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THE DIAGNOSTIC CAPABILITIES OF NON-INVASIVE FECAL BIOMARKERS OF NSAID-INDUCED INTESTINAL LESIONS IN PATIENTS WITH OSTEOARTHRITIS

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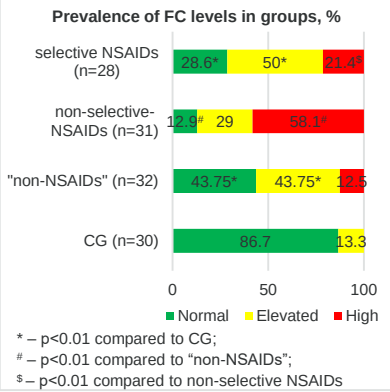
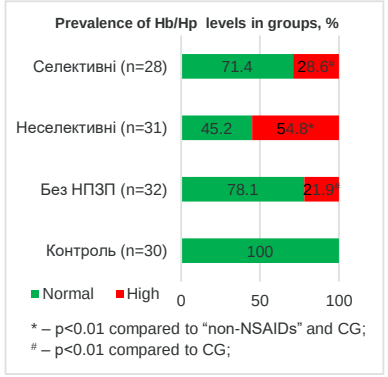
Introduction: Osteoarthritis (OA) is a common disease among the population, especially the elderly, requiring frequent nonsteroidal anti-inflammatory drugs (NSAIDs), which are harmful to the upper and lower parts of the gastrointestinal tract.

Aims & Methods: To analyze the diagnostic possibilities of non-invasive fecal biomarkers of NSAID-induced intestinal lesions in patients with OA and to check the possibility of predicting the presence of such lesions based on fecal biomarkers. We investigated 91 patients with OA of different localizations and degrees (then divided into three subgroups depending on NSAIDs use and their selectivity) and 30 people without OA as a control group (CG). We studied the following fecal biomarkers: calprotectin (FC) (RIDASCREEN® Calprotectin), secretory immunoglobulin A (sIgA) (RIDASCREEN® sIgA), and hemoglobin/haptoglobin (Hb/Hp) complex (now discontinued) (ELISA method).

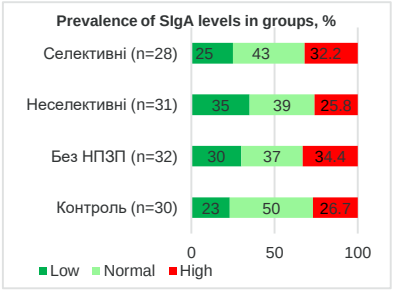
Results: The FC content in OA patients was significantly higher than in CG (147.19 (IQR 132.76-161.8) mg/kg vs 20.91 (IQR 19.5-32.53) mg/kg (p <0.001). It was 68.78 (IQR 61.48-90.3) mg/kg in those not taking NSAIDs, 259.65 (IQR 234.67-294.99) mg/kg in those taking non-selective and 111.93 (IQR 105.31- 149.63) mg/kg in those taking selective NSAIDs. We found a significant difference between all three subgroups from the CG (p <0,01). NSAIDs subgroups differed from the "non-NSAIDs" (p <0,01). In "non-NSAIDs" subgroup patients, the elevated (50-200 mg/kg) level of FC was significantly more common than in CG (OR = 4.92; 95% CI 1.273-23.965; p = 0.0012); non-selective NSAIDs subgroup had a significantly higher prevalence of high FC level (>200 mg/kg) than "non-NSAIDs" subgroup.



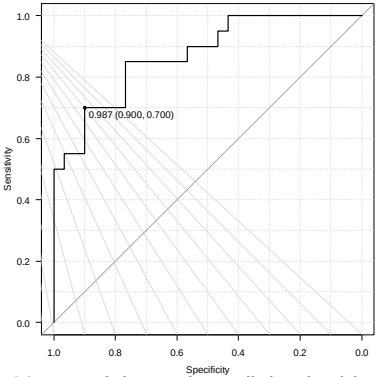
Hb/Hp complex content in CG was 0.73 (IQR 0.65-0.79) mg/kg vs 4.77 (IQR 3.41-6.81) mg/kg in the OA group. In OA-"non-NSAIDs" - 1.88 (IQR 1.23-2.6) mg/kg, non-selective-NSAIDs - 9.38 (IQR 7.47-13.29) mg/kg and in selective NSAIDs - 2.98 (1.34-4.62) mg/kg. OA-non-selective-NSAIDs differed significantly from CG and "non-NSAIDs". The OA-selective-NSAIDs differed from the non-selective and CG (p <0,05). OA patients had high Hb/Hp complex while in the CG it was not high in all cases. OA-non-selective-NSAIDs had high levels of Hb/Hp complex significantly more frequent than CG (p<0.001) and "non-NSAIDs" (OR=4.229; 95% CI 1.288-15.289; p<0.001).



SIgA content differed in OA patients from the CG (1088.83 (IQR 986.0-1.291.25) mg/kg vs 593.57 (IQR 549.0-761.91) mg/kg, p <0.01), but not in subgroups (p> 0.05), where there was no difference neither in quantitative, nor in qualitative comparison.



The developed logistic models allows to predict the risk of NSAID-induced intestinal lesions. It looks like **ln(P/(1-P)) = -2.168+0.2986*(Hb/Hp) + 0.0083*FC**. AUC of the model is 0.872 (95% CI 0.773 - 0.97), p<0.05; the optimal threshold = 0.987. At the chosen threshold, the sensitivity of the model is 65% (95% CI 40.8% - 84.6%), specificity 90% (95% CI 73.5% - 97.9%), Positive Predictive Value - 81.2% (95% CI 54.4 - 96), Negative Predictive Value - 79.4% (95% CI 62.1 - 91.3).



ROC curve of the test for predicting the risk of NSAID-induced intestinal damage

Conclusion: the NSAID enteropathy manifests in increased FC and Hb/Hp complex content. Our model can predict such lesions. These markers are slightly increased in OA patients even if they do not take NSAIDs. SIgA content is not affected by NSAIDs intake.

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