1. Isotretinoin and the risk of IBD

Data on isotretinoin (a vitamin A derivative used to treat acne) as a cause of IBD has been controversial and largely based on small case-control studies. Nevertheless, the issue has received a lot of media attention due to some substantive individual awards resulting from litigation suites against its main manufacturer. Investigators have now analyzed the association between isotretinoin (IST) and IBD using a large French administrative database covering approximately 75% of the population. Recent use of IST was compared between incident IBD cases (n=7,593) and controls without IBD matched for age, sex and calendar year (n=30,372). By logistic regression analysis, IST use was not associated with an increased risk of UC (OR 1.36) but, interestingly, was associated with a decreased risk of Crohn’s disease (OR 0.45). Results were robust when controlled for contraceptive use or other antibiotics used to treat acne or when the analysis was limited to individuals aged < 40 or who had recent endoscopy or surgery to confirm their initial diagnosis.

Comments: This is so far the largest study looking at the relationship between IST use and development of IBD and fortunately, the results point towards a lack of a causality. It is interesting to note that the use of isotretinoin was very uncommon in this population (0.3%), although the large number of subjects included provided adequate statistical power. It is also noteworthy that, as it was noted in previous studies, there appears to be a risk differential between UC and CD although other confounders may account for this. Unfortunately this study came out a little late as is pointed out in the excellent accompanying editorial. Not only was the drug removed from the market by its manufacturer but a number of very substantial awards have been paid to plaintiffs and their attorneys based on limited evidence restricted to case reports and FDA warnings. As physicians, it is very sobering to see how the legal aspects of medical practice are frequently disconnected from the scientific evidence.


2. Comparison of MRE and Deep Enteroscopy for Small Bowel Crohn’s disease

MR Enterography has emerged as a useful imaging modality in patients with Crohn’s disease. In addition to a more nuanced level of information about structural bowel abnormalities (inflammation vs. fibrosis) the study is also devoid of radiation exposure which is why it is
preferred by some for younger patients. Although its accuracy has been compared with other studies and primarily with CTE, a comparison with deep enteroscopy has not been reported. This study from Japan sought to determine the sensitivity and specificity of MRE for mucosal and luminal anomalies in a prospective study including 100 patients with CD. MRE was performed first to keep the radiologists blinded. All patients underwent either SBE or DBE within 3 days (almost all on the same day). The two of them were compared for mucosal inflammation, ulcers, scarring and stricturing, using deep enteroscopy as the gold standard. Most patients were in clinical remission and 36% were receiving biologics. Deep enteroscopy reached the proximal ileum (more than 10 cm from the IC valve) in 98% of patients and the jejunum in 40%. The sensitivity of MRE for small bowel inflammation was between 67-82% with a specificity of 87-95% compared with DBE. However, the sensitivity and especially specificity were much lower in the colon. The sensitivity and specificity for severe stenoses were 59% and 90% but for all stenoses only 41% and 94%, respectively. MRE missed a 2 cm long, 2 mm diameter stricture in the proximal ileum and another 1 cm long, 2 mm stenosis at the IC valve. As expected there was poor correlation of the endoscopic score with CDAI and fair correlation with CRP. Given the fact that the prevalence of bowel stenoses was low (7%), the negative predictive value of MRE for severe stenosis was high at 97% whereas the PPV was low (31%).

**Comments:** Despite its limitations, this is an important study because it provides an estimate of the accuracy of MRE in patients with active and inactive CD. Its obvious appeal notwithstanding, MRE appears to be significantly inferior to endoscopy for both active inflammatory lesions and especially for strictures. Although the indication for MRE was not specified in this study, it is likely that this is a selected cohort with relatively well controlled disease and limited structural damage. I suspect that in patients with more significant bowel damage, the negative predictive value of MRE will be much lower (i.e. the false negative rate much higher). The MRE is more likely to miss short strictures and particularly those < 1-2 cm regardless of diameter unless they are associated with proximal dilation. Physicians need to keep this information in mind when they interpret the results of imaging studies in patients with suspected or established CD. Particularly in cases where there is high suspicion for small bowel disease, complementary studies such as capsule endoscopy or deep enteroscopy should be considered.


**3. Can we treat Crohn’s disease with diet?**

Although elemental diet has been effective to induce remission in children with Crohn’s disease, studies in adults have been largely disappointing. Therefore a recently published article on this topic was received with quite a bit of interest. The authors report a retrospective series of children and adults with CD who were treated with a mixture of polymeric diet (commercially available) and an original “Crohn’s Disease Elimination Diet” in combination with
immunomodulators. The “inspiration” for this original diet is not provided but apparently it
derives from an also original “Bacterial Penetration Cycle Hypothesis” and it excludes, among
others, “all products with an expiration date”. Neither the hypothesis nor the diet have been
adequately studied. The authors report remission rates in excess of 70% including a drop in
inflammatory markers in all patients. Although this is a seriously flawed study, I suspect it will
receive some attention in press as it has the necessary frazzle and sensationalism required for
an impact in the lay media: avoidance of major pharma drugs, relatively inexpensive, easy to
follow diet, promotional of healthy supplements as well as some “scientific evidence” derived
from an interesting yet completely speculative hypothesis. As we have discussed in JC’s before,
the best diet for IBD patients is a balanced diet that is well tolerated and includes essential
nutrients. Whether any particular diet has a therapeutic effect in IBD patients remains
completely unproven and relatively unlikely.

Source: Sigall-Boneh R, Pfeffer-Gik T, Segal I, et al. Partial enteral nutrition with a Crohn's
disease exclusion diet is effective for induction of remission in children and young adults with