High-dosed intravenous iron replacement therapy does not hinder drug-induced amelioration of disease activity in IBD patients with iron deficiency anaemia

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Background: Iron deficiency and iron deficiency anaemia (IDA) are common complications of inflammatory bowel disease, impacting quality of life, hospitalisation rates and time lost from work. Anaemia in IBD is caused by chronic blood loss and impaired iron intake/absorption. While oral iron is convenient and ostensibly inexpensive, it fails to compensate continuous iron loss in the presence of inflammation, and may cause gastrointestinal side-effects including abdominal pain and nausea. Studies show that non-absorbed iron can exacerbate mucosal inflammation. Intravenous (IV) iron has been shown to be safe, effective and well tolerated in IBD patients. IV ferric carboxymaltose (FCM; Ferinject®) can be given in weekly 15-min infusions of ≤1000 mg/week. In this multicentric, prospective, non-interventional, post-marketing study, the effect of high-dosed IV FCM on inflammatory activity in IBD patients in routine clinical practice was assessed.

Methods: Patients were enrolled in 101 centres in Germany based on medical need for IV iron therapy with FCM as prescribed by the treating physician. Primary outcomes included response rates and AEs. In addition, changes in clinical disease indices (CDAI/CAI), CRP values, and self-reported disease-related symptoms (fatigue, concentration lack, headache, paleness of mucous membranes, hair loss, dyspnoea, sleeping disorders, restless legs syndrome), were evaluated and classified as 1–4 for severity, were analysed. Patients were stratified in baseline CRP subgroups (<5 mg/l, >5 mg/l, 5–10 mg/l, >10 mg/l).

Results: In total, 224 subjects (127 CD; 97 UC) received IV FCM for ca. 12 weeks. Mean total dose was 1139 mg (100–4800 mg), with 76.7% receiving 500–2000 mg. Concomitant drugs included aminosalicylates (89 patients/46.1%), corticosteroids (84/43.5%), immunosuppressants (36/18.7%) and biologics (36/19%). While patients (n = 97) with elevated clinical disease activity indices (CDAI ≥150; CAI ≥ 5) had lower mean Hb at baseline compared with those with normal indices, mean Hb at EOS was similar. Baseline CRP was higher in subjects with higher vs. lower activity indices (6.1 mg/l vs. 3.6 mg/l). Mean CRP levels decreased significantly from 6.4 mg/l to 3.5 mg/l (median 1.9–1.0 mg/l), indicating a reduction in inflammatory activity, independent of baseline Hb. CRP change was statistically significant in patients with high disease activity, CD/UC patients with total dose 500–1000 mg, and patients completing therapy. Amelioration of inflammatory activity was confirmed by reduced CDAI/CAI. Patients in both CRP subgroups showed increases in Hb, s-ferritin and TSAT, but reduced CRP levels and fewer symptoms.

Conclusions: High-dosed FCM therapy does not appear to inhibit drug-induced amelioration of inflammatory activity in patients with IBD and iron deficiency anaemia.

The impact of thiopurine drugs on the natural history and surgical outcome of ulcerative colitis: A cohort study

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Background: Thiopurines are used as maintenance therapy in ulcerative colitis, but whether these drugs influence the natural history of the disease is unknown. We aimed to assess the effect of thiopurines in terms of colectomy, hospital admission, progression in disease extent and anti-TNF therapy within 10 years.

Methods: Patients diagnosed with ulcerative colitis within the Örebro University Hospital catchment area, during 1963–2010 (n = 1007), who initiated thiopurines (n = 253) were included. To overcome the risk of confounding by indication, we used a novel approach and compared patients who stopped treatment within 12 months because of an adverse reaction (n = 76) with patients who continued therapy or discontinued due to other reasons (n = 177). Long-term outcomes were assessed by Cox-regression analyses with adjustments for confounding factors including sex, age, hospital admission at diagnosis, disease extent, and previous medication at first thiopurine exposure.

Results: No significant difference in baseline characteristics was observed between the two groups. The cumulative probability of colectomy within 10 years was 19.5% in tolerant patients compared with 29.0% in intolerant, (adjusted HR: 0.43; 95% confidence interval (CI) 0.20 to 0.99). The probability of hospital admission was 34.0% in tolerant vs. 56.2% in intolerant patients (adjusted HR: 0.43; 95% CI 0.25 to 0.59). The risk for progression in disease extent was 20.4% in tolerant patients compared with 29.0% in intolerant, (adjusted HR: 0.43; 95% CI 0.24 to 0.79). Within 10 years, 16.1% of tolerant and 27.5% of intolerant patients received anti-TNF therapy, (adjusted HR: 0.43; 95% CI 0.24 to 0.79).

Conclusions: Based on the novel approach of comparing patients tolerant and intolerant to thiopurines, we, for the first time, reveal that thiopurines have a profound beneficial impact of the natural history and long-term colectomy rates of ulcerative colitis.