Inflammatory bowel diseases: are we ready to recommend a preventive diet for infants?

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Environmental factors throughout life play a critical role in the development of IBD (Crohn's disease (CD), UC). The past decade has witnessed an acceleration of environmental research in IBD with several landmark prospective cohorts identifying dietary and other lifestyle determinants of disease. In parallel, we have also made substantial progress in identifying how the environment contributes to IBD through microbiome-dependent and microbiome-independent effects. Adding to this literature is a study in *Gut* examining the impact of early life diet on risk of IBD.[1] Guo *et al* use the All Babies in Southeast Sweden study and the Norwegian Mother, Father and Child Cohort Study to examine the association between early life diet and risk of IBD. These large prospective cohorts administered comprehensive questionnaires assessing early life diet (at 12–18 months and 30–36 months) covering intake of meat, fish, fruits and vegetables, breast milk, baby foods and sweets and snacks. The main predictors of interest were overall diet quality using the modified Healthy Eating Index and intake of individual food groups. Cases of CD or UC were identified by linkage to the patient registries. The final analysis included 81 282 children with complete dietary data at 1 year of age among whom 307 developed incident IBD (131 CD, 97 UC, 79 IBD-unclassified). Adjusting for parental IBD history, sex, origin, education and maternal comorbidities, a medium-quality (HR 0.74, 95% CI 0.57 to 0.97) or high-quality (HR 0.73, 95% CI 0.55 to 0.97) diet was associated with a reduced risk of IBD compared with a low-quality diet. Separately, there was no association between diet quality and risk of CD (HR 0.63, 95% CI 0.27 to 1.47) or UC (0.83, 95% CI 0.50 to 1.38), although the point estimates were supportive of an inverse association. Interestingly, diet quality at 3 years of age was not associated with incident IBD (HR 1.02, 95% CI 0.76 to 1.37) suggesting that perhaps the impact of diet on disease development is greatest at a young age. In terms of individual components, a high intake of fish (HR 0.66, 95% CI 0.46 to 0.93) and vegetables (HR 0.72, 95% CI 0.55 to 0.95) was associated with a reduced risk of IBD. In contrast, intake of some (compared with no) sugar-sweetened beverages was associated with an increased risk of IBD (HR 1.42, 95% CI 1.05 to 1.90). The strengths of this work include the large sample size and rigorous follow-up. However, an important limitation is that the diet questionnaire used has not been qualitatively or quantitatively validated against other more conventional methods. The questionnaire also lacks the granularity to capture relevant exposures like additives and emulsifiers common in baby foods, that may be relevant to IBD pathogenesis. In addition, accurate quantitative ascertainment of intake is inherently difficult in infants and small children. The emerging use of biomarkers to quantify early life exposures may be a particular important scientific advance to ascertain risk factors in this age group.

There is considerable interest in the impact of early life (and in utero) exposures as relevant to development of IBD. This elegant study by Guo *et al* adds to the data regarding the importance of this period in IBD development. Although in the present study there was no association between diet at 3 years and development of IBD (in contrast to the association observed for dietary intake at 1 year), other prospective cohorts of adult-onset IBD have demonstrated an inverse association between vegetable[2] or fish[3] intake and reduced risk of CD while sugar-sweetened beverages have been linked to a higher risk of IBD.[4] Thus, the impact of these dietary factors does not seem to be restricted purely to infancy and there is broad consistency that these factors are associated with incident IBD irrespective of the life period of exposure.

Are we ready to recommend a preventive diet to infants (and adults) at risk for development of IBD? Recommendations for primary prevention of IBD are still derived primarily from observational cohorts that demonstrate factors associated with disease. While such studies do not establish causation, many of these observations are backed up by experimental evidence demonstrating biological plausibility. Despite the absence of gold standard interventional data demonstrating a benefit of dietary interventions in preventing disease, in my opinion, it may still be reasonable to suggest such interventions to motivated individuals that incorporate several of the dietary patterns associated with lower risk of IBD from this[1] and other studies. This includes ensuring adequate dietary fibre, particularly from fruits and vegetables, intake of fish, minimising sugar-sweetened beverages and preferring fresh over processed and ultra-processed foods and snacks. In a recent study in adult-onset IBD, adherence to a healthy lifestyle was hypothesised to prevent nearly 50% of CD and UC.[5] However, several existing gaps remain important for the field to address. The durability of benefit of dietary (or other) interventions is unknown, and whether that differs by the age of adoption. An intervention that needs to be sustained indefinitely to modify disease risk may have lower acceptance than those that can be episodic. It remains to be established if there are periods of high vulnerability where lifestyle modifications may exert a greater and more durable influence than later in life. If so, the in utero and early life period may represent one such susceptibility window; clinical trials are currently exploring this hypothesis.[6] This period represents the time where there is greatest instability of the microbiome, and thus vulnerability to external influences.[7] The early life period is also an important phase in immune maturation which has implications for the development of IBD and other immune-mediated diseases.[8 9] In prior studies, early life exposure to antibiotics has been associated with an increase in risk of IBD, with an effect size that is greater when exposure occurs at a young age compared with adulthood.[10] Similarly, other exposures specific to the early life period such as breast feeding[11] have demonstrated a stronger magnitude of association with disease than later life factors. Tailoring interventions to such periods may be the most cost-effective strategy for disease prevention.

It is also important for the field to develop surrogate markers of IBD risk (eg, serological, metabolomic or proteomic profiles) that can serve as end points for

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intervention studies of environmental modification in diverse populations. Such studies are likely to be more feasible and provide us with meaningful data on which to base our clinical practice. Randomised controlled trial evidence for diet in preventing IBD is unlikely to be practical given the relatively low incidence of IBD, even in high-risk individuals. However, most of the components of preventive recommendations for IBD are safe and may confer a spectrum of other well-proven health benefits (such as reducing cardiovascular disease and promoting longevity) irrespective of their impact on IBD incidence. Thus, there seems to be only upside to adopting this strategy.

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