Essential Fatty Acids: Not Just for Dermatologists Anymore

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Basics of EFAs for the practitioner

The essential fatty acids are polyunsaturated fatty acids (PUFA). They are termed essential since they cannot be produced from other fatty acids by the body. They have unique medicinal properties in that dietary supplementation is considered to be a way to possibly redirect certain aspects of the body's metabolism in a way that is beneficial to the therapy of certain conditions. This is because the PUFA are linked to inflammation in the body. They are the essential elements in the production of various inflammatory mediators.

The omega 6 family (linoleic acid is primary source) produces a variety of pro-inflammatory products in that cyclooxygenase acts on it to produce a variety of prostaglandins and thromboxane A2. Omega 6 also includes arachnidonic acid. On the other hand the omega 3 family (linolenic acid) is mainly acted upon by lipoxygenase to produce less inflammatory leukotrienes. The predominant forms of Omega 3 fatty acids marketed include varying amounts of EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid).

For these dietary supplements to have an effect they must have sufficient time to incorporate into the cell membrane. There is competition by the PUFAs for conversion by the various enzymes into eicosanoids, therefore the more Omega 3 present the less very inflammatory products are produced. This means that a considerable amount of time (months) may elapse before they become effective. The exact mechanism in which these supplements work is still under investigation. It is still unknown if the absolute quantity that is given is the main factor in efficacy of if the ratio of Omega 3 to Omega 6 is the main factor. Some research would point to a Omega 6:Omega 3 ratio of between 5:1 to 10:1 being optimal to reduce inflammation. Feeding an appropriate diet may have some benefits over addition of supplements.

Dermatologic uses: A quick review

Many studies have shown that PUFAs can help with a variety of inflammatory and pruritic skin problems. Benefit has been shown in between 20 to 40% of patients being treated. Generally Omega 3/Omega 6 supplements are not able to control pruritus completely as a sole agent, but can be a very useful adjunctive therapy especially when antihistamines are being used. This effect has also been seen with cats that have pruritus, miliary dermatitis and eosinophilic granuloma complex lesions. Excessive supplementation with Omega 3 is probably not appropriate as it may in fact reduce the anti-inflammatory effect.

Use in orthopedic problems

A study did suggest that use of an EFA supplement could be of benefit in the treatment of hip arthritis. Approximately 50 % of dogs had a good to excellent response when treated. There was no blinding or placebo control in this study. A study on the influence of Omega 6:Omega 3 ratio in dogs with elbow DJD did not show any benefit in varying the ratio.

Use in cardiology

Initially it was tempting to use EFA supplements to help with thrombosis in cats with cardiomyopathy as EFA supplements have been shown to inhibit platelet function significantly in a variety of animal species. In humans considerable benefit is seen with diets rich in fish oil. Giving 1 g of omega 3 a day in 11,300 patients resulted in a reduction of fatal and non-fatal cardiac events by 10-15%. Recently research has been performed that showed no effect of omega 3 supplementation on clotting in cats, so that it is not likely to be of benefit in preventing thrombosis in this species.

An antiarrhythmic effect has been seen with increased n-3 levels in people. This has been a very significant finding. Experimental studies in animals using ischemia and reperfusion to induce arrhythmias have shown a benefit in regard to arrhythmias, independent of the effect of these fatty acids on atherosclerosis. These effects can be seen with the acute infusion of the fatty acids so that the effect does not even completely depend upon incorporation of the fatty acids into the cell membranes. Certainly the exact mechanism by which this benefit is seen is unknown. It is also very uncertain if this would be of any benefit to our patients as infarction is rarely a problem in dogs and cats. It has been shown that omega 3 supplementation can significantly reduce the number of VPCs Boxers with arrhythmogenic right ventricular cardiomyopathy have.

A more unique and probably very useful indication for n-3 supplementation in dogs with heart disease has recently been reported. Cachexia is a major problem in dogs with CHF. This will of course cause the owner to perceive a reduction in the quality of life in their pet that might lead to euthanasia. Giving 27 mg/kg/day EPA and 18 mg/kg/day of DHA when compared to placebo resulted in reduced cachexia, probably by decreasing various cytokines.

Use in urology

There is considerable controversy in regard to n-3 and n-6 fatty acids in renal disorders. Some studies have shown a preservation of renal function in experimentally induced renal failure dogs given increased n-3 amounts when compared to high n-6 diets or diets rich

in saturated fats. Hyperlipidemia is a common sequela to renal failure in animals and this seems to improve with use of n-3 supplements. In other studies increased n-6 supplementation resulted in increased GFR.

Fish oil supplementation also seems to have some effect on acute renal failure. In an experimental model, fish oil supplementation reduced acute renal failure induced by ischemia. With gentamicin induced renal failure benefits were not seen with n-3 supplementation.

In IgA nephropathy in people, fish oil supplementation did decrease the rate at which renal function was lost. It would seem from experimental studies that benefit of n-3 supplementation does seem to exist with glomerular disease especially.

Hypertension is a common consequence of renal disease. It has been seen in people that blood pressure decreases with fish oil supplementation, whether this applies in pets is unknown.

Use in cancer therapy

Much as in heart failure, with cancer cytokine levels increase that then lead to many of the clinical signs including cachexia. Supplementation with n-3 fatty acids has been shown to be of benefit in people with cancer associated cachexia. There may also be benefits in regard to metastasis and the cancer itself. Recently there has been some research done that showed improved survival in dogs with lymphoma fed a diet enriched with fish oil and arginine.

Use in gastroenterology

The use of EFA supplements and dietary manipulation of n-6:n-3 ratios has only been sparsely investigated in pets. It would not be surprising if some benefit would be seen with chronic inflammatory bowel disease. In people, fish oil supplementation has been shown to decrease relapses of Crohn's disease. There has also been information that EFA supplementation is helpful with ulcerative colitis in people.

Potential adverse effects

A variety of potential side effects need to be considered. One that has been raised is an increased bleeding tendency, however a recent study in cats showed no effect on platelets even when given in large quantities (1.126 g EPA, 0.624 g DHA, later increased to 1.689 g EPA and 0.936 g DHA). Dogs also did not have any changes in clotting when their diet was altered from a n-6:n-3 ratio of 100:1 to 5:1. Extreme fish oil supplementation can increase bleeding times, however this does not necessarily translate into spontaneous problems (the same applies to aspirin).

Another potentially deleterious effect is reduction of host immune response. In some experimental models, increasing the PUFA amount can increase susceptibility to certain infections and reduce survival. Studies in dogs have not shown a negative effect on immunity in dogs fed a diet containing a ratio of 5:1 (n6:n3). Since cytokine reduction is a major therapeutic benefit hoped to be achieved with PUFA supplementation and cytokines are involved in immune responses, some degree of immune compromise may occur, though if clinically significant is unknown.

Common adverse effects with PUFA supplementation are effects on the GI system such as nausea, vomiting and diarrhea. These can usually be avoided if lower dosages are used initially.

Summary

The use of PUFA supplements would seem to offer some very interesting possibilities. Unfortunately to date in many cases the exact amount of supplementation needed or if dietary ratio adjustment is the way to go has not been clarified. Certainly in certain conditions such as skin disease and with various forms of cachexia benefit has been shown. In other diseases it is more uncertain. In theory it should be quite helpful with glomerular diseases, diseases which tend to be quite frustrating to deal with in the first place. With chronic renal failure at this time there is opposing information if n-6 or n-3 such be increased. With inflammatory bowel disease PUFA can offer an adjunctive therapy. Most diets formulated for GI problems now do try to achieve an "optimal" level of PUFAs. Many more studies are under way. Whether they will clear up the waters or only make them more murky remains to be seen.

References

Available upon request from the author.