

# **Anti-inflammatory effects of a low arachidonic acid diet and fish oil in patients with rheumatoid arthritis**

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FROM ABSTRACT

Patients with rheumatoid arthritis (RA) improve on a vegetarian diet or supplementation with fish oil.

We investigated the effects of both dietary measures, alone and in combination, on inflammation, fatty acid composition of erythrocyte lipids, eicosanoids, and cytokine biosynthesis in patients with RA.

## Methods

Sixty-eight patients with definitive RA were matched into two groups of 34 subjects each.

One group was observed for 8 months on a normal western diet (WD) and the other on an anti-inflammatory diet (AID) providing an arachidonic acid intake of less than 90 mg/ day.

Patients in both groups were allocated to receive placebo or fish oil capsules (30 mg/kg body weight) for 3 months in a double-blind crossover study with a 2-month washout period between treatments.

**[A 200 lb person is about 91 kg; 91 kg X 30 mg = 2730 mg]**

Clinical examination and routine laboratory findings were evaluated every month, and erythrocyte fatty acids, eicosanoids, and cytokines were evaluated before and after each 3-month experimental period.

## Results

In AID patients, as compared to WD patients, fish oil led to a significant reduction in the numbers of tender (28% vs 11%) and swollen (34% vs 22%) joints.

## Conclusion

A diet low in arachidonic acid ameliorates clinical signs of inflammation in patients with RA and augments the beneficial effect of fish oil supplementation.

## THESE AUTHORS ALSO NOTE:

"Arachidonic acid (AA) present in cell phospholipids is the precursor of pro-inflammatory eicosanoids, and supplementation with arachidonic acid results in stimulated prostaglandin (PG) formation."

"Western diets (WD) are high in AA, which derives exclusively from nutrients of animal origin."

"N-3 fatty acids from fish oil inhibit cytokine and eicosanoid formation by competing with n-6 fatty acids for incorporation in cell phospholipids and for the binding sites of cyclo-oxygenase [COX] and lipoxygenase [LOX]."

Patients with RA improve on a vegetarian diet.

Several studies have found modest but consistent improvement in clinical symptoms and laboratory findings in RA patients who are given fish oil. [8 references].

In the diet group, to reduce AA intake to <90 mg per day, meat intake was limited to a maximum of two servings per week.

## RESULTS

This was an 8-month study.

Animal fat intake was 21 g/day less in the AID group than the WD group.

"Dietary EPA intake was low in both groups, as only lean fish was eaten."

In the WD group, fish intake was higher and their diet contained on the average 66.2 mg/day of EPA, as compared to 36.6 mg/day in the AID group. [EPA is eicosapentaenoic acid, a 20 carbon long omega-3 fat that is anti-inflammatory. This means that the western diet group had more anti-inflammatory EPA because they ate more fish].

Linoleic acid [18 carbon long omega-6] intake was up to 60% higher in the AID group. [Linoleic acid is an omega-6 precursor to pro-inflammatory AA, and the AID ironically consumed more of it than did the WD group in their diet].

The AID group consumed 70% less AA in their diet than did the WD group.

"At the first visit, CRP was higher in WD than in AID patients ( $2.2 \pm 2.5$  mg/dl vs  $1.6 \pm 1.5$  mg/dl)." [C-reactive protein is a blood marker for systemic inflammation, and some contend it is the most important marker for cardiovascular event risk.]

"Fish oil treatment reduced CRP in AID patients but not in WD patients."

**[IMPORTANT: This means that taking more anti-inflammatory fish oil will not reduce systemic inflammation if one does not reduce pro-inflammatory omega-6 AA in the diet].**

Patients on the AID diet consumed less meat, and therefore had significantly less AA in their erythrocytes.

"The EPA increased during supplementation with fish oil by 217% in the WD group and by 244% in the AID group." "Administration of fish oil reduced the disease activity in both groups." **[IMPORTANT]**

In AID patients, treatment with fish oil for 3 months resulted in a significant decrease in LTB<sub>4</sub>.

[LTB<sub>4</sub> is a pro-inflammatory bad guy that is derived from omega-6 AA]

"When fish oil was given from months 6–8, TNF-alpha decreased in both WD and AID patients." **[This would suggest that therapeutic benefit might require fish oil supplementation for 6-8 months.]**

"The reduction of corticosteroid and/or NSAID consumption was not a primary goal of the study." However, in patients on fish oil during months 6–8, a "significant reduction of NSAID medication was advised by the physician." **[IMPORTANT]**

"The corticosteroid doses were reduced during fish oil treatment in the AID and WD groups; the reduction was significant after 3 months of treatment with fish oil." **[This would suggest that therapeutic benefit might require a minimum of 3 months of fish oil supplementation].**

## DISCUSSION

"Our results demonstrate an enhancement of the beneficial effect of fish oil in a low AA diet in patients with RA."

"Several studies demonstrate an improvement in clinical signs of inflammation in patients with RA on vegetarian diets."

"A meta-analysis of clinical studies confirmed a modest but consistent benefit with regard to the number of tender joints and to morning stiffness in patients with RA during supplementation with n-3 fatty acids."

"In previous studies, effective doses were between 2.6 g and 6 g per day."

"The EPA:AA ratio in cell lipids determines the degree of competitive eicosanoid inhibition and presumably the therapeutic effect."

“In the present study, a significant increase in the EPA:AA ratio was found in erythrocyte lipids after EPA supplementation in AID and WD patients.”

“There was a significantly greater increase in the ratio with AID, which contained markedly less AA and more linoleic acid than WD.” **[Again, this implies that the benefit of fish oil supplementation is significantly enhanced if one reduces their consumption of pro-inflammatory AA].**

There is more efficient absorption of EPA when there is low dietary AA.

“In industrialized countries, the percentage of AA in plasma phospholipids averages 16% of total fatty acids, compared to only 2% in populations with traditionally high fish consumption.”

The prevalence of RA in these high fish consumption-low AA consumption populations is considerably lower than in inhabitants of industrialized countries.

“The AA present in lipid stores derives from exogenous (nutrients of animal origin) and endogenous (anabolism of linoleic acid) sources.”

“More than 80% of ingested AA is transported to peripheral cells for eicosanoid production [PGE2].” **[IMPORTANT]**

The endogenous conversion of linoleic acid (18 carbon long omega-6 fat found in corn, sunflower, safflower, and soy oil, etc.) to AA is decreased by other polyunsaturated fatty acids, including alpha-linolenic acid (18 carbon long omega-3 fat found in flax, hemp, and walnut oils, etc.).

**[This is why one should consume some flax oil daily].**

“Arachidonic acid is the precursor of several pro-inflammatory eicosanoids and considered to be a main determinant of eicosanoid formation.” **[IMPORTANT]**

These authors found a significant correlation between AA intake and the clinical signs of joint inflammation.

NSAID are known to depress renal PGE2 formation, and this may have obscured potential actions of the study diets on this eicosanoid. [This is an important point: it is difficult to assess the reduction of PGE2 with fish oil supplementation when the patients are also taking NSAIDs, which also inhibit the production of PGE2].

“In a previous study, supplementation with 2.6 g/day of n-3 fatty acids in subjects with RA led to a significant improvement in patients’ global evaluations and physicians’ assessments of pain after 3 months, while an improvement in grip strength was observed only after 6 months of treatment.” **[IMPORTANT]**  
These results are confirmed by this study.

"The greatest improvements in clinical parameters of arthritis and the most impressive reductions in eicosanoid and cytokine biosynthesis were found in AID patients given fish oil during months 6–8 of the study, indicating that fish oil efficacy is enhanced with lower AA stores." **[IMPORTANT]**

"This time-dependent effect most probably results from the fact that EPA accumulates only slowly in membrane phospholipids, due to the higher oxidation rate that EPA shares with all n-3 fatty acids **[take your antioxidants]** than with n-6 fatty acids."

"In conclusion, this study suggests a synergism between low AA intake and fish oil supplementation."

"We found a significant improvement in our RA patients" with fish oil supplementation and reduction of AA in the diet.

"It appears that the effect of AID is time-dependent, becoming manifest after 2 months on the diet."

"Clinical improvement and inhibition of eicosanoid formation were more pronounced in patients given EPA for months 6–8, pointing to the EPA:AA ratio as being decisive for clinical effectiveness."

#### KEY POINTS FROM DAN MURPHY

- 1) Patients with rheumatoid arthritis improve on a vegetarian diet or supplementation with fish oil.
- 2) Meat diets are high in arachidonic acid. Arachidonic acid is a 20-carbon long omega-6 fat that is converted into PGE2 and other pro-inflammatory substances that cause the joint pathology in RA patients.
- 3) Arachidonic acid is found only in foods of animal origin, and is not found in vegetarian foods.
- 4) However, linoleic acid, an 18 carbon long omega-6 fat precursor to AA is found in grain oils including corn, sunflower, safflower, cottonseed, soy, etc.
- 5) Omega-3 fatty acids from fish oil inhibit pro-inflammatory cytokine and prostaglandin formation by competing with omega-6 fatty acids for enzymes.
- 6) Supplementation with about 3,000 mg of EPA/DHA fish oil resulted in significant improvement in RA signs, symptoms, and lab assessment of pro-inflammatory cytokines and prostaglandins after 3 months, and best results were seen between 6-8 months. This is because EPA accumulates quite slowly in membrane phospholipids.

- 7) Supplementation with these fish oils allowed these RA patients to reduce their dependence on NSAIDs and corticosteroid drugs.
- 8) Best results were achieved in these RA patients with a combination of fish oil supplementation and reduction of AA in the diet by reducing the consumption of meat.
- 9) Other positive studies on RA patients with fish oil supplementation used doses between 2.6 g and 6 g per day.
- 10) More than 80% of ingested AA is transported to peripheral cells for eicosanoid production, like PGE2.
- 11) Alpha-linolenic acid (18 carbon long omega-3 fat found in flax, hemp, and walnut oils, etc.) reduces the conversion of linoleic acid (18 carbon long omega-6 fat found in corn, sunflower, safflower, and soy oil, etc.) to AA. This is one reason I like the omega-3 oils produced by Nutri-West, as it contains alpha-linolenic acid. I use their **COMPLETE HI-POTENCY OMEGA-3 LIQUID**. Their phone number is **800-443-3333**.
- 12) EPA is highly susceptible to oxidation, so take anti-oxidants. Nutri-West makes an antioxidant product called **COMPLETE OMEGA-3 CO-FACTORS** that is specifically formulated to protect the double bonds of essential fatty acids from oxidation.

#### COMMENT FROM DAN MURPHY

The most recent information that I am aware of [Sears, Barry,(Ph.D), The Anti-Inflammation Zone, ReganBooks, 2005], indicates that the most important blood test for everyone is to determine one's level of silent inflammation with the

Arachidonic Acid:Eicosapentaenoic Acid ratio, or AA:EPA

The optimal ratio it is 1:1

A 3:1 ratio is acceptable

The average American is a ratio of 30:1

The average chronic pain patient has a ratio of 50:1

Schizophrenics have a ratio that averages 70:1

To have your AA:EPA tested, check out [www.siptesting.com](http://www.siptesting.com)

Dan