Is Fish Oil Protective Against AIDS?

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Polyunsaturated Fatty Acids and Macrophage Activity

Considerable evidence has accumulated showing omega-3 fatty acids suppress the harmful activities of macrophages. For example, monocytes from human volunteers given fish oil supplements had sharply reduced production of interleukin-1 and tumor necrosis factor (Endres et al, 1989), platelet activating factor (Sperling et al, 1987), leukotriene B4 (Kremer et al, 1987), superoxide ion and monocyte chemiluminescence (Fisher et al, 1990), and arachidonic acid derived prostaglandins (Fischer, 1989). Fish oil retards murine systemic lupus erythematosus, a macrophage linked autoimmune disease, in NZBxNZW F1 mice (Prickett et al, 1981). In mice with macrophage mediated glomerulonephritis, fish oil supplements blocked kidney damage (Lefkowith and Schreiner, 1987). Fish oil, by suppressing macrophage activity, reduced streptozocin induced insulin dependent diabetes in mice (Linn et al, 1989). Furthermore, fish oil reduced mouse peritoneal macrophage production of prostaglandin E-2 (PGE-2) by 65% (Lokesh and Kinsella, 1987).

In contrast, linoleic acid, the dominant omega-6 fatty acid from vegetable oils, activates macrophages. For example, unstimulated splenic macrophages from mice fed linoleic acid for 30 days had a 250 fold increase in PGE-2 production over controls (Ogle et al, 1990). This rate was more than 9 times higher than for stimulated splenic macrophages from controls. In addition, linoleic acid increases kidney damage in mice with macrophage mediated glomerulonephritis (Lefkowith and Schreiner, 1987) and streptozocin induced insulin dependent diabetes in mice (Linn et al, 1989).

Macrophage Control of Lymphocyte Activity

PGE-2 produced by macrophages, sti-
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mulates the proliferation of T suppressor cells and impairs T helper and B cell proliferation (Ogle et al, 1990). Tumor necrosis factor, secreted by activated macrophages, inhibits T helper cell activity and appears to have autocrine stimulatory effects resulting in increased production of PGE-2 and interleukin-1 (Pryjma et al, 1989). Interleukin-1, by directly influencing the hypothalamus and pituitary to produce more ACTH, causes increased adrenal secretion of Cortisol (Goetzl et al, 1988). Macrophages also make ACTH, providing a redundant stimulatory pathway for Cortisol secretion (Nathan, 1987). The immunosuppressive properties of Cortisol are well known (Guyton, 1981). Transforming growth factor-beta, another product of activated macrophages, impairs lymphocyte function at extremely low concentrations while at the same time it stimulates monocytes (Wahl, 1989). Clearly, activated macrophages can powerfully suppress lymphocytes.

Perez et al (1987) have found that diets enriched with linoleic acid reduced allograft rejection in mice, a profound sign of lymphocyte immunosuppression. In a landmark experiment (Alexander et al, 1986), burned guinea pigs fed linoleic acid compared to fish oil had significantly greater weight loss, a higher metabolic rate, heavier adrenals, and lighter spleen. Furthermore, cell mediated immunity was 60% lower and opsonic index was 50% lower than the fish oil group. Macrophage activation induced by linoleic acid is the most likely mediator of the lymphocyte suppression.

Human Applications

A controlled study of 50 burn patients using different tube feeding formulations has been reported by the Shriners Burns Institute (Alexander and Gottschlich, 1990). Two groups received Osmolite-Promix or Traumacal, having 9% and 16% of the calories from linoleic acid, respec-
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Is Fish Oil Protective Against AIDS? A third group was given the Shriners' Burn Diet which contained 3.6% of the calories from linoleic acid and 4.5% from eicosapentaenoic acid, along with some added arginine, histidine and cysteine. The Shriners' Burn Diet group had significantly fewer deaths, wound infections, pneumonia, total infectious episodes and days in hospital. Total number of infectious episodes was two times higher in the 9% linoleic acid group and three times higher in the 16% linoleic acid group. It appears the lymphocyte suppressive properties of linoleic acid are of more than theoretical interest.

The dietary ratio of omega-6 fatty acids (linoleic acid) to omega-3 fatty acids (linolenic acid, eicosapentaenoic acid, docosahexanoic acid) for all of human history prior to the 19th century has been estimated to be about 1:1 (Leaf and Weber, 1987). Fish, wild game and leaves contain omega-3 fat. After 1800 the consumption of omega-6 fat began to rise and after 1930 rose rapidly. Nuts, seeds, grains, grain fed animals, and polyunsaturated vegetable oils are rich sources of omega-6 fat. Currently the ratio of omega-6 to omega-3 fat in industrialized nations hovers around 5:1.

Our linoleic rich diets are historically unprecedented. The evidence cited above indicates excessive linoleic acid is macrophage activating and lymphocyte suppressing. Hence over the past 200 years, most industrialized nations have gradually adopted immunosuppressive diets. At the present time, because of our huge intake of polyunsaturated vegetable oils, industrialized nations may be consuming some of the most immunosuppressive diets in human history.

Japan is an exception due to their prodigious fish consumption along with low animal and vegetable fat intake. Japan's unique disease incidence may be reflective of their low omega-6 to omega-3 dietary fat ratio. For example, diseases of macrophage activation, such as atherosclerosis (Bowyer and Mitchinson, 1989), rheumatoid arthritis (Harris, 1990), and possibly depression (Smith, 1991) have remarkably low incidence there. Furthermore, AIDS, a disease of lymphocyte suppression, is extremely rare in Japan. As of July, 1990, only 189 cases of AIDS have been reported in Japan, compared to 137,385 reported AIDS cases in the United States (Anonymous, 1990).

These astonishing differences in AIDS incidence can be conveniently attributed to cultural factors. On the other hand, Japan's low rate of AIDS may indicate a much more effective immune defense against HIV infection. If so, we may in part be seeing the immunological difference between the excessive linoleic acid consumption in the U.S. and the high fish intake in Japan.

Conclusion

The omega-6 to omega-3 ratio of fatty acids in the body could be a critical factor in the immune system defense against HIV infection and AIDS expression. Linoleic acid would assist HIV in suppressing lymphocytes, thereby increasing the rate of infection. Macrophages are one of the first cells infected with HIV and they are instrumental in the propagation and invasion of HIV into other tissues, especially brain (Gendelman et al, 1989; Ho, 1989). Macrophage activating linoleic acid probably facilitates the macrophages in their deadly work. Possibly anything that activates macrophages may increase die susceptibility to HIV infection and accelerate its progression to AIDS. If so, then casein may be another important dietary factor, since there are peptides in casein that directly activate gastrointestinal macrophages (Migliore-Samourand Jolles, 1988). Fish oil, because it calms down macrophages and permits a more competent lymphocyte response, should reduce HIV infectivity and AIDS progression. There is an important need to test these ideas with clinical trials.

References


