animal studies(9).

There is little evidence of the relative efficacy of plant sources of n-3 PUFA in the form of ALNA such as green leafy vegetables, flaxseeds, rapeseeds & canola oils. One study has demonstrated that 18g of ALNA/day for 8 weeks significantly decreased the stimulation & proliferation of lymphocytes in healthy adults (10). However this dose was greatly in excess of current average intakes (1-2gm/day) in United Kingdom's adult population (11) & would be very difficult for most individuals to achieve through dietary change. As the conversion of plant sources of n-3 to EPA is relatively inefficient, it is likely that large doses would be required to affect

immunological responses (7). Many plant oils are rich in n-6linoleic acid. Metabolism of this acid produces gamma-linolenic acid (GLA), which is converted to dihomo-gamma-linolenic acid (DGLA) & AA. In human inflammatory cells, GLA is converted to DGLA and accumulates in these cells that do not contain the necessary enzymes for the subsequent conversion to AA (12). Thus increased dietary GLA reduces the synthesis of potent mediators of inflammation from AA and increases anti-inflammatory action through some of the DGLA-derived eicosanoids (7). A number of studies have examined whether certain plant seeds oils that contain relatively large amounts of GLA may have anti-inflammatory actions, notably those extracted from the seeds of evening primrose oil (EPO), black currants & borage plants.

In general vitamin E (alpha-tocopherol) deficiency & low tissues vitamin E content enhances components of the inflammatory response & suppresses components of the immune response (13, 14). Dietary vitamin E supplementation has been reported to bring about the opposite effect (15). Miehle et al. (16) have proposed that free radical production increases in a dose-dependent manner depending on the severity of the condition & the number of the joints and that this could explain the graded effect of alpha-tocopherol. Patients with RA should be encouraged to increase their consumption of vitamin E rich cereals, fruits & vegetables.

Vitamin C (ascorbic acid) is an extra cellular scavenger of free oxygen radicals and as such play an important role in antioxidant defenses (17). In animal studies biochemical markers of antioxidant defense mechanisms were increased with vitamin C supplementation (18) & infiltration of

inflammatory cells into synovial fluid were decreased (19).

Serum selenium fluctuated in most of the patients during the course of the disease, with low levels in the period of high disease activity and normal levels in periods of low activity. It is hypothesized that selenium levels drop in response to inflammation & that supplementation may have anti-inflammatory effects (20). In immune cells, the major function of selenium appears to control excessive production of peroxidative substrates and it may also down-regulate cytokine signaling (21) with high doses possibly causing immunosuppression(20).

Low plasma levels of pyridoxal-5-phosphate (PLP), metabolically active form of vitamin B6 have been reported in RA patients (22) who may be associated with the elevated TNF-alpha production and subsequent elevated energy expenditure seen in RA (22). It has been suggested that vitamin B6, in conjuncture with folate and vitamin B12 supplementation may be beneficial to a subgroup of RA with high homocysteine metabolism. Elevated levels of homocysteine occur commonly in RA patients, and may contribute to the increased cardiovascular risk associated with the disease (23). Low levels of serum zinc have been reported in patients of RA (24), which may not be fully accounted by low dietary zinc intake (25).

### CONCLUSION

Dietary advice for patients with RA should be focused on achieving current daily recommendation for the population at large, with a varied balanced diet containing foods rich in anti-oxidants, providing adequate intake of iron, calcium, vitamin D & the B-

complex vitamins and boosting n-3 PUFA intake to reduce the severity of RA symptoms and improve overall health. Elimination diets are usually preceded by a period of fasting, which may confound the reported improvement in symptoms. Fasting is known to suppress inflammation (5). The mechanism by which this operates is not completely understood, but may involve a reduction in the release of inflammatory cytokines, reduced leukotrienes formation (26) and altered intestinal permeability. This may decrease the penetration of immunostimulants from the intestines (5). Such diets must be developed with expert dietetic support in order to preserve the nutritional quality of the diet. Patients with RA should be discouraged from taking self-imposed elimination diets; which may compromise nutritional status.

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