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6-THIOGUANINE MEASUREMENT ALLOWS OPTIMISATION IN MANAGEMENT OF IBD PATIENTS ON AZATHIOPRINE

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Introduction Azathioprine is widely used in the management of Inflammatory Bowel Disease (IBD). The ideal dose for a patient is usually calculated by weight, but the rate of metabolism of azathioprine to its active metabolite 6-thioguanine (6TGN) varies between individuals. In addition, therapy may be limited by non-compliance, side effects or relapse of disease while on treatment. This retrospective study evaluates whether measuring 6TGN levels alters the management of patients on azathioprine for IBD.

Methods A search of laboratory records identified a cohort of 41 patients with IBD that had been tested for 6TGN levels. 48 tests had been performed as 7 patients were tested twice. Electronic and, when required, paper records were reviewed to record demographics and diagnosis. The reason for checking 6TGN level and how this altered management was evaluated.

Results The cohort was mainly young adults, with an age range of 18–73 years (median 36 years), and a slight female predominance (22 F:19 M). 66% of patients had Crohn's disease, the remainder Ulcerative Colitis (UC). Tests were performed because patients were symptomatic, suspected of non-compliance, had abnormal liver biochemistry or to confirm a therapeutic dose.

Of the 48 tests performed, 12 (25%) identified low 6TGN levels. Compliance was addressed in 3 cases. Dose of azathioprine was increased in 6 cases and management was altered in 2 cases.

20 tests (42%) were within the therapeutic range and azathioprine dose was only increased following 3 of these tests. 4 patients required escalation of treatment to alternative medication or surgery.

16 tests (33%) were above the recommended level of 6TGN, despite all the patients receiving <2.7 mg/kg of azathioprine and 4 patients receiving less than 2 mg/kg. 5 patients with high 6TGN levels were subsequently switched to an alternative agent for maintenance therapy.

29 (60%) of all tests were performed on symptomatic patients to confirm adequate dosing before declaring a treatment failure. By weight calculation, 11 of these patients were receiving subtherapeutic doses of azathioprine. However, contrary to expectation, only 5 of 11 had low levels of 6TGN.

Conclusion Calculation of azathioprine dose by weight does not address individual variation in metabolism to the active component, 6TGN. In this retrospective study, management was altered in 51% of patients as a result of measuring 6TGN, with either alteration of dose, or change of therapy. The cost of the assay (£29) limits its use, and currently we would recommend the use of 6TGN as a useful adjunct to established measures for azathioprine dose adjustment, such as clinical response and haematological indices.

Competing interests None.

Keywords 6-thioguanine, azathioprine, Crohn's disease, thiopurine, ulcerative colitis.