Increasing weight and body mass index adversely affect thioguanine nucleotide levels in inflammatory bowel disease

Introduction Inflammatory bowel disease (IBD) often requires long-term immunosuppressive therapy with thiopurines such as azathioprine (AZA) or mercaptopurine (MP) and anti-tumour necrosis factor (TNF) agents. Despite the variable response to thiopurines and anti-TNF agents, few predictive factors of response have been identified. A lower body mass index (BMI) has been associated with a better outcome for azathioprine therapy, infliximab and adalimumab. Obese IBD patients are more likely to have active disease or be hospitalised. This study examined the association between weight and thiopurine therapy by examining 6-thioguanine nucleotide (6-TGN) levels.

Methods We conducted a retrospective analysis of patients who were treated at the Royal Liverpool University Hospital with a thiopurine. The dose of thiopurines was adjusted as tolerated to a maximum of 2.5 mg/kg for AZA and 1.5 mg/kg for MP. Eligible patients had a 6-TGN measurement with their height and weight recorded at the same time. Associations between 6-TGN, BMI, weight, patient demographics and biochemical indices were estimated using a multivariable linear regression model. Body fat index was calculated as described previously. All tests were declared statistically significant if p < 0.05.

Results 106 patients (48 male, 58 female) were included and contributed 133 measurements. 55% had Crohn’s disease and 45% had ulcerative colitis. 91% were on AZA and 9% were on MP. After adjustment, a one kilogram increase in weight was associated with a 1.62 unit decrease in 6-TGN levels (95% CI: 0.40 to 2.82, p = 0.0094). Body fat index correlated strongly with weight for both males and females (0.8345 and 0.8860 respectively) and a significant difference was found between BMI for each sex (p < 0.001) with females, on average, having a higher BMI. Weight, BMI and BFI differed significantly across sub-therapeutic, therapeutic and supra-therapeutic 6-TGN groups (Table 1).

Conclusion 6-TGN levels decreased significantly with increasing weight and BMI despite a similar weight based dosing. This may explain the previously noted adverse outcomes in obese IBD subjects and underscores the importance of thiopurine metabolite testing.