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Is there a role for fish oil in inflammatory bowel disease?

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Abstract

A number of animal and human studies suggest omega 3-fatty acids are anti-inflammatory. As a result they may have a therapeutic role in inflammatory bowel disease (IBD). The aim of this review is to briefly assess the literature about the utility of poly-unsaturated fatty acids (PUFAs) in the management of IBD. Taken together, almost all studies suggest some beneficial effects of n-3 PUFAs in IBD but the mechanism remains controversial. In addition, clinical benefit seems to be largely confined to ulcerative colitis. However all studies have concluded that these compounds have no potential for a steroid/aminosalicylic acid sparing effect or to maintain remission. Now the question arises as to whether this treatment is of real value to IBD patients? Clearly they have some therapeutic potential but further work is needed.

Key words: Fish oil; Ulcerative colitis; Crohn's disease; Treatment; n-3 poly-unsaturated fatty acids

Core tip: Fish oil supplements are probably of benefit to patients with ulcerative colitis. They have a much less certain role in Crohn's disease.

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INTRODUCTION

Both animal and clinical work suggest that omega 3-fatty acids are anti-inflammatory in their action and so have the potential to be of use in the treatment of inflammatory bowel disease (IBD). In particular, they appeal to patients who see them as both safe and natural. The purpose of this review is to survey the literature and assess the utility of poly-unsaturated fatty acids (PUFAs) in the management of IBD.

THE UTILITY OF PUFAS IN THE MANAGEMENT OF IBD

The aetiology of IBD remains unclear but local mediators including arachidonic acid metabolites, cytokines and altered cell mediated immunity are likely to contribute to the disease. The rationale for the prescription of n-3 PUFA to promote a healthy gastrointestinal tract has been linked to their suggested anti-inflammatory properties. Different strategies have been adopted in various clinical trials to evaluate n-3 PUFA in patients with IBD. Inhibition of natural cytotoxicity, changes in interleukin 2 (IL-2) and arachidonic acid metabolites, *e.g.*, LTB_4 are the main chemotactic signals seen in the mucosa during a relapse. All are known to mediate the natural killer activity. A second hypothesis is based on the possible deficiency of essential fatty acids (EFAs) in IBD and its effect on cell membranes[1]. A further possibility is that fish oil ameliorates oxidative stress in IBD.

In a randomised crossover trial from four units which

involved 18 patients with ulcerative colitis (UC) fish oil supplements reduced LTB_4 levels in a rectal dialysate. Histology improved and patients' weight increased[2].

Conversely, a small Canadian trial of 11 patients found that addition of fish oil was of clinical benefit in UC but did not reduce mucosal LTB_4[3]. However, over a six month period serum LTB_4 was insignificant while there was a simultaneous fall in NK cell cytotoxicity[4].

An American study of 47 patients with long-standing bowel problems looked at the frequency of essential fatty acid deficiency. The majority had Crohn's disease. Compared to 56 control subjects, patients' metabolism was comparable to that seen in essential fatty acid deficiency (EFAD). Patients had: (1) 7% lower PUFA levels; (2) Lower concentrations of saturated and monounsaturated fatty acids.

The authors suggested patients with IBD should be assessed for EFAD and receive significant quantities of supplements with a high EFA content[5]. In contrast, a Japanese study found that EFAD rarely occurs in Crohn's disease[6]. A United Kingdom prospective study based on 26000 recruits living in Norfolk showed that total dietary n-3PUFAs, eicosapentaenoic acid and docosahexaenoic acid were associated with a reduced risk of ulcerative colitis[7]. This was not found in a small cross-sectional study of 51 patients with inflammatory bowel disease from Hungary[8].

To gauge whether fish oil can reduce oxidative stress in ulcerative colitis a Brazilian crossover study of nine patients on conventional treatment with sulfasalazine also received omega-3 fatty acids or placebo for two months separated by two months. They were compared with nine healthy people. Disease activity was examined through a range of standard serological measures as well as endoscopy and histology. The results showed that fish oil can act as a free radical scavenger and so protect patients[9]. The influence of monounsaturated, n-3, and n-3 + n-6 polyunsaturated fatty acids on histology, mucosal defence, mucosal prostaglandin E2 and LTB_4 in a rat model was investigated in Spain. It concluded that n-3 PUFAs can prevent inflammation but cause a decrease in the colon's defence system leading to oxidative injury[10]. Therefore, although it seems likely that these compounds have anti-inflammatory effects, the mechanism by which they achieve this needs further exploration.

There are some important considerations which should be borne in mind before promoting their use in the clinical care of patients with IBD: (1) Do they decrease disease activity? (2) Do they maintain remission? (3) Can they be used as an alternative to steroids or aminosalicylic acid (ASA) compounds?

There are studies which demonstrated a reduction in disease activity with these compounds, *e.g.*, a pilot study in United Kingdom evaluated their effectiveness both in terms of disease activity and histological scores when compared with pre-treatment measures[11,12]. In a German trial 5-ASA compounds were stopped in 64 patients who had ulcerative colitis and had been in remission for three months. They received a fish oil supplement and their clinical course was followed for 24 mo with colonoscopies at the beginning and end of the study. Freedom from disease activity was only seen in two of the 24 mo and the overall relapse rate was similar for active treatment and placebo groups. It seems that n-3 PUFAs can temporarily retard but not prevent relapse in UC[12]. Another randomised blinded control study of 87 patients from United Kingdom found fish oil had some benefit. Corticosteroid requirements were reduced for those 53 patients who had active disease on trial entry. Fish oil induced faster remission, although this trend did not reach significance. In contrast there was no difference in relapse rates if patients were in remission. So, it appears fish oil supplementation has a modest benefit in active disease allowing use of smaller doses of corticosteroids. In contrast they seem to have no role in maintenance[13]. A randomised controlled multicentre trial of 204 patients with Crohn's disease in Germany confirmed that omega-3 fatty acids had no role in prolonging remission[14,15]. Confirmation of the limited benefit in ulcerative colitis and absence of effect in Crohn's disease was first suggested in 1989 in a study of 39 patients[16]. The multicentre EPIC study from North America and Europe which included 738 patients with Crohn's disease again confirmed that omega 3 free fatty acids had no role in maintenance[17]. Support for such an interpretation comes from 3 systematic reviews[18-20]. However, this might not be the case in children and young people. In a study of 38 patients addition of enteric coated omega-3 fatty acids to 5-ASA treatment appeared of benefit[21]. Support for their role in Crohn's disease also came from a rigorous trial in 78 patients[22].

Ten patients with moderately active colitis were assessed in a study which used a randomized cross-over methodology. The treatments were either sulfasalazine or omega-3 fatty acids for 2 mo. Response was measured by endoscopic assessment, histological review and whole-body protein turnover. Treatment with omega-3 fatty acids alone led to a less objective improvement than conventional treatment. This shows that for active ulcerative colitis sulfasalazine is better than omega-3 fatty acids[23].

CONCLUSION

Taken together, almost all studies suggest some beneficial effects of n-3 PUFAs in IBD but the mechanism remains controversial. In addition, clinical benefit seem largely confined to UC. However all studies have concluded that these compounds have no potential for a Steroid/ASA sparing effect or to maintain remission. Now the question arises as to whether this treatment is of real value to IBD patients? Clearly they have some therapeutic potential but further work is needed with larger numbers and more highly powered trials.

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