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Predictors of thiopurine treatment failure in ulcerative colitis

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Background: Immunomodulators such as azathioprine (AZA) and 6-mercaptopurine (6-MP) have been used for induction and maintenance treatment of Ulcerative colitis (UC). In non-responsive patients to AZA or 6-MP, biologic agents or surgical treatment could be considered. This study was to evaluate the predictive factors of response to AZA/6-MP in patients with moderate-to-severe UC.

Methods: Among total 254 patients who were managed as UC in Korea University Ansan Hospital through 2005 to 2015, 113 patients with UC who used AZA/6-MP were analysed in the study. Patients' medical records including baseline characteristics, disease extension of UC, severity, treatment agents, and surgical treatments were reviewed retrospectively. Thiopurine treatment failure was defined as retreatment with steroids, therapeutic escalation to anti-TNFα agents or need for surgery.

Results: Among 113 patients with UC who received AZA/6-MP treatment, 37 patients (32.7%) failed thiopurine treatment (19 treated with steroids, 17 treated with anti-TNFα, 4 treated with surgical treatment). On multivariate Cox regression analysis, Mayo score was the only significant risk factor for thiopurine treatment failure (HR 1.28, 95% CI 1.04–1.58, *p*-value 0.023). In present study, patients who had undergone thiopurine treatment for ≤6.2 months due to worsening clinical findings were defined as early thiopurine treatment failure, based on the lowest quartile cut-off limit. Family history of UC was significantly associated with early treatment failure (HR 6.48, 95% CI 1.31–32.2, *p*-value 0.022).

Conclusions: AZA/6-MP treatment is effective on induction and maintenance treatment in UC. However, high Mayo score is significantly associated with treatment failure and family history is associated with increased risk of early treatment failure. Early therapeutic escalation such as biologic treatment should be considered in patients with these risk factors.

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Clinical outcomes and prognostic factors of methotrexate therapy in combination with anti-TNF agents in inflammatory bowel disease

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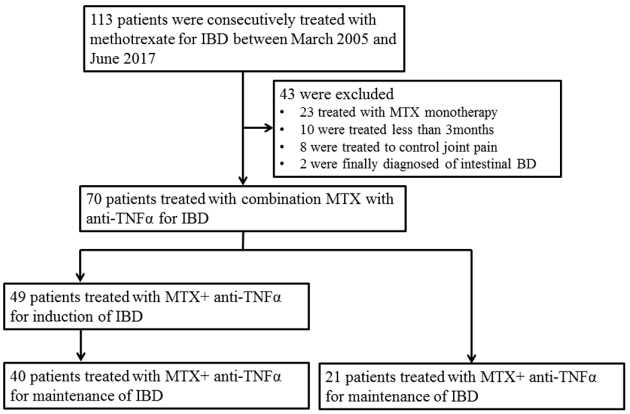
Background: Combination therapy with an immunomodulator and anti-tumour necrosis factor (TNF) is one of the crucial therapeutic strategies for inflammatory bowel disease (IBD) management. Methotrexate (MTX) is a second-line immunomodulator and has received much attention in recent years due to several advantages over thiopurine. We aimed to investigate clinical outcomes and prognostic factors of MTX therapy when combined with anti-TNF in IBD patients.

Methods: We retrospectively reviewed 70 IBD patients (Crohn's disease [*n* = 57], Ulcerative colitis [*n* = 13]) (age, 18–63 years) treated with MTX in combination with anti-TNF agents for induction or maintenance therapy at Severance and Gangnam Severance Hospital, Seoul, Korea. 22 (31.4%) were initially commenced on oral and 48 (68.6%) started subcutaneous route. Initial MTX dosage was 7.5–25.0 mg/week. Drug data for MTX therapy and outcomes data for clinical efficacy were analysed. Moreover, sustained clinical benefit of MTX therapy which was defined as ongoing use of MTX or intentional discontinuation of successful therapy before last follow-up was also evaluated.



Recruitment algorithm.

Results: A total of 49 patients were selected for the analysis of induction therapy, and steroid free clinical remission was achieved in 22 (44.9%) of the 49 patients at 3 months, 13 (50.0%) of the 26 patients at 12 months, and 4 (44.4%) of the 9 patients at 24 months. Co-therapy with second line anti-TNF agent was associated with a failure of clinical remission at 3 months (odds ratio [OR]: 0.084, 95% confidence interval [CI]: 0.009–0.838). Meanwhile, 60 patients were selected for the analysis of maintenance therapy, and 17 (28.3%) patients experienced relapse during follow-up period of 3–26 months. Anaemia (Haemoglobin < 11 mg/l) at maintenance initiation was independent predictor of relapse (hazard ratio [HR]: 3.847, 95% CI: 1.153–12.829). Factors related with failure of sustained clinical benefit of MTX in combination therapy were obesity (≥23 kg/m^2) (HR: 4.117, 95% CI: 1.380–12.296), concomitant adalimumab (vs. infliximab) therapy (HR: 3.872, 95% CI: 1.419–10.571), and female sex (HR: 3.271, 95% CI: 1.119–9.561). Adverse event related with MTX occurred in 24 (34.3%) patients, and 3 (4.3%) patients discontinued MTX due to adverse event.

Conclusions: MTX therapy in combination with anti-TNF was relatively well tolerated. The type of combined anti-TNF agents and baseline patient characteristics rather than the MTX dosage and administration route were crucial factors in determining clinical outcome.

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A comparative analysis of low bioavailability steroids in inducing clinical response and remission in ulcerative colitis: Budesonide MMX as the safest option

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