PURPOSE

Many patients with Crohn's Disease (CD) and Ulcerative Colitis (UC) who have a high 6-methylmercaptopurine/6-thioguanine (6-MMP/6-TGN) ratio receive allopurinol 100 mg in addition to thiopurines to optimize metabolite concentrations. However, some patients do not tolerate allopurinol at this dosage.

The aim of this study was to determine the intrapatient effect of reducing the allopurinol dosage from 100 to 50 mg, in terms of metabolite concentrations, enzyme activities, efficacy and tolerability.

METHODS

A prospective non-inferiority one-way crossover study was performed. CD and UC patients with stable disease using a thiopurine and allopurinol 100 mg were switched to 50 mg for one month. Primary outcomes were thiopurine metabolite concentrations. Secondary outcomes were enzyme activities of xanthine oxidase, thiopurine methyltransferase and hypoxanthine guanine phosphoribosyltransferase, disease activity and tolerability.

RESULTS

Twenty-two patients were included. Treatment with allopurinol 50 mg compared to 100 mg resulted in a significant decrease in mean 6-TGN levels (761 to 625 pmol/8* 10^8 RBC; p=0.005) and a significant increase in mean 6-MMP levels (451 to 665 pmol/8*10^8 RBC; p=0.01). However, mean metabolite concentrations were still therapeutic. Enzyme activities, disease activity scores and patient experiences did not alter significantly. Generally, UC patients were more positive about their improved treatment than CD patients.

CONCLUSION

Combination therapy with 50 mg allopurinol led to a decrease of 6-TGN levels compared to 100 mg allopurinol. Disease activity, side effects and patient experience, however, were similar between allopurinol 100 and 50 mg. UC patients seem to benefit and prefer lower doses whereas the contrary is seen in CD patients.

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