Rome III criteria for IBS-D. In Group 1 the prevalence of IBS and its differing subtypes (IBS-D, IBS-C, mixed IBS (IBS-M) and unspecified IBS) were determined using the Rome III Diagnostic Questionnaire. In groups 2 and 3, demographic data and diagnostic yield of any investigations undertaken as part of the diagnostic workup were evaluated. Statistical analysis was performed using SPSS version 17.0 (SPSS Inc, Chicago, IL) with Fisher’s exact test used to compare categorical data, and an unpaired T-test used to compare continuous data.

Results IBS prevalence in healthy volunteers (Group 1) was 6% (60/1002), with 80% being female (p < 0.0001). Mixed IBS was the most common IBS subtype (Table 1), with IBS-C patients being significantly older than other patients with IBS (mean age 45 vs 30 years, p = 0.027). When comparing Groups 2 and 3, patients with IBS-C underwent a total of 56 additional investigations (including radiological, endoscopic investigations, breath tests, SeHCAT scan, faecal pancreatic elastase), significantly lower than the number of investigations undertaken in the IBS-D group of 885 (p < 0.001). Whilst further investigations in Group 3 identified an alternative diagnosis to IBS-D in 25%, the 56 additional tests undertaken in the IBS-D group of 885 (p < 0.001). Investigations undertaken in the IBS-D group of 885 (p < 0.001).

Conclusion This is the first study to evaluate the population prevalence of differing IBS subtypes within a UK population. Whilst, further investigation of IBS-D patients may lead to an alternative diagnosis and instigation of an appropriate management strategy, the merits of further investigation in IBS-C patients is to be questioned.

Disclosure of Interest None Declared

Abstract PTU-134 Table 1 Prevalence rates of differing types of IBS in Group 1 (n = 1002)

<table>
<thead>
<tr>
<th>Subtype of IBS</th>
<th>Number of Patients</th>
<th>Prevalence (%)</th>
<th>Sex (F:M)</th>
<th>Mean Age</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBS-D</td>
<td>14</td>
<td>1.4</td>
<td>7:7</td>
<td>32</td>
<td>18</td>
</tr>
<tr>
<td>IBS-C</td>
<td>7</td>
<td>0.7</td>
<td>6:1</td>
<td>45</td>
<td>21</td>
</tr>
<tr>
<td>IBS-M</td>
<td>27</td>
<td>2.7</td>
<td>24:3</td>
<td>32</td>
<td>15</td>
</tr>
<tr>
<td>Unspecified IBS</td>
<td>12</td>
<td>1.2</td>
<td>11:1</td>
<td>25</td>
<td>7</td>
</tr>
</tbody>
</table>


REFERENCE
1. Gastro. 2011. Supported by Ironwood Pharmaceuticals Inc and by Forest Laboratories Inc. Medical writing assistance was provided by Complete Medical Communications, funded by Almirall.

PTU-136 MECHANISM OF ACTION FOR LINACLOTIDE-INDUCED ABDOMINAL PAIN RELIEF
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Introduction Cyclic GMP (cGMP) is a 2nd messenger produced in intestinal epithelial cells in response to guanylyl cyclase C receptor (GCC) activation. Linaclotide (LIN), an investigational GCC agonist (GCCA), improved constipation and reduced abdominal pain in patients with irritable bowel syndrome with constipation (IBS-C) in clinical trials. We have shown that exogenous extracellular cGMP has contrasting effects on colorectal (CR) afferent mechanosensitivity.1 Here we assessed the effects of GCCAs on CR afferent mechanosensitivity in healthy and chronic visceral hypersensitivity (CVH) mouse models.

Methods We investigated CVH in healthy mice and CVH 28 days post -TNBS administration, when inflammation had resolved and nociceptors were mechanically hypersensitive. Mechanosensory responses of CR splanchnic nociceptors and pelvic mucosal afferents were compared in vitro ± GCCAs STc (3, 50, 250, 1000nM) and LIN (1, 50, 100, 300, 1000nM), which were applied individually to the CR mucosal surface. GCC expression in the CR mucosa was determined via qRT-PCR.

Results In healthy mice, STc dose-dependently (50, 250, 1000nM) reduced nociceptor mechanosensitivity (max. effect at 1000nM [n = 10], -38%; p < 0.001). This effect was more potent in CVH, with various doses of STc (1, 50, 250, 1000nM) all significantly reducing mechanosensitivity (max. effect at 1000nM [n = 10], -53%; p < 0.001). In healthy mice, LIN significantly reduced nociceptor mechanosensitivity at doses of 300nM and 1000nM (max. effect at 1000nM [n = 7], -48%; p < 0.01). In CVH this effect was dose-dependent and more potent, with LIN (100, 300, 1000nM) significantly reducing nociceptor mechanosensitivity (max. effect at 1000nM [n = 5], -59%; p < 0.01). By contrast, in pelvic nerves STc increased low-threshold pelvic mucosal afferent mechanosensitivity in healthy mice (n = 7; p < 0.001), an effect completely lost in CVH (n = 7; p > 0.05). qRT-PCR analysis revealed abundant GCC expression in CR mucosa of both healthy and CVH mice.

Conclusion STc and LIN significantly reduced colonic nociceptor mechanosensitivity, with greatest effect in CVH. Although these overall effects mirror those of exogenously applied cGMP, GCCAs are more potent at inhibiting nociceptors. Overall, LIN induced the greatest inhibitory effects on nociceptors, particularly in CVH. Reducing colonic nociceptive input would help to reduce pain, which supports LIN clinical data showing a significant reduction in abdominal pain in humans with IBS-C. Increased mucosal afferent sensitivity may help coordinate defecation.


REFERENCE
1. Gastro. 2011. Supported by Ironwood Pharmaceuticals Inc and by Forest Laboratories Inc. Medical writing assistance was provided by Complete Medical Communications, funded by Almirall.
Conclusion FGIDs accounted for over 40% of a Gastroenterologist’s workload in clinic. Given that some of these conditions have a similar prevalence in the community, the disparity in prevalence among individual FGIDs seen in a Gastroenterology outpatient clinic suggests that General Practitioners are more comfortable dealing with some FGIDs than others.

Disclosure of Interest None Declared

PTU-137 'NUTRIENT SENSING IN THE HUMAN GUT: INVESTIGATION OF THE CO-LOCALIZATION RATE BETWEEN CASR, T1R1 AND GPR43 RECEPTORS WITH SATIETY PEPTIDES IN THE HUMAN ANTRUM, TERMINAL ILEUM AND ASCENDING COLON.'

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Introduction Increasing evidence from animal studies show that apical nutrient sensing receptors, expressed in gut enteroendocrine cells, play a key role in the release of satiety peptides1,2. Early human studies indicate a similar expression pattern of these receptors and role in peptide release3. In this study the anatomical relationship between amino acid sensing (CaSR), carbohydrate sensing (T1R1), and short chain fatty acid sensing (GPR43) receptors and appetite regulating peptides GLP-1, PYY, 5-HT was investigated in human studies.

Methods Healthy full thickness human gut sections were incubated with primary and fluorescent secondary antibodies and they were viewed under the fluoroscopic microscope to investigate co-localization of the CaSR, T1R1 and GPR43 with the GLP1, PYY and 5HT.

Results The co-localization rate between CaSR and PYY, GLP1 and 5HT was 0%, <1% and 43% in the antrum, 20%, 12% and 82% in the ileum and 26%, 14% and 91% in the colon, respectively. Co-localization of T1R1 and GLP1 was observed only in the antrum and the colon. GPR43 was not expressed.

Conclusion CaSR is expressed at protein level and is colocalized with PYY, 5HT and GLP1 in the human antrum, terminal ileum and ascending colon. T1R1 expression at protein level is very limited in the antrum, terminal ileum and ascending colon. T1R1 expression at protein level is very limited in all the tested tissues. GPR43 expression was not observed.

Disclosure of Interest None Declared

REFERENCES

PTU-138 CENTRAL OBESITY AND WAIST BELT CAUSE PARTIAL HIATUS HERNIA AND SHORT SEGMENT ACID REFLUX IN HEALTHY VOLUNTEERS
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Introduction Epidemiology demonstrates an association between obesity, hiatus hernia and acid reflux but mechanism is unclear. We have examined the structure and function of the gastro-oesophageal (GO) junction in healthy subjects with and without obesity and the effects of elevating intra-abdominal pressure with belt.

Methods We recruited 8 subjects with normal (< 94 cm males < 80 cm females) and 8 with increased (> 102 cm males > 88 cm females) waist circumference, matched for age and gender. To allow accurate monitoring of location of the GO junction and its proximal movement during TLOSRs, a magnet (2x1 mm) was endoscopically clipped to the SCJ. Combined assembly of locator probe, high-resolution pH catheter and slimline manometer was passed nasally. After a standard meal, recording seated upright and also of the diaphragm. There was marked proximal migration of the SCJ during TLOSRs with its magnitude being less in obese vs. non-obese, both with and without belt. The effect of belt was assessed by comparing obese vs. non-obese, both with and without belt. The effect of belt in obesity was assessed by comparing belt-on vs. off in obese subjects. All results were in mean (SEM).

Results Location of the SCJ (P = 0.006) and pH step-down (P = 0.01) were displaced proximally in obese vs. non-obese but the diaphragm was not displaced as reflected by peak LOS pressure (pLOS) and pressure inversion point (Pip) (Figure). With belt-on vs. off, there was similarly proximal displacement of SCJ and pH step-down and also of the diaphragm (P = 0.006) and LOS (upper and lower border, P = 0.01 and 0.03 respectively). In obese subjects with belt-on vs. off, there was proximal displacement of SCJ, pH step-down and diaphragm. There was marked proximal migration of SCJ during TLOSRs with its magnitude being less in obese vs. non-obese (4.2 vs. 6.8 cm, P = 0.04) and belt-on vs. off (3.9 vs. 5.5 cm, P = 0.01), consistent with its resting position being already proximally displaced. At traditional site (5 cm above LOS), the mean % time pH < 4 was minimal (0 – 0.5%) in all studied groups, however, acid exposure above the SCJ but below upper border LOS was increased in belt-on vs. off (6.2% vs. 1.6%, P = 0.01) and in obesity with belt-on vs. off (9.7% vs. 3.0%, P = 0.04) but not obese vs. non-obese (P = 0.2).