TREATMENT OF IRON DEFICIENCY WITHOUT ANEMIA WITH FERRIC CARBOXYMALTOSE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: PROSPECTIVE EVALUATION OF CLINICAL AND PATIENT-REPORTED OUTCOMES IN SPAIN

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BACKGROUND

Iron deficiency without anemia (ID-noA) in patients with Inflammatory Bowel Disease (IBD) might impose important clinical implications with significant impact on patients' well-being[1] and the role of parenteral treatments requires further research in real world practice.

OBJECTIVE

This study aims to assess the benefit-risk profile of ferric carboxymaltose (FCM) in IBD patients with ID-noA, including changes in their reported health-related quality of life (HRQoL).

METHODS

- An observational, multicentric, prospective research was conducted including consecutive IBD patients (ulcerative colitis-UC- and Crohn disease-CD-) with inactive or mild disease activity suffering from ID-noA being treated with FCM according to routine clinical practice (n=98).
- Exclusion criteria: patients with a disease that could contribute to iron deficiency -ID- [severe cardiopulmonary, hepatic or renal]; active moderate-to-severe IBD; non-steroidal anti-inflammatory drugs within 3 months prior to the study or taking anticoagulant drugs; taking FCM for diseases other than IBD; cases who had been given intravenous iron, erythropoietin or blood transfusion within 3 previous months; allergic or intolerant to FCM or any of its excipients; pregnant; and patients <18 years of age.
- Intervention: patients received a single 500 mg dose of FCM for the treatment of ID-noA. Treatment was administered on an outpatient basis in the hospitals of the participating centres. FCM was administered over ≥15 minutes following approved use.[2]
- The diagnosis of CD and UC was established by clinical, radiological, histological and endoscopic criteria, and disease severity was classified using the Montreal classification.
- Key variables for benefit-risk analysis: the partial Mayo score and the Harvey–Bradshaw index were used to define clinical activity in UC and CD, respectively, before FCM infusion (baseline) and 1 month after treatment. Also, blood tests (i.e., ferritin, serum iron, transferrin saturation index [TSAT]), patient's self-reported ID-symptoms and HRQoL [Short Form-12 (Physical Component Summary-PCS- and Mental Component Summary-MCS-) and EQ-5D-3L] were registered at same time periods.
- **Statistical Approach:** differences from baseline were tested with non-parametric tests (Wilcoxon signed-rank and McNemar's test). The statistical analysis was performed using the software package R 4.0.3 for Windows.

RESULTS

- Patients' characteristics are shown in detail in Table 1.
- A clear benefit in clinical parameters was observed (Table 2, p<0.001). This benefit was consistent among CD and UC patients (all: p<0.01). Also, a percentage of patients with TSAT<16% dropped from 73.75% to 8.75%, p<0.001).

Table 1. Sample description

Variable	N=98
Mean age [SD], years	43 [12.41]
Sex, Female, n [%]	70 [71.43]
Diagnosis, n [%]	
Crohn's disease	66 [67.35]
Ulcerative colitis	32 [32.65]
Harvey–Bradshaw index, n [%]	
Remission [score 0–4]	53 [54.07]
Mild [score 5–7]	10 [10.20]
Moderate [score 8–16]	3 [3.06]
Severe [score >16]	0
Partial Mayo Scoring Index; n [%]	
Remission [score 0–1]	18 [18.36]
Mild [score 2–4]	10 [10.2]
Moderate [score 5–6]	3 [3.06]
Severe [score 7–9]	1 [1.06]
Previous surgery, Yes n [%]	26 [26.53]
Mean CRP [SD], mg/L	4.12 [6.16]
Mean faecal calprotectin [SD], µg/g	333.21 [647.64]

Variable	N=98
Mean Hb [SD], g/dL	13.44 [1.02]
Mean s-ferritin [SD], µg/L	48.38 [64.60]
Mean s-iron [SD], µg/dL	51.92 [41.03]
Mean TSAT [SD], %	12.78 [4.19]
Mean vitamin B12 [SD], pg/mL	346.91 [270.79]
Mean folic acid [SD], ng/mL	7.01 [3.34]
IBD Treatment, n [%]	
• Mesalazine	31 [31.63]
• Steroids	6 [6.12]
• Thiopurines	24 [24.49]
• Methotrexate	4 [4.08]
• Anti-TNF	38 [38.78]
• Vedolizumab	6 [6.12]
• Ustekinumab	11 [11.22]
• Apheresis	2 [2.04]

CRP, C-reactive protein; PMI, Partial Mayo Scoring Index; SD, standard deviation; s-ferritin, serum ferritin; s-iron, serum iron; TSAT, transferrin saturation index; TNF, tumour necrosis factor

Table 2. Effects of ferric carboxymaltose administration on iron parameters

	Pre-FCM	Post-FCM	MD (95% CI)	p-value*
Mean s-ferritin, µg/L; [n (pre/post) = 93/87]	48.4	175.0	126.6 (97.5, 137)	<0.001
Mean s-iron, µg/L; [n (pre/post) = 85/84]	51.9	84.4	32.5 (28.5, 44)	<0.001
Mean TSAT, %; [n (pre/post) = 80/75]	12.8	27.2	14.4 (11.6, 17)	<0.001

FCM, ferric carboxymaltose; n, number of patients with lab values before and after FCM treatment; s-ferritin, serum ferritin; s-iron, serum iron; TSAT, transferrin saturation; CI, confidence interval; MD, mean difference; *Wilcoxon-signed-rank test.

- Self-reported symptoms improved four weeks after treatment. Average increase of 7.5 points in VAS score (p<0.01), 0.102 points in EQ-5D index score (p<0.001), 2.9 points in the PCS (p<0.01) and 7.3 points in the MCS (p<0.01). Overall, all differences were statistically significant. The same analysis was performed for separate cohorts of patients with Crohn's disease and ulcerative colitis, producing comparable results.

Figure 1. Benefit observed in Patient-reported symptoms related to iron deficiency -ID- (percentage of patients reporting any problem)

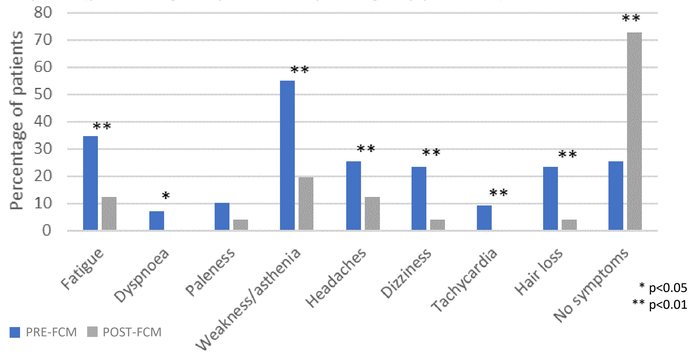


Figure 2. EQ-5D 3L descriptive system

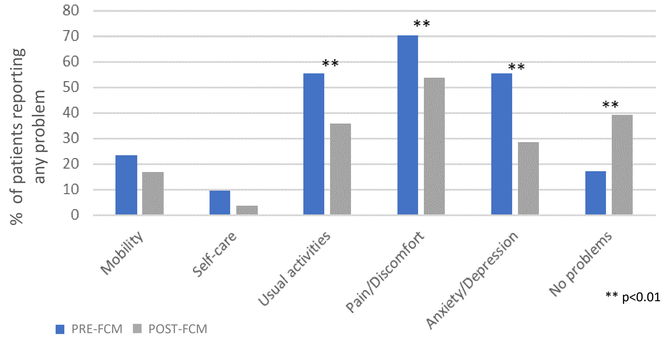
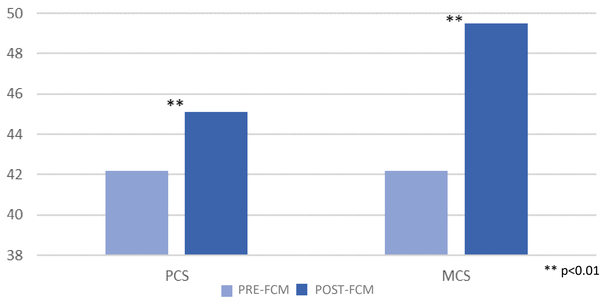


Figure 3. Effects of FCM on patients' HRQoL (SF-12)



CONCLUSIONS

- Treatment with FCM for ID-noA IBD patients was associated with a high effectiveness due to a prompt response of iron parameters with meaningful clinical improvements.
- FCM can very quickly improve patient-reported symptoms and HRQoL.
- Given the increasing prevalence of this complex disease, early diagnosis of ID and administration of FCM could contribute to reducing the social and economic burden of IBD on health systems.

REFERENCES

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