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Has body composition any effect on thiopurine level in IBD?

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Background: Thiopurines are the most commonly used immunosuppressive therapies in mild-to-moderate IBD. Azathioprine (AZA) is a prodrug, metabolised in 6-thioguanine (6-TG), which has therapeutic effect and 6-methylmercaptopurine (6-MMP), which causes toxic side-effects. Dosage of thiopurines should start gradually, later based on current recommendations dosage, has to be 2–2.5 mg/kg. The effect of body composition on 6-TG level was never been studied. Therapeutic concentration of 6-TG is between 235 and 450 pmol/l × 10^10 red blood cell count (RBC). Our aim was to evaluate thiopurine blood level's connection with weight, body-surface area and different body composition parameters measured by bioelectrical impedance analysis.

Methods: This is a cross-sectional study involving 26 IBD patients (7 Ulcerative Colitis, 19 Crohn’s Disease). Thiopurine metabolite blood level was measured with high liquid chromatography (HPLC) and body composition analysis was performed with bioelectrical impedance analysis.

Results: Patients involved in this study received immunosuppressive therapy in a mean 5.3 years and they have been diagnosed with IBD in a mean 10.3 years. In one case the therapy was 6-MP (75 mg) and in the other cases AZA (50–200 mg). Concomitant therapy was given in 20 cases (77%): 5-ASA 1 (3.8%), cyclosporine 1 (3.8%), biological therapy 12 (46%), steroid plus 5-ASA 2 (7.7%), steroid plus anti TNF agents four cases (15.4%). Considering patients’ weight seven patients (27%) were overweight, 2 (7.7%) patients were underweight. Therapeutic concentration of 6-TG was found in 23 patients (88.5%), they received AZA for a mean 4.3 years. Three patients (11.5%) has lower blood 6-TG level, they received AZA for an average of 14.3 years. The level of AZA metabolite 6-TG correlated with both body weight-based and body-surface area-based AZA doses (p = 0.005 and p = 0.011, respectively). However, no correlation was found with any of the investigate body composition parameters (total body water, intra-, extracellular water, skeletal muscle mass, body fat mass).

Conclusions: Our study revealed that body composition parameters have no effect on the active AZA metabolite blood level. Therefore, there is no need to modify the current, well-tried dosing scheme of AZA.

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Benefits of implementing a rapid access clinic in a high-volume inflammatory bowel disease centre: Accessibility, resource utilisation and outcomes

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Background: IBD impacts on patient’s physical health, social functioning and quality of life, contributing to the health-economic burden associated with the disease, especially in emergency situations. We aimed to prospectively measure indicators of quality-of-care, after implementation of a new rapid access clinic (RAC) at a tertiary care IBD centre.

Methods: Consecutive patients from the McGill University Health Centre who accessed the RAC via email were prospectively included, between June and September 2017. Time to medical appointment, utilisation of imaging, endoscopy, laboratory, treatment decisions and need for unplanned emergency room (ER) visits or admissions 30–90 days after consulting the RAC was assessed.

Results: Seventy-four patients (35% men, mean age: 35 years, CD: 72%, L3: 59%, B2–3: 39%, UCE3: 48%, biological therapy: 76%, previous surgery: 23%) were included. Seventy-five per cent of requests were considered appropriate for an RAC appointment. Outpatient visits were a median 2 days (mean 3.3) after the email request. Five patients required an ER visit within 30 days after the RAC appointment, out of which 3 were initiated during the rapid appointment. Two of three patients required admission and underwent urgent IBD-related surgery. No patients required an ER visit within 90 days. Treatment was modified in 40 patients (72%). Laboratory assessment including FCAL (65%) and therapeutic drug monitoring (30%) was performed as appropriate. The need for subsequent accelerated assessment was infrequent. Fast-track endoscopy was performed in four patients, and two patients had an abdominal/pelvic CT for assessment.

Conclusions: Implementation of an RAC improved healthcare delivery by avoiding unnecessary ER visits and patient care by increasing access to an IBD centre.

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White cell count (WCC) and mean corpuscular volume (MCV) as surrogate markers for thiopurine monitoring in inflammatory bowel disease (IBD) treatment: A single-centre experience

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Background: Thiopurines (TPs) are commonly used in treatment of IBD. Optimal dosing is determined by patients’ weight and commonly titrated to achieve target range of 2–2.5 mg/kg. Levels of 6-thioguanine nucleotide (6-TGN), an active metabolite breakdown of thiopurines
and 6-methylmercaptopurine (6-MMP), an inactive metabolite, can be measured to check for efficacy and toxicity, respectively, but this is not widely available. WCC, lymphocyte count (LC) and MCV have emerged as surrogate markers to monitor TP efficacy. Previous studies have suggested WCC <4 × 10^9/l and MCV > 100 fl correlate with 6-TGN level and reduced risk of disease relapse. The aim of our study is to assess these surrogate parameters in our patients on TPs.

Methods: A total of 200 IBD patients being treated with azathioprine (AZA) were included in this retrospective, observational study. Data were obtained from our IBD database and review of medical notes. Recent WCC, LC, and MCV were recorded, along with body weight, AZA dose and concomitant treatment with biologic therapy (mainly anti-TNF agents). Disease activity index was assessed using Harvey Bradshaw index (HBI) for Crohn’s disease (CD) and partial Mayo score for ulcerative colitis (UC) at time of blood testing.

Results: There were 108 (54%) females and 92 (46%) males. Of the 200 patients, 144 (72%) were diagnosed with CD, 55 (27.5%) UC and 1 (0.5%) indeterminate colitis. One hundred and seventeen patients (58.5%) were on AZA monotherapy with 83 patients (41.5%) on combination therapy with a biologic. The mean age for our study population was 49 (19–81). The mean WCC count was 6.81 × 10^9/l (2.8–14.2). Mean LC was 2.86 × 10^9/l (0.5–8.8) with mean MCV of 91.1 fl (78–104). Seven of 200 (3.5 %) patients had WCC < 4 × 10^9/l and 7 of 200 (3.5%) also had a MCV > 100 fl. In the IBD AZA monotherapy group, 4 of 117 patients (3.4%) had leucopenia and the same number 4 of 117 had macrocytosis and only one patient (0.9%) had both leucopenia and macrocytosis. In patients on combination therapy, 3 of 83 (3.6%) had leucopenia and the same number of patients, 3 of 83, demonstrated macrocytosis. None in this group had both leucopenia and macrocytosis. The mean AZA dose to body weight was 1.7 mg/kg. The mean HBI score was 2.9 and partial Mayo score 1.7.

Conclusions: A very small percentage of our study population had leucopenia, lymphopenia or macrocytosis suggesting that many may be sub-therapeutic. Notwithstanding this, the majority of patients were in clinical remission. There was no significant difference in these measured parameters between the AZA monotherapy or combination therapy groups. It is not clear how assidious we should be in escalating TP dose to target MCV and WCC/LC in order to maximise efficacy in IBD patients. Work is underway to correlate these surrogate markers with TP metabolites levels and disease activity indices.

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Relative frequency of relapses in patients with ulcerative colitis and Crohn’s disease treated with mesenchymal stromal cells: Five-years of follow-up

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Background: Numerous studies have shown that mesenchymal stromal cells (MSCs) have a high potential for differentiation and immunosuppressive properties. Currently under phases I–III clinical trials evaluating the efficacy and safety of MSCs in the treatment of patients with inflammatory bowel disease (IBD) – ulcerative colitis (UC) and Crohn’s disease (CD). To compare the frequency of relapses and duration of remission for 5 years of follow-up in patients with luminal Crohn’s disease (CD) and the total defect of ulcerative colitis (UC) receiving therapy with mesenchymal stromal cells (MSCs) and bone marrow.

Methods: We compared the frequency of relapses in patients with luminal form CD (colitis and ileocolitis), with a group of patients with UC (total lesion) receiving MSCs. A group of patients (CD) aged 22–36 years (Me-28) (n = 24) received MSC culture scheme (0–1–2 weeks, then every 26 weeks). The second group of patients with UC (n = 26) aged 20–62 years (Me-28) received the culture of MSCs in a similar way. Evaluation of the effectiveness of therapy for relapse frequency was carried out at 12, 24, 36, 48, and 60 months after initiation of therapy.

Results: Among the patients in first group relapse in the 12 months of observation occurred in 2 of 24 patients (8.3%) in 2 group, relapse occurred in 3 of 26 (11.5%) (OR –0.72; 95% CI 0.13–3.96, p = 0.92). After 24 months in the group of patients (group 1) receiving MSC, relapse occurred in 5 of 24 (20.8%) in group 2 patients with recurrent disease in 7 of 26 (26.9%) (OR –0.77; 95% CI 0.13–3.96, p = 0.92). After 36 months in group 1 patients with a relapse of the disease in 8 of 24 (33.3%) in group 2 relapsed in 14 of 26 (53.8%) (OR –0.62; 95% CI 0.32–1.21; p = 0.24). After 48 months in group 1 receiving MSC, relapsed in 11 of 24 (45.8%) in group 2 relapsed in 18 of 26 (69.2%) (OR –0.6; 95% CI 0.37–0.97, p = 0.048). After 60 months in first relapse in 16 of 24 (66.6%) in group 2 relapsed in 22 of 26 (84.6%) (OR –0.63; 95% CI 0.44–0.90, p = 0.013).

Conclusions: MSCs transplantation longer contributes to clinical remission in patients with Crohn’s disease luminal shape compared with a group of patients suffering from ulcerative colitis.

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Loss of response to anti-TNF in inflammatory bowel disease in a Portuguese centre


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Background: Tumour necrosis factor antagonists (anti-TNFs) are a mainstay in inflammatory bowel disease (IBD) treatment but a significant proportion of patients will not respond or will lose response to these therapies over the time.

Methods: Single-centre retrospective study that included all patients that initiated anti-TNF maintenance therapy for treatment of IBD. Loss of response (LOR) was defined the occurrence of one of the following: dose escalation, discontinuation, switching, corticosteroids use or surgery. The aim of this study was to determine the prevalence of LOR among patients with IBD treated with anti-TNFs.

Results: One-hundred-and-forty-six patients with IBD that initiated anti-TNFs were included: 90% Crohn’s disease and 10% ulcerative colitis; 80% infliximab, 19% adalimumab and 1% golimumab. The mean follow-up was 39 months. LOR occurred in 58% patients (84/146). The reasons for LOR were lack of clinical remission in 83%, side effects in 11% and lack of endoscopic/imaging remission in 7%. 70% had dose escalation, 8% discontinuation, 8% switching, 7% surgery and 6% corticosteroids use. The mean time to LOR was 21 months. Among the 84 patients with LOR, 31 (37%) had a second LOR after a mean period of 15 months: 87% for lack of clinical remission, 10% for side effects and 3% for lack of endoscopic/imaging remission. Switch to another anti-TNF

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