

Fish Oils and Kidney Disorders

Summaries of the latest research concerning fish oils and kidney disorders

What is IgA Nephropathy?

IgA nephropathy is a fairly common kidney disorder. It is caused by an inflammation (glomerulonephritis) in the network of blood capillaries involved in the filtration of waste products from the blood. More specifically, it manifests itself through the deposit of the antibody immunoglobulin A (IgA) in the mesangial cells, which support the walls of the capillaries. The IgA deposits and accompanying lesions to the capillaries interfere with proper filtration of waste products from the blood. IgA nephropathy is more common in men than in women and its incidence peaks between the ages of 16 and 35 years. IgA nephropathy is associated with a gradual decline in kidney function leading to end-stage renal disease within 5 to 25 years of diagnosis in 20-40% of patients. The disease is usually diagnosed after blood or excess protein is observed in the urine. Serum creatinine levels are abnormally high in IgA nephropathy because the kidneys are unable to filter creatinine (a waste byproduct of creatine, a protein that supplies energy for muscle contraction) out of the blood and excrete it in the urine. A doubling in serum creatinine level corresponds to a 50% decline in kidney function. There are no pharmaceutical drugs that will slow down or reverse the progression of IgA nephropathy.

Low-dose fish oil therapy effective in IgA nephropathy

ROCHESTER, MINNESOTA. Researchers at the Mayo Clinic previously reported that supplementation with 1.9 grams/day of EPA (eicosapentaenoic acid) plus 1.4 grams/day of DHA (docosahexaenoic acid) is effective in retarding the progression of IgA nephropathy. The researchers have now carried out another clinical trial to determine whether doubling the daily dose of fish oil supplement would be even more effective. Their randomized clinical trial involved 73 patients with biopsy-diagnosed IgA nephropathy. Ten of the patients had quite severe disease as indicated by a baseline serum creatinine level of 3.0-4.9 mg/dL while the remaining 63 patients had moderate disease (serum creatinine between 1.5-2.9 mg/dL). The fish oil supplement used in the trial was supplied by Pronova in Norway (trade name ? /Omacor/) in the form of highly purified ethyl esters of EPA and DHA. At the end of the 2-year study period the serum creatinine level in the low-dose group (1.9 g/day of EPA plus 1.5 g/day of DHA) had increased by 0.08 mg/dL per year while patients in the high-dose group (3.8 g/day of EPA plus 3.0 g/day of DHA) saw an average yearly increase of 0.10 mg/dL. Rapid deterioration in kidney function (creatinine increase of more than 0.5 mg/dL per year) was observed in 70% of the patients with severe disease as compared to only 23% in the group with moderate disease. There was no significant difference in the number of patients in the low and high dose groups who developed end-stage renal disease (ESRD). At the end of 2 years 86% in the low-dose group and 80% in the high-dose group were still free of ESRD. The corresponding numbers after 3 years were 73% and 76%. The 2-year number of about 85% ESRD-free compares to only 63% ESRD-free in a previously investigated placebo group. The /Omacor/ supplement was generally well-tolerated, but two patients (out of 73) did discontinue their treatment as a result of gastrointestinal intolerance. There were no unfavourable effects on serum lipid profiles (cholesterol levels), hematocrits, peripheral blood leucocytes or platelets. The researchers conclude that low-dose and high-dose fish oil supplementation is equally effective in slowing the progression of IgA nephropathy. *Donadio, JV, et al. A randomized trial of high-dose compared with low-dose omega-3 fatty acids in severe IgA nephropathy. Journal of the American Society of Nephrology, Vol. 12, 2001, pp. 791- 99/*

Fish oils slow progression of IgA nephropathy

ROCHESTER, MINNESOTA. In 1994 researchers at the Mayo Clinic reported that fish oils (eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) are effective in slowing the progression of IgA nephropathy. The follow-up period during the initial trial was 4 years. The Mayo researchers have now extended the follow-up period to 6.4 years. As in the earlier trial the patients took either placebo (olive oil capsules) or fish oil capsules providing 1.9 grams/day of EPA and 1.4 grams/day of DHA. The primary end point of the trial was an increase of 50% or more in serum creatinine and the secondary end point was the development of end-stage renal disease (ESRD). At the end of the follow-up period 17 patients in the fish oil group reached the primary end point versus 29 patients in the placebo group, i.e. a 41% reduction in the number of patients experiencing an increase in serum creatinine of 50% or more. Eight patients in the fish oil group developed ESRD versus 19 patients in the placebo group or a 58% reduction in the number of patients whose disease progressed to ESRD. The researchers conclude that early and prolonged treatment with fish oils slows the progression of renal disease in high-risk patients with IgA nephropathy. They believe that the main mechanism by which fish oils works is through competition with arachidonic acid for the enzyme required to produce eicosanoids. Arachidonic acid is metabolized to eicosanoids that engender inflammation while fish oils result in the production of eicosanoids that combat inflammation. The "good" eicosanoids likely slow renal disease progression by reducing glomerular and interstitial inflammation, mesangial cell contractility, platelet aggregation and vasoconstriction in response to renal injury. *Donadio, JV, et al. The long-term outcome of patients with IgA nephropathy treated with fish oil in a controlled trial. Journal of the American Society of Nephrology, Vol. 10, 1999, pp. 1772-77/*

Fish oils benefit kidney patients

ROCHESTER, MINNESOTA. IgA nephropathy is a common kidney disease that often follows a viral infection of the gastrointestinal or upper respiratory tract. There is no known cure for the disease and treatment with steroids, antibiotics, anticoagulants, antiplatelet drugs, and phenytoin has been ineffective. About 20 to 40% of all IgA nephropathy patients develop renal failure 5 to 25 years after diagnosis. Researchers at the Mayo Clinic report that supplementation with fish oils, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), is highly effective in slowing down the progression of the disease. Their clinical trial involved 106 patients who had been diagnosed with IgA nephropathy. Fifty-five of the patients were randomized to receive 12 fish oil capsules daily (providing 1.87 grams of EPA and 1.36 grams of DHA in total) while the remaining 51 patients received 12 olive oil (placebo) capsules daily. The progression of the disease was judged by regularly measuring the level of creatinine in blood serum during the two years of the trial. A clear difference was observed. While the patients in the fish oil group had an average median increase in serum creatinine of only 0.03 mg/dL the patients in the placebo group experienced an increase of 0.14 mg/dL annually indicating that their disease was progressing significantly faster. After four years 40% of the patients in the placebo group had died or developed end-stage renal disease as compared to only 10% in the fish oil group. No adverse effects of fish oil supplementation were observed. The Mayo Clinic researchers conclude that fish oil supplementation retards the progression of IgA nephropathy. NOTE: This study was partially funded by Merck, Sharp & Dohme, a manufacturer of pharmaceuticals, and Seven Seas Health Care, a producer of fish oils. *Donadio, James V., et al. A controlled trial of fish oil in IgA nephropathy. New England Journal of Medicine, Vol. 331, November 3, 1994, pp. 1194-99 van Ypersele de Strihou, Charles. Fish oil for IgA nephropathy? New England Journal of Medicine, Vol. 331, November 3, 1994, pp. 1227-29 (editorial)/*

IgA nephropathy associated with fatty acid deficiency

ROCHESTER, MINNESOTA. The fatty acid composition of cell membranes is a crucial indicator of overall health and studies have shown that abnormalities in the relative concentrations of essential fatty acids (EFAs) are associated with many common diseases such as diabetes and rheumatoid arthritis. The EFA profile of cell membranes is usually measured in the phospholipid phase of blood plasma. Researchers at the Mayo Clinic report that patients with IgA nephropathy have an abnormal EFA profile and that this abnormality can be corrected by supplementation with fish oil. Their clinical trial involved 15 patients with IgA nephropathy and 100 controls. All participants had their EFA profile analyzed at entry to the study and at 6 weeks, 6 months, and 12 months following entry. The analyses at baseline indicated that IgA nephropathy patients had significantly less omega-3 fatty acids in their cell membranes (20% less) than did controls. The shortfall in DHA (docosahexaenoic acid) was particularly significant at 25%. The difference in omega-6 fatty acid content between patients and controls was quite small with patients having a shortfall of 4%. The mean melting point of the membrane EFAs in the patients was 19.1 degrees C versus 14.8 degrees C in controls indicating that patients' cell membranes were less fluid than those in the controls. Supplementation with 6 to 12 grams per day of menhaden oil for a year dramatically increased membrane content of omega-3 fatty acids, specifically DHA and EPA (eicosapentaenoic acid). The content of the main omega-6 fatty acid, linoleic acid, declined slightly at 6 weeks and 6 months, but by 12 months had returned to normal. The content of the omega-6 fatty acid, arachidonic acid, on the other hand, was close to normal at entry, but declined thereafter. This is of particular interest in that arachidonic acid is the precursor for inflammatory eicosanoids while EPA is the precursor for anti-inflammatory eicosanoids. The researchers also measured protein excretion in the urine and glomerular filtration rate before and after fish oils supplementation. Both are important indicators of kidney function. Protein excretion rate (proteinuria) was markedly decreased and glomerular filtration rate significantly improved following supplementation. The researchers conclude that the treatment of IgA nephropathy should include a balanced and enhanced intake of essential fatty acids. *Holman, RT, et al. Essential fatty acid deficiency profiles in idiopathic immunoglobulin A nephropathy. American Journal of Kidney Diseases, Vol. 23, May 1994, pp. 648-54/*

Kidney transplant patients benefit from fish oils

HONOLULU, HAWAII. IgA nephropathy is likely to recur in patients who receive a kidney transplant as a result of having developed end-stage renal disease. It is estimated that recurrence rates are as high as 60% and that the transplant eventually fails in 30-60% of patients with IgA nephropathy. It is therefore not uncommon for these patients to have two transplants separated by 10 years or less. A medical researcher at the University of Hawaii now reports that transplant failure can be postponed quite significantly by supplementation with fish oils. He describes the case of a 34-year-old man who was observed to have blood in his urine (hematuria) in 1979. His kidney function deteriorated, by March 1986 he required dialysis treatments, and 2 months later he received a kidney transplant and was then put on prednisone and cyclosporine. In 1991 he was diagnosed with IgA nephropathy and a year later he was again put on dialysis, and subsequently received a second kidney transplant; thus his first transplant lasted 6 years. In May 1997, 5 years after the second transplant, the patient again developed IgA nephropathy and was then placed on fish oil supplementation (2.1 grams/day of EPA plus 1.4 grams/day of DHA). The amount of protein in his urine (proteinuria) decreased from 3299 mg/day before fish oil therapy to 458 mg/day after therapy. A normal value is less than 165 mg/day. Ten years after the second transplant there was no sign of rejection and the man's kidney function was well preserved. The researcher points out that this case clearly indicates the progressive nature of IgA nephropathy even if the kidney is replaced. It also clearly demonstrates a beneficial effect of fish oil therapy on post-transplantation IgA nephropathy, but this effect needs to be confirmed in larger trials. *Ng, Roland. Fish oil therapy in recurrent IgA nephropathy. Annals of Internal Medicine, Vol. 138, June 17, 2003, pp. 1011-12/*

Dialysis patients benefit from fish oils

CATSKILL, NEW YORK. Patients with kidney failure require long-term hemodialysis in order to remove waste products from the blood. It is estimated that about 350,000 patients in the USA alone require regular dialysis treatments. Although modern dialysis methods are effective in cleaning up the blood they do produce side effects. Uremic pruritus or renal itch (localized or generalized itch in patients with chronic kidney disease) affects up to 80% of patients on dialysis. A recent clinical trial found that patients given 6 grams/day of fish oil had significantly less severe itching than did patients given a similar daily dose of olive oil or safflower oil. The researchers doing the trial speculate that fish oils prevent itching by displacing arachidonic acid from cell membranes. Fish oils and arachidonic acid compete for the same enzymes (cyclooxygenase and lipoxygenase) used in the production of eicosanoids. If arachidonic acid "wins" more pro-inflammatory compounds (series 2 prostaglandins and series 4 leukotrienes) are produced whereas if fish oils gain the upper hand the result is the production of more anti-inflammatory compounds (prostaglandin E3 and leukotriene B5). The anti-inflammatory eicosanoids would be less likely to cause itching than would the pro-inflammatory ones. Because dialysis patients leave some blood in the dialysis machine at each treatment they are given the hormone erythropoietin in order to stimulate the production of new red blood cells. A small pilot study involving 20 dialysis patients was recently carried out to see if fish oil supplementation would reduce the need for erythropoietin. The patients were given 6 grams/day of emulsified fish oil (3 pouches of /Coromega/) for 8 weeks. At the end of the study the average erythropoietin requirement had declined by 16% and serum albumin had increased by 3.6%. Researchers at Emory University have found that dialysis patients who reported eating fish at least once in a 3-day period were about half as likely to die during the 3-year study period, as were patients who did not report any fish consumption. Fish oils are generally considered safe in daily intakes of as much as 12 grams. According to the Food and Drug Administration supplementing with EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid), the main components of fish oil, is safe provided the *combined* daily intake does not exceed 3 grams. (Note: This would correspond to about 10 grams of fish oil). There is no evidence that fish oils increase bleeding time; however, it would be prudent to adjust the dose of heparin used during dialysis if fish oil supplementation is used. *Vergili-Nelsen, JM. Benefits of fish oil supplementation for hemodialysis patients. Journal of the American Dietetic Association. Vol. 103, September 2003, pp. 1174-77/*

Fish oils for dialysis patients

ROCHESTER, MINNESOTA. Hemodialysis in patients with kidney failure requires that the blood to be cleaned is drawn from the body, pumped through the dialysis machine, and then returned to the body. Because relatively large amounts of blood are handled, it is necessary to use large catheters to draw and return the blood. In order to avoid the discomfort, pain and inconvenience of repeated puncture of the veins most patients on long-term maintenance dialysis now have a permanent access system (graft) made from /Gore-Tex/ (polytetrafluoroethylene) implanted in the arm. While this is convenient, the implant is also a potent breeding ground for blood clots and tends to become obstructed over time. It is estimated that the annual cost of maintaining dialysis access exceeds 1 billion dollars and that more than 50% of all access grafts experience thrombosis within one year after placement. Researchers at the St. Louis University School of Medicine now report that fish oil supplementation is highly effective in helping to avoid thrombosis and maintaining unobstructed access in grafts. Their clinical trial involved 24 patients with newly implanted polytetrafluoroethylene access grafts. Half the patients were randomized to receive 4 grams/day of fish oil (1.8 g EPA + 1.0 g DHA) while the other half received 4 grams/day of corn oil. At the end of the 12-month follow-up period the researchers found that access was still unobstructed in 76% of the patients given fish oil as compared to only 15% of those given corn oil. They conclude that fish oils possess unique biologic properties that make them effective in the prevention of graft access thrombosis. / Schmitz, PG, et al. Prophylaxis of hemodialysis graft thrombosis with fish oil: double-blind, randomized, prospective trial. Journal of the American

Society of Nephrology, Vol. 13, 2002, pp. 184-90 / Coromega *Additional References* 1. Donadio J.V. et al. IgA Nephropathy. *New England Journal of Medicine*, Vol. 347, September 5, 2002, pp. 738-748 *Conclusion:*A comprehensive review of the causes, pathology and treatment options for IgA nephropathy. 2. Donadio J.V. n-3 Fatty acids and their role in nephrologic practice. *Current Opinion in Nephrology and Hypertension*, Vol. 10, 2001, pp. 639-642 *Conclusion:* A review of the applications for fish oils in the treatment of kidney disorders. 3. Donadio, J.V. Use of fish oil to treat patients with immunoglobulin A nephropathy. *American Journal of Clinical Nutrition*, Vol. 71 (suppl), 2000, pp. 373S-375S *Conclusion:* A summary of clinical trials involving the use of fish oils in the treatment of IgA nephropathy. *OILOFPISCES.COM*
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