Letter to the Editor

Cholestyramine Treats Primary Sclerosing Cholangitis–Associated Inflammatory Bowel Disease

Polychronis Pavlidis*, Michael Heneghanb, Bu’Hussain Hayeea

a Gastroenterology Department, King’s College Hospital, London, UK
b Institute of Liver Studies, King’s College Hospital, London, UK

The use of cholestyramine to treat pruritus in four patients after liver transplantation (LT) for primary sclerosing cholangitis (PSC) was associated with a rapid and sustained drop in levels of fecal calprotectin (FCAL).

All patients had inflammatory bowel disease (IBD) in association with the PSC, all suffering repeated flares of disease post-LT despite anti-rejection therapy. All were therefore receiving optimized anti-TNF therapy for IBD [median duration of treatment 26 (16, 55) months], prior to cholestyramine. Levels of FCAL were high pre-treatment (indicating partial or non-response to anti-TNF agents) and no dose optimization had taken place within 6 months of therapy with cholestyramine. No other agents were changed or initiated around this time.

Figure 1 shows the rapid fall in FCAL (in one case observed at 2 weeks, but 2-month time point shown for standardization). After discussion with all patients and the transplant multidisciplinary team, cholestyramine therapy was continued once daily for 6 months. In one patient, infliximab could be stopped 12 months after introducing cholestyramine (‘deep remission’ and mucosal healing achieved, no relapse to date, follow-up 18 months). In two patients, the infliximab dose was reduced to 5mg/kg every 8 weeks, with no further relapses, lower FCAL results, and no ulceration seen on colonoscopy. One patient experienced a severe IBD flare after stopping cholestyramine. She did not benefit from high-dose intravenous steroids and underwent a colectomy.

Cholestyramine is a bile acid (BA) sequestrant used for the management of dyslipidemia and pruritus. However, it can also attenuate intestinal ulceration in animals with non-steroidal anti-inflammatory drug enteropathy, a well-described model of IBD. Colesevelam, another BA sequestrant, has been found to exert its metabolic effects through activation of the membrane bile acid receptor TGR5. This finding supports the hypothesis that alternative pathways, besides the attenuation of the potentially deleterious topical effects of toxic BA, may be implicated in cholestyramine’s anti-inflammatory effects.

Although treating an element of BA malabsorption, a well-described cause for diarrhea in IBD, could explain symptom resolution in our patients, it would not account for the drop in the FCAL and the endoscopic improvement.

To our knowledge, this is the first report on the beneficial role of a BA sequestrant on intestinal inflammation in humans, suggesting that an intervention targeting BA may benefit PSC-associated IBD and IBD in general.

References


Figure 1. Cholestyramine effects on FCAL and Mayo score at different time points after commencement