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Oral butyrate plus inulin improve serum metabolomic profile and gut microbiota composition in ulcerative colitis and celiac disease
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Background: Intestinal microbiota is most probably involved in the development and maintenance of autoimmune inflammation in ulcerative colitis (UC) and celiac disease (CD). Gas chromatography-mass spectrometry (GC-MS) of serum generates comprehensive metabolic profiles, reflecting integrated human and gut microbial metabolism which may be altered in disease states.

We aimed to investigate the effects of an orally administered butyrate plus inulin on GC-MS-based serum metabolomic profiles and gut (fecal) microbiota composition in UC patients, CD patients and healthy controls (HC).

Methods: Serum metabolomic profiles and fecal samples were collected from 75 individuals: 20 patients with mild-moderate active UC, 35 CD patients, and 20 healthy controls. ROC curve analysis, some multivariate analysis techniques such as principal components analysis (PCA) were used to identify of biomarkers and to assess differences between groups. The quantitative real-time polymerase chain reaction (qRT-PCR) was used for quantitative fecal microbiota assessment.

Results: We characterized 84 serum metabolites to differentiate between UC, CD and HC cohorts. 18 metabolites at least have a combined (human plus microbial) origin. In serum of UC patients, phenylacetic acid (PAA), 4-hydroxyphenylacetic acid (4-HPAA), 3-indolyacetic acid (IAA), succinic acid (SA) and fumaric acid (FA) were the metabolites most prominently increased, whereas 3-phenylpropionic acid (PPA) was significantly decreased. Serum of CD patients showed significant increases in IAA, 3-indolepropionic acid (IPA), SA and FA.

Differences in serum metabolite levels of UC patients, CD patients and controls may indicate the difference in the metabolic activity of gut microbiota (Clostridia and Bacteroides spp.) involved in phenylalanine and tyrosine metabolism. Increased serum levels of succinic acid, produced abundantly by some Bacteroides spp., suggest its possible damaging effect on intestinal mucosa especially in UC. Orally administered butyrate plus inulin (Zacofalk NMX, Dr. Falk Pharma GmbH, 3 tablets per day for 4 weeks) as supplement to mesalazine in UC or gluten free diet (GFD) in CD was effective in reducing disease activity with a marked improvement of serum metabolomic profiles (including succinic acid reduction) and gut microbiota (including reduction of Bacteroides fragilis/Faecalibacterium prausnitzii ratio and butyrate-producing bacteria increase) in both conditions. There were no any adverse events.

Conclusions: Oral butyrate plus inulin can be effectively used in UC, as well as in CD, improving symptoms, serum metabolomic profile and gut microbiota composition. Quantitative metabolomic profiling of serum using GC-MS discriminates between UC patients, CD patients and healthy controls.

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Opportunistic infections in anti-TNF treated IBD patients: analysis from three tertiary centers in Romania
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Background: Anti-TNF agents, together with the classic immunosuppressors, are the mainstay of treatment in IBD; deriving from their action mechanism, there is an increased risk for infection and malignancy. Because Romania is a high prevalence country for tuberculosis (even if the exact incidence of latent tuberculosis is not known), the standard procedure for immunosuppressive treatment initiation in Romania includes screening for hepatitis B virus, hepatitis C virus, HIV, and tuberculosis. Even though, we are facing a number of opportunistic infections in these patients. This is why we intended to evaluate the safety of the immunosuppressor treatment, in general, and of anti-TNF agents, in particular, in Romanian patients with IBD.

Methods: We performed a retrospective analysis of 113 consecutive patients with moderate to severe ulcerative colitis and Crohn’s disease admitted to three tertiary centers in Bucharest between 2009–2013, who received anti-TNF agents (infliximabum or adalimumabum) with/without classic immunosuppressors (azathioprine, methotrexate or 6 mercaptopurine) associated; we intended to determine the incidence of opportunistic infections and the possible risk factors.

Results: We analyzed 113 patients – 82 (72%) with Crohn’s disease and 32 (28%) with moderate to severe ulcerative colitis. We found 27 opportunistic infections: 5 cases of Clostridium difficile infection (4.5%), 2 cases of CMV colitis (1.8%), 2 cases of TB reactivation (1.8%) – 1 peritoneal TB and one intestinal TB and 2 cases of perianal abscesses (in patients with ulcerative colitis) [3 (2.7%) cases of herpes zoster and 16 (14.1%) cases of upper respiratory tract and urinary tract infections. All patients were treated according to the guidelines, severe infections being admitted to the hospital and resolved with treatment; none of the patients had complications and there were no deaths. 17.5% of the patients had latent TB and received standard chemoprophylaxis before antiTNF (including those with intraabdominal TB).

Conclusions: The association between anti TNF agents and classic immunosuppressors increased the risk of infection. The risk of TB reactivation was significant, even with a correct chemoprophylaxis. The duration of immunosuppressor therapy did not influence the rate of infection.

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Outcome of infliximab discontinuation in IBD patients and therapy rechallenging in relapsers: Single centre preliminary data
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Background: Tumor necrosis factor antagonists (TNF-A) have dramatically changed our concept of treating inflammatory bowel disease (IBD). One of the ongoing controversies, still debated, is whether and when stop treatment with TNF