

Fish oil for OA? Don't give up yet

I read with interest the article by Hill *et al*,¹ with the accompanying editorial by Felson and Bischoff-Ferrari.² The point made by the editorialists was that the absence of a difference in osteoarthritis outcomes could have been due to the comparator group, which was high in oleic acid. Hill *et al* chose sunola oil for the comparator with fish oil as they believed that the absence of polyphenols would make it less likely that there would be a therapeutic effect from the sunola oil.

We published a trial of the effects of supplementation with what we termed low- and high-dose fish oil, versus olive oil.³ While we found a greater therapeutic effect of high-dose fish oil (mean of 6.8 g of n-3 per day) versus 'low dose' fish oil (mean of 3.4 g per day) versus 6.8 g of olive oil, we also found that there were several notable clinical and immune effects in the olive oil group including substantial decreases in both ionophore-stimulated leukotriene B4 (LTB4) and interleukin 1 (IL-1) production. While the decreases in these, and other parameters measured, were greatest in the high-dose fish oil group, it was apparent that the oleic acid supplementation had considerable potential to alter the immune responses from baseline. Of course both LTB4 and IL-1 production from patient's lipopolysaccharide stimulated peripheral blood mononuclear cells would have considerable potential to affect the clinical manifestations of osteoarthritis as well.

There is in fact a rather rich history of oleic acid-induced changes in immune parameters. Olive oil has been demonstrated to result in significant clinical improvements in the MLR/lpr mouse model of autoimmune disease,⁴ and to be associated with significant clinical improvements in rheumatoid arthritis (RA) in another trial.⁵

It is thus quite possible that the patients with OA in the laudable trial by Hill and colleagues were in fact given two active interventions. While the authors lament in their discussion that there is perhaps no ideal placebo oil, they could of course have used corn or safflower oil (n-6 fatty acids) as we had in some of our fish oil trials in patients with RA.^{6,7}

Finally, the dose of fish oil used could have been higher. Dose-dependent effects of fish oil have been described in hypertension⁸ and in our trial in RA.³ While the typical capsule available commercially does contain only 300 mg in 1 g, high-dose omega-3 capsules are now readily available. These capsules

contain 950 mg of n-3 per 1350 mg capsule. It is thus possible for a patient to take 6–7 of these divided between meals, and fairly easily consume a dose that would better test the hypothesis of a benefit of n-3 fatty acids at higher doses when compared with a corn oil supplement.

Given the relative paucity of therapeutic interventions for OA, it would be regrettable if the trial by Hill *et al* was viewed as proving with finality that there is no discernible benefit from fish oil in osteoarthritis.

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