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Levels of serum free thiols are superior to fecal calprotectin in predicting endoscopic disease activity in Inflammatory Bowel Disease

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Conclusion: Clinicians are well aware of the risk of POR in Crohn's disease and tight endoscopic control within twelve months is often proposed. After a first ileocolonoscopy without POR, most respondents reported relying on fecal calprotectin for routine monitoring. The surprisingly high rate of immediate postoperative prophylactic therapy with biologics, even in the absence of clear endoscopic recurrence or clinical risk factors for POR, highlights the need for a randomized trial comparing immediate prophylaxis with endoscopy-driven therapy.

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P0350 INTERLEUKINS LEVELS: ARE WE ON THE ROAD TO TAILORED THERAPY IN INFLAMMATORY BOWEL DISEASE?

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Introduction: There is a rising interest in identifying easy to dose disease markers to predict response to therapy in inflammatory bowel disease (IBD) patients.

Several markers have been studied, but none of them has been validated.

Aims & Methods: The aim of our study was to understand the role of inflammatory interleukins in predicting the response to immunosuppressive or biological therapy. A monocentric prospective study was conducted. Forty IBD patients who needed to start immunosuppressive or biological drugs were included. For each patient serological levels of interleukin (IL)1-B, IL4, IL6, IL8, Il10, IL12p70, IL17, IFN-gamma, TNF-alfa, TGF-beta-1 were dosed at the time of enrollment (T0) and after three months of immunosuppressive or biological therapy (T3). To dose these cytokines, multiplex Bio-Plex® system was used.

Results: Among the 40 enrolled patients, 32 (80%) were suffering from Crohn's disease (CD) and 8 from Ulcerative Colitis (UC); the mean age was 46.6 years (18-79 years).

IL1-B T0 was detectable only in CD patients (mean value 0.05 pg/ml), with no difference due to illness localization.

Serological T0 TNF-a levels correlated with pre-treatment endoscopic activity: among patients with moderate or severe endoscopical activity median value was 20.94 pg/ml while among mild activity or remission group median value was 13 pg/ml (p=0,034).

T0 IL8 levels correlated both with pre-treatment fecal calprotectin (p=0,03; r= 0.437) and endoscopic activity (median value 28,07 pg/ml for moderate to severe activity vs 5,79 pg/ml median value for mild activity/remission; p=0,023)

T0 TGF-b1 levels were significantly lower in CD patients than in UC patients (p = 0.0076).

Low levels of IL6 at T0 (< =0.54 pg/ml) predicted a negativization of fecal calprotectin after three months of adalimumab (ADA) administration (area under the curve [AUC] = 0.89; p=0,001; sensitivity = 72.7%; specificity = 100%). Low levels (median value = 0.54 pg/ml) of T0 IL6 correlated with a higher probability to response to azathioprine (AZA) too (p = 0.049). T0 IL6 >=0.9 pg/ml correlated with higher response to vedolizumab (VEDO).

Patients who responded to AZA had undetectable T0 serological levels of IFN-g, while the ones who did not respond had a median IFN-g level of 0.11 pg/ml (p = 0.043).

T0 serological levels of TGF-b1 correlated with response to AZA (< 4.7 pg/ml) and to ADA (>6.57 pg/ml) (p = 0.027).

Low IL12p70 levels predicted a better response to therapy at all (p = 0.0095), but not for each drug separately.

T0 IL8 levels predicted response to vedolizumab therapy: at ROC curve analysis we observed for >6,6 pg/ml levels of IL8 a response to VEDO in all patients (AUC = 1; sensitivity 100%; specificity 100%; p=0.0001).

Conclusion: IFN-g and TGF-b1 may be useful to identify AZA responders and IL8 and IL6 levels could be good predictors of response to both biological and immunosuppressive drugs. Our study is a first step for tailored therapy in IBD patients.

Disclosure: Nothing to disclose

P0351 MEASURING INFLIXIMAB DRUG LEVELS CONSISTENTLY: ALIGNMENT TO THE 1ST INTERNATIONAL STANDARD MATERIAL (NIBSC 16/170) USING IDKMONITOR® INFLIXIMAB DRUG LEVEL ELISA LEADS TO AN INCREASE IN THE MEASURED INFLIXIMAB CONCENTRATION

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Introduction: Measuring the concentration of infliximab drug levels in IBD patients is widely practiced. Variability between assays has previously been a problem as inconsistent results are obtained between different laboratories, depending on the methodology and manufacturer used.

Introduction of the 1st International Standard infliximab material (NIBSC 16/170) should allow for alignment of the methods for measuring infliximab, and ultimately more consistent results between laboratories.

Immundiagnostik has aligned the IDKmonitor® Infliximab drug level ELISA by re-calibrating with the International Standard infliximab material (NIBSC 16/170). The impact of this change upon clinical results is explored.

Aims & Methods: The aim of this work is to determine the change in the measured concentration of infliximab using the IDKmonitor® Infliximab drug level ELISA kit before and after alignment with the 1st International Standard infliximab (NIBSC 16/170).

Serum samples received through the routine infliximab monitoring service (n=80) were measured using the IDKmonitor® Infliximab drug level ELISA, using kits manufactured before and after calibration with the 1st International Standard infliximab (NIBSC 16/170). Regression and correlation results were obtained.

Results: Regression analysis of results before and after the calibration provide are good (R2 = 0.99). Correlation of the data shows that when aligned to the 1st International Standard infliximab (NIBSC 16/170), the measured concentration of infliximab is higher than that obtained with the kit manufactured before the calibration (i.e. post calibration result = 1.35x pre-calibration result + 0.81).

Conclusion: International standardisation of infliximab drug level concentrations is now possible due to the introduction of the 1st International standard infliximab. This is a step change towards consistency of measuring infliximab drug levels.

However, clinicians who are using this test for monitoring need to be aware of this change and consider patient results carefully in the light of this information.

Disclosure: Nothing to disclose

P0352 LEVELS OF SERUM FREE THIOLS ARE SUPERIOR TO FECAL CALPROTECTIN IN PREDICTING ENDOSCOPIC DISEASE ACTIVITY IN INFLAMMATORY BOWEL DISEASE

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Introduction: Oxidative stress is considered to play a pivotal role in the pathogenesis of Inflammatory Bowel Diseases (IBD). Serum free thiol groups (R-SH) reliably reflect systemic oxidative stress, since they are readily oxidized by reactive species. Endoscopic examination is the gold standard to determine disease activity in IBD. In clinical practice, fecal calprotectin (FC) levels are most widely used as surrogate marker for endoscopically proven disease activity.

However, its diagnostic accuracy and applicability are still subject to de-

bate. Systemic biomarkers for disease activity are urgently sought to improve disease activity monitoring and to avoid repeated endoscopic examination.
Aims & Methods: In this study, we aimed to establish concentrations of serum free thiols in IBD and assessed their potential utility as a discriminating biomarker for different grades of endoscopic disease activity. Serum free thiol concentrations were measured in 78 IBD patients (31 patients with Crohn's disease (CD) and 47 patients with ulcerative colitis (UC)) and 50 healthy controls, adjusted for serum albumin. Albumin-adjusted serum free thiols were analyzed for associations with clinical and biochemical disease parameters. Endoscopic disease activity was assessed by the Simple Endoscopic Score for CD (SES-CD) and Mayo endoscopic subscore for UC, that were merged to create an IBD composite endoscopy score. Nonparametric ROC estimation with cross-validated areas under the curves (AUCs) was used to assess the discriminative value of serum free thiols regarding the degree of endoscopic disease activity (n=54) and to compare this to fecal calprotectin (n=28) in patients for which those data were available.
Results: Mean serum free thiol concentrations were significantly decreased in both CD and UC as compared to healthy controls (19.4±3.1 and 17.8±3.4 vs. 21.1±1.9 µmol/g of albumin, $P < 0.001$). Albumin-adjusted serum free thiols significantly inversely associated with age ($r = -0.49$, $P < 0.01$), platelet counts ($r = -0.29$, $P < 0.01$) and fecal calprotectin levels ($r = -0.32$, $P < 0.05$). Patients with severe endoscopic disease activity demonstrated significantly lower serum free thiol concentrations compared to patients having mild disease activity (16.2±3.1 vs. 20.4±3.4 µmol/g of albumin, $P < 0.01$). Finally, serum free thiols highly accurately discriminated between mild and moderate-to-severe disease activity, better than fecal calprotectin (FC) levels (AUC=0.87, $P < 0.001$ vs. AUC=0.76, $P < 0.05$, respectively). After cross-validation, serum free thiols maintained their predictive accuracy (AUC=0.89, $P < 0.001$).
Conclusion: Serum free thiols are reduced in IBD as compared to healthy controls and strongly correlate with the degree of endoscopic disease activity. Quantifying systemic redox status in IBD may be a promising, minimally invasive strategy to monitor IBD disease activity. Future studies are warranted to further explore free thiols as potential biomarker for IBD disease activity in larger, prospective patient cohorts and serially assess their predictive value in relation to disease course and therapeutic interventions.
Disclosure: Nothing to disclose

P0353 VALIDATION OF NOVEL FECAL INFLAMMATORY MARKER FOR ASSESSMENT OF INFLAMMATORY BOWEL DISEASE ACTIVITY

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Introduction: Diagnosis of inflammatory bowel disease (IBD) require combination of patient history and physical examination in association with laboratory, endoscopic, histologic, and radiographic investigations. Although ileocolonoscopy is the preferred method of diagnosis, assessing disease extent, activity and follow up after therapy but repeated endoscopy is neither practical nor feasible, being invasive, time consuming, and not always well tolerated or accepted.
Therefore, employment of non-invasive biomarkers is needed. No single marker is ideal. Many studies focus on fecal calprotectin (FC) in IBD and confirm its value in diagnosis, disease activity evaluation, effect evaluation, and relapse monitor.
Neopterin, is a metabolite of cyclic guanosine monophosphate that is released by activated T lymphocytes and macrophages after induction by interferon γ. Neopterin release from activated macrophages may provide, at least theoretically by its intrinsic mechanism of release, an advantage over calprotectin which is not secreted and represents a neutrophil-derived protein.
Aims & Methods: ts specificity and sensitivity to To investigate the relation between fecal neopterin (fNeo) excretion and IBD clinical and endoscopic activity indices and compare its specificity to that of fecal calprotectin.
60 patients were included: 30 patients with ulcerative colitis (UC) (15 clinically in remission, 15 active) and 30 patients with Crohn's disease (CD) (15 clinically in remission, 15 active) and 20 healthy control subjects.
FC and fNeo were detected in stool samples by enzyme-linked immunosorbent assay (ELISA).
The following indices were calculated at enrollment: for Crohn's disease the Crohn's disease activity index (CDAI) and simple endoscopic score for Crohn's disease (SES-CD); for ulcerative colitis, Simple Clinical Colitis Activity Index (SCCAI) and ulcerative colitis endoscopic index of severity (UCEIS).
Results: Among UC patients, fNeo was higher in those with either clinically active or inactive disease than in control subjects (P=0.001, P=0.040 ; for active and inactive disease vs. controls respectively) but there was no significant difference between both UC groups (P=0.225). For CD patients, fNeo concentration was higher in those with active disease than in those with inactive diseas (P< 0.001) or healthy controls (P=0.001). Nonsignificant trends toward greater fecal neopterin concentration were observed with increased colonic disease involvement. Neopterin was not found to be significantly correlated with all laboratory tests done (Heamoglobin, platelets, white blood cells, ESR, CRP, serum albumin, fecal calprotectin). fNeo was significantly correlated with CDAI (r=0.604, P< 0.001) , SES-CD (r=0.600, P< 0.001) in CD patients but not with SCCAI, UCEIS in UC patients. fNeo was found to have comparable sensitivity and overall accuracy to FC in predicting endoscopic disease activity in CD patients but less in UC and combing both stool tests together increases the sensitivity and specificity of either alone.
Conclusion: Stool neopterin could be used to assess disease activity in CD but not in UC patients as it correlates positively with disease activity indices in CD but not in UC. Thus its measurement represents a novel reliable biomarker useful to detect and monitor the severity of mucosal affection in CD patients more than UC.
Disclosure: Nothing to disclose