

OC-050

ORIGIN OF INCREASED FECAL SERINE PROTEASE IN PATIENTS WITH IRRITABLE BOWEL SYNDROME AND DIARRHOEA (IBS-D)

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Introduction Patients with IBS-D have been reported to have increased faecal serine protease activity which could induce visceral hypersensitivity and increase gut permeability by activating proteinase activated receptor-2 (PAR-2). These proteases could be either endogenous (pancreatic or mast cell) or bacterial in origin.

Aim To define the type and origin of proteases using a proteomic method.

Methods *Study 1:* Serine protease activity in stool supernatant from 36 patients meeting the Rome III criteria for IBS-D and 9 healthy controls was evaluated using a previous published method.¹ Patients completed a one week stool diary and a hospital anxiety and depression score. *Study 2:* Serine proteases from a subset of 8 pooled patient samples were purified using a combination of affinity chromatography and SDS-PAGE. Protease identification using proteolysis and mass-spectrometry was performed. *Study 3:* Assessment of stool amylase and elastase was performed using two commercially available ELISAs.

Results *Study 1:* Serine protease activity was significantly increased in patients, 621 ± 94 versus 211 ± 46 units of trypsin/mg protein in controls, $p = 0.04$. Serine protease activity was significantly correlated with anxiety $r = 0.5$ $p = 0.002$. *Study 2:* The predominant proteases were pancreatic in origin including trypsin, elastase and carboxypeptidase-B. Additionally there was abundant pancreatic amylase. *Study 3:* Stool amylase but not elastase was significantly increased in IBS-D 183 ± 35 103 units/ml versus controls 78 ± 44 . Amylase also correlated with serine protease activity, $r = 0.33$, $p < 0.05$.

Conclusion We confirm previous reports of increased serine proteases in IBS-D but these appear to be of pancreatic origin and associated with increased anxiety. Anxiety may cause rapid transit which reduces degradation by colonic bacteria and increases fecal protease.

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Keywords faecal elastase, faecal amylase, irritable bowel syndrome, serine proteases.

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