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Azathioprine dosing and metabolite measurement in paediatric inflammatory bowel disease—does one size fit all?
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Background: Azathioprine (AZA) is an effective immunomodulatory maintenance therapy in children with inflammatory bowel disease (IBD). Current recommended dosing is 2–2.5 mg/kg/dose in the presence of normal thiopurine methyltransferase (TPMT) level. Elevated levels of the AZA metabolites 6-TGN and 6-MMP have been associated with increased risk of myelotoxicity and hepatotoxicity, however evidence suggests that monitoring metabolites can help optimise effectiveness and safety of thiopurines. We aim to assess association between AZA weight-based dosing, thiopurine metabolites and disease activity index in a cohort of paediatric IBD patients.
Methods: Retrospective data review (2015–2017) from the paediatric gastroenterology department at Evelina London Children's Hospital. Children with IBD who were taking AZA and had regular thiopurine metabolites measurement were included. PCDAI and PUCAI were used to assess disease activity.
Results: A total of 41 patients, 38% female, 62% male with mean (±SD) age of diagnosis 12.2 (±3.4) years, were included. Twelve patients had ulcerative colitis (UC), 27 Crohn's disease (CD) and 2 very early onset IBD (VEOIBD). Mean AZA dose, in mg/kg (±SD), 0.7 (±0.4). Mean 6TGN value (±SEM) 260 (±25.2), and mean MMT value (±SEM) 1023 (±168). Thiopurine metabolites were measured at (mean ± SEM) after 75 ± 13.5 days after starting AZA, 5 patients had elevated 6TGN levels >450. Mean lymphocyte count at time of metabolite measurement was 2.3 (±0.8). Activity index at the start of thiopurine were (±SD) 22.5 (±16.3) and when metabolites were measured 8.1 (±12).
Conclusions: We have identified that the majority of our patients maintain clinical remission (defined by an activity index—PUCAI/PCDAI—of less than 10) on lower AZA doses than currently recommended. We have also identified a number of patients with elevated 6TGN levels without signs of myelosuppression. Higher doses of AZA are associated with higher metabolite levels, and we propose that regular routine measurement of AZA metabolites will help optimise therapy, minimise side effects and identify children at risk of hepato- and myelotoxicity.

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Risk of malnutrition in patients with inflammatory bowel diseases: Results from an Italian multi-centre observational cross-sectional study
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Background: Prevalence of malnutrition in patients with inflammatory bowel diseases (IBD) has not yet been well defined, ranging from 6 up to 75% in various studies based on different criteria used. Malnutrition universal screening tool (MUST) is the recommended tool to define the risk of malnutrition, but it has never been applied to IBD patients. Aim of the study were to define the prevalence and risk of malnutrition in IBD patients, and to evaluate nutritional interventions in malnourished or at risk patients.
Methods: All consecutive IBD adult patients afferent evaluated in 14 centres in a 2-week period were enrolled. Patients with short-bowel syndrome and those who had received artificial nutrition in the previous 6 months were excluded. For all the patients demographic, IBD history, physical and laboratory data were recorded, together with body mass index (BMI) and MUST score. A BMI less than 18.5 kg/m2 identified malnourished patients and a MUST score ≥1 patients at risk of malnutrition. Patients with BMI ≥ 18.5 kg/m2 and MUST score ≤ 1 were considered as controls. Clinical disease activity was measured by CDAI and DAI scores. Statistical analysis was performed by using chi-square, Fisher exact, and Kruskal–Wallis tests.
Results: A total of 295 patients with IBD were enrolled, 148 Crohn’s disease (CD) (66 males, 44 ± 14 years) and 147 ulcerative colitis (UC) (81 males, 49.6 ± 15.7 years). Most patients were evaluated in an outpatient setting (95% of CD and 99% of UC patients). The overall prevalence of malnutrition was 6.4%, with no significant difference between CD and UC patients (8.1% vs. 4.8%, p > 0.05). Patients at risk of malnutrition were 16.6% (18.2% in CD and 14.9% in UC, p > 0.05). Significant differences were found among the three groups regarding disease activity and CRP levels (see Table). A comprehensive nutritional assessment was offered only to one-third of patients with malnourished or at risk CD and to one fourth of patients with UC at risk of malnutrition. Artificial nutrition was started in 8% of malnourished CD patients, 15% of CD patients at risk of malnutrition and in 10% of UC patients at risk of malnutrition.
Conclusions: The prevalence of malnutrition in IBD patients is lower than previously reported, but there is 17% of patients at risk of malnutrition mostly related to clinical disease activity. Nutritional interventions are currently offered to a small proportion of malnourished or at risk patients. Physicians should be taken into greater account the nutritional aspects of IBD patients.

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Risk factors for disease relapse after stepping down from combination to anti-TNF monotherapy in children with IBD
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Background: Stepping down from combination therapy of anti-TNF and immunomodulator drug to monotherapy is common practice in IBD. The aim of our study was to define risk factors for disease exacerbation after withdrawal from combination therapy in children with IBD.