increase of fecal pellet output (1.5 fold change, p<0.05), of mucosal pro-inflammatory cytokine (IL-1β, TNFa and CXCL-1) mRNA levels and of myeloperoxidase (MPO) activity was found. Colonic permeability also increased (1.5 fold change, p<0.05) while expression of tight junction proteins, occludin and ZO-1, was reduced. In post-TNBS mice, pro-inflammatory cytokine mRNA levels were increased until two weeks after TNBS injection but were restored to control levels at day 28. In contrast, colonic permeability remained higher at day 28 in post-TNBS mice compared with control mice (3 fold change, p<0.05). In both models (WAS at day 10, post-TNBS at day 28), an increased proteasome trypsin-like activity compared with respective control mice was found, while other proteasome activities remained unaffected. Proteasome composition was also modified with an increased ratio of inducible β2 / constitutive β2 subunits (1.5 and 3 fold change in WAS and post-TNBS mice, respectively, both p<0.05) that are responsible of trypsin-like activity. In conclusion, we observed similar alterations of proteasome system with increased trypsin-like activity in both IBS models. Further experiments should be performed to investigate the role of UPS in the occurrence of IBS symptoms.

Su2050

Supernatants of Mucosal Biopsies From Irritable Bowel Syndrome Patients Impair Human Colonic Smooth Muscle Contractility

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Backgrounds: Irritable bowel syndrome (IBS) is a multifactorial disorder characterized by abdominal pain/discomfort and changes in bowel habit. Although changes in intestinal motor function are thought to play an important role in IBS pathogenesis, little is known about smooth muscle contractility in this disorder. Aim of the study was to investigate the effect of IBS mucosal supernatants on human colonic muscle contractility. Methods: Supernatants were obtained from biopsies of 14 IBS patients, 7 constipation- (IBS-C) and 7 diarrhoea-predominant IBS (IBS-D), and 6 healthy volunteers used as controls. Human colonic circular smooth muscle strips and cells, obtained from disease-free surgical specimens, were exposed to control or IBS supernatants. Spontaneous phasic contractions on strips and morpho-functional parameters on cells were evaluated in basal conditions and in response to acetylcholine (Ach). To investigate the possible role of the signalling pathways involved in muscle relaxation, cells exposure was performed in the presence of the cAMP- and/or cGMP-cyclase inhibitors, 2',5'-dideoxyadenosine and LY83583 respectively. Besides, to evaluate the influence of inflammation and oxidative stress, incubation with IBS-supernatants was conducted in the presence of the NFkB inhibitor MG132 (0.1uM) or catalase (1200U/ml). Data are expressed as mean±SE. Results: Control supernatants had no effect on muscle strip and cell contraction. Following exposure to IBS supernatants, in respect to untreated strips, basal tone significantly decreased only in IBS-C (31±15%) whereas Ach-induced contraction significantly decreased both in IBS-C and D (27±13 and 24±13%). In parallel, compared to controls cells, IBS-C and -D supernatants caused a significant cell shortening, with a major effect of IBS-C (19±2 and 16±2% respectively). Conversely, in cells, the inhibition of Ach contraction was more pronounced in IBS-D than IBS-C (37±9 and 17±4%). Dilution of IBS supernatants partially restored the effects on both strips and cells of about 50%. The cellular effects of IBS supernatants were not reverted by inhibition of the cAMP- and cGMP signaling pathways neither by the presence of MG132 or catalase. Finally, a 24 h washout in IBS supernatant-free medium did not restore morphofunctional cell resting parameters. Conclusions: Supernatants obtained from mucosal biopsies of IBS patients concentration-dependently impair human colonic contractility, not involving muscle relaxation, inflammation or oxidative stress. Mediators released from the IBS mucosa might likely affect colonic contractility through a receptor-dependent mechanism.

Su2051

Combined Polyethylene Glycol and Sodium Picosulphate for Disimpaction in Children With Chronic Constipation and Palpable Faecaloma

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Introduction: Polyethylene glycol (PEG) is the gold standard for oral faecal disimpaction. Compliance is a problem as large volumes (1-2L/day) must be taken. Colon cleansing for colonoscopy is achieved by combining PEG and a stimulant. The stimulant sodium picosulphate (SPS) produces disimpaction in 81% of constipated patients and is a liquid easily taken by children. **Aim:** Determine stool output produced by combined PEG and SPS in children with chronic constipation with a palpable faecaloma. **Methods:** Inclusion criteria: 2 year's chronic constipation, ongoing laxatatives, palpable faecaloma confirmed by enlarged stool-filled rectum on x-ray. Children recorded daily diary with laxative dose, defecation frequency, stool volume and consistency (Bristol stool scale, BSS) for wk before & 2 wks treatment. Laxatives dose (based on child's age & stool volume in colon/rectum in x-ray on day 1) was high concentration (4-8 sachets) of Movicol (PEG + electrolytes 14.7g/sachet) on day 1&2. Each sachet was dissolved in 125ml water then equal volume of juice/milk plus 10-20 drops of SPS (Dulcolax SP). Children drank 125-250ml per half hour using a fun approach (MOTIVATE method) and continued on 1 sachet of Movicol plus 10 drops of SPS for 14 days. **Results**: 22 children (12 male, 4-15 yrs, median 8) recruited from tertiary teaching hospital. All had hard stools palpable in rectum (faecaloma) & enlarged rectum in x-ray (rectal:pelvic ratio >0.6). Disimpaction started with high dose of Movicol on day1. Using the MOTIVATE method, children were easily able to drink the large volume of PEG solution & compliance was high. Stool consistency increased from (mean ±SD) BSS 4±2 to 5±1. Stool volume (median) increased from 1.0L/wk pre to 2.3L/wk during the disimpaction week. Subjects produced maximal stool volume on day2, 0.5- 4.0L of stool over day1-4 and ≥250ml of stool/day in the following 10 days, with (mean±SEM) of 4.2±0.6L total stool produced over 14days. Despite producing a large volume of soft stool, 15/22 still had a palpable faecaloma on day8 but faecalomas were smaller than on day1. There was a weak positive relationship between BMI:Movicol dose, Movicol dose:stool output and a moderate relationship between BMI: stool output. This suggests a larger dose was required. **Conclusion:** For disimpaction in children with a palpable faecaloma and rectal enlargement, combined PEG and SPS given at high dose on day 1 and 2 are effective in producing large volumes of stool. The MOTIVATE method provided a fun way to drink the large volume of osmotic and stimulant laxatives. The dosage of PEG and SPS used was effective in removing the faecaloma in 1/3 of children but a higher dose should be tested. The method was well tolerated and with further refinement of dose could provide a method of disimpaction in children with chronic constipation and large solid stools in the rectum.

Su2052

Annual Costs of Care for Pediatric Irritable Bowel Syndrome and Functional Abdominal Pain (Syndrome)

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OBJECTIVES: Irritable bowel syndrome (IBS) and functional abdominal pain (syndrome) (FAP(S)) are common pediatric disorders that can significantly impair quality of life of children and their families. IBS and FAP(S) are thought to impose a large economic burden. However, to date, pediatric data are not available. Aim of this study was to investigate annual medical and non-medical costs of treatment for children with IBS and FAP(S). **METHODS**: Baseline data from children with IBS or FAP(S) who were included in a multicenter trial (NTR2725) in the Netherlands were analyzed. Patients' parents completed a questionnaire with a 4-week recall period concerning the use of health-care resources, travel costs, out-of-pocket expenses, productivity loss of parents and supportive measures at school. Use of abdominal pain related prescription medication was derived from case reports forms. Total annual costs per patient were calculated as the sum of direct and indirect medical and non-medical costs. Costs of initial diagnostic investigations of abdominal pain were not included in the analysis. **RESULTS**: A total of 258 children were included in the analysis, of which 183 (70.9%) were female. Median age was 13.4 years (±5.5). Total annual costs per patient were estimated to be ¤2622. Inpatient and outpatient health care use were the major cost driver, accounting for 22% and 33% of total annual costs, respectively. Furthermore, parental productivity loss accounted for 24% of total annual costs. **CONCLUSIONS**: Pediatric abdominal pain related functional gastrointestinal disorders impose a large economic burden on patients' families and health care systems. Approximately half of the total annual costs of IBS and FAP(S) consists of inpatient and outpatient health care use.

Su2053

Is Cystic Fibrosis Associated With Gastroparesis? A Systematic Review of Observational Studies.

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Introduction: Although cystic fibrosis(CF) is associated with gastrointestinal dysmotility such as gastroesophageal reflux, intestinal pseudoobstruction and constipation, the finding of gastroparesis is not always consistent. Some studies show gastric emptying(GE) delay while others show rapid GE. Our systematic review aims to determine whether CF patients have slower or faster GE compared to healthy controls. Methods: Pubmed, EMBASE, Web of Science, Scopus and abstracts from major gastroenterology and CF meetings in USA and Europe were reviewed. All studies assessing GE in patients with CF were included. Data was extracted recording the following variables: number of patients with CF plus controls, age, sex, presence of diabetes(DM) and pancreatic insufficiency(PI), diagnostic modality, and type of GE measurements. Two authors rated existing studies with the Newcastle-Ottowa Scale (NOS) to assess risk of bias. The diagnosis and prevalence of gastroparesis was analyzed using all available studies. GE times were compared with healthy controls using a random effects model. Subgroup analysis stratified results by method used to measure GE. I^2statistic assessed heterogeneity between studies. Results: 29 studies from 12 different countries met inclusion criteria(17 case-control studies, 12 case series). A total of 833 subjects were included(508 CF, 325 controls). Diagnostic modalities were diverse: Technetium scintigraphy(12), C-Octanoic breath test(7), ultrasound(4), capsule endoscopy(2), and other techniques(4). Using all available studies and their interpretation, 44.7% (176/394) of patients with CF had gastroparesis. With respect to case-control studies, 252 CF patients and 325 controls were included. In the CF group, 54.9% patients were male, 3% had DM and 97.6% had PI (49.8% male, 0% DM and 0% PI in control group). Overall, 7 studies reported slower GE in CF, 4 reported faster GE in CF, and 6 reported no difference. Pooled comparison of 7 studies reporting 1 or 2 hours retention rates(RR1 and RR2) did not showed difference between patients and controls(-0.1(CI -0.7, 0.1) and 0.4(-1.5, 2.4)respectively). *Figure 1*. Results were highly dependent on diagnostic modality. Using RR1 and RR2 measurements, scintigraphy identified more rapid GE in CF. No difference in GE was found when comparing half GE times(T1/2). All studies had small sample sizes(mean 22.5), and had significant methodologic limitations (mean NOS was 4.4). Heterogenity was significant, I^2 ranged from 89 to 94%. Conclusion: Patients with CF may have a higher prevalence of gastroparesis compared to healthy controls. However as a group there was no significant difference between GE in CF patients versus the normal healthy population. Scintigraphy also identified more rapid GE in some CF patients, but more robust studies are needed to further evaluate gastric motility in this population.