P085-F | Antioxidative and anti-inflammatory effects in the realization of hepatoprotective properties of derivative of drug Xymedon with L-ascorbic acid

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The inflammation and activation of peroxide oxidation of lipids are important components in the pathogenesis of liver diseases. In our previous investigations was shown that pyrimidine derivative, Russian drug Xymedon (I) have hepatoprotective properties [1]. We synthesized derivatives of Xymedon with biogenic molecules to improvement of hepatoprotective properties [2,3]. The derivative of Xymedon with L-ascorbic acid (II) leads to the most pronounced decrease of areas of liver injury [3,4]. However, the mechanism of hepatoprotective action of (II) didn't studied.

In present work we studied expression of superoxide dismutase (SOD1) and glutathione peroxidase (ISO1) as parameters of antioxidative mechanism and cytokines level as parameters of anti-inflammatory mechanism. Parameters were investigated in liver lysates obtained from rats that have been subjected to toxic damage by CCl_4 and treated with (II). SOD1 and ISO1 were determined by immunoblotting method, cytokines – by multiplex analyzer MagPix and Merck kits.

After administration of CCl_4 the SOD1 expression was increased in 10 times, ISO1 was decreased in 2·7 times. On the 3rd and 21st day the SOD1 level in control was down but stayed higher then initial one in 2 times. ISO1 remained at a reduced level. The elevated level of SOD1 in groups injected with (II) stayed up to 21st day. (II) was no effect on ISO1. In control, cytokines IL-1α, IL-3 and IFNγ were increased after CCl_4 administration and remained at an elevated level for 3 days. The level of proinflammatory cytokines IL1-α, IL1-β in groups treated with (II) was lower than in control.

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P086-F | Gut microbiota in chronic constipation disease: a new therapeutic target

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Background: Chronic constipation (CC) is a prevalent, burdensome gastrointestinal disorder whose etiology remains poorly understood and is most likely multifactorial with most significant contribution of imbalance in intestinal microbiota and failure of gut motor function. We have recently shown endotoxemia and morphological pathology in the colonic wall in constipated patients. The aim of this study was to characterize mucosal microbiota and contractility of colonic muscle in CC patients.

Methods: Colonic tissue samples were obtained from patients undergoing colectomy for CC and contractile activity was analyzed. Outcome was compared with the intestinal muscle contractions of patients undergoing colorectal surgery for gut diseases not associated with disorder of motor function. The juxta-mucosal microbiota was studied with culture-based and 16S rRNA pyrosequencing techniques.

Results: In CC patients, the spontaneous contractions were higher in both longitudinal (12·3 ± 4·4 vs 1·9 ± 0·9 g/s) and circular (13·47 ± 3·3 vs 5·8 ± 2·2 g/s) smooth muscle strips compared to controls. Moreover, the carbachol-induced response was also increased in CC in both longitudinal (EC50 0·50 ± 0·05 vs 0·65 ± 0·14 μM) and circular (EC50 0·76 ± 0·06 vs 2·01 ± 1·05 μM) muscle layers compared with those of the control group. The microbiota in constipated patients was dominated by bacteria belonging to the phyla Firmicutes (31–68%) and Bacteroidetes (5–57%), followed by Proteobacteria (1–48%) and Actinobacteria (1–17%). No definitive association between constipation and the abundance or lack of certain prokaryotic taxa in the gut microbiome was observed. Yet, we identified some microbes which may affect motility via production of methane (Methanobrevibacter), hydrogen sulfide (Desulfovibrio, Bilophila), butyrate (Clostridiales), propionate (Bacteroides), and acetate (many taxa).

Conclusions: Our findings suggest that alterations of the microbiota might affect gut motility via altered microbial-derived metabolites, and the restoration of disturbed microbiota may be a novel therapy strategy for CC.

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