JOURNAL WATCH

1. Efficacy of Amitriptyline in Pediatric Functional Abdominal Pain Disorders: A Randomized Placebo-Controlled Trial

Seetharaman J, Poddar U, Yachha SK, Srivastava A, Sen Sarma M. Efficacy of Amitriptyline in Pediatric Functional Abdominal Pain Disorders: A Randomized Placebo-Controlled Trial. J Gastroenterol Hepatol. 2021 Dec 21. doi: 10.1111/jgh.15765. Epub ahead of print. PMID: 34935191.

Functional abdominal pain disorders (FAPD) still remain a challenge for the pediatric gastroenterologists. With a prevalence of 10–13%, it is a major cause of parental anxiety and poor quality of life (QOL) in the affected children. Amitriptyline, a tricyclic antidepressant, has been approved for functional abdominal pain in adults and one previous study in children, though with a small sample size, has shown good efficacy. The present study was done incorporating 194 children from age 6–18 years who were diagnosed with FAPD as per ROME IV criteria. The main aim of this study was to assess the efficacy of amitriptyline in terms of pain relief in children with FAPD. Pain assessment was done using pain score table and a responder was defined as the reduction in pain scores more than 50% of baseline values following drug administration. Study was done in two parts, in the first 4 weeks of base line observation parents/children were advised to enter the pain score table at home during each episode of pain followed by a medication period of 12 weeks after randomization. Amitriptyline was administered once a day in a dose of 10 mg and 25 mg in children with weight less than and more than 35 kg respectively and were followed up for one year. It was observed that the treated group showed a significant reduction in the pain score ($p < 0.001$) after 3 months of treatment as compared to the placebo group. Improvement was seen more in the irritable bowel syndrome group but not in the functional dyspepsia group. No serious adverse effects were observed. The study has limitations in terms of being an opened labelled study where there are possibilities of biases, and that compliance was not assessed in the treated group. The author concluded that low-dose amitriptyline for 12 weeks is effective in sustained pain relief and improving QOL in children with FAPD. However, more multicentric and blinded studies are needed before the validation of this study.

2. Drugs in Focus: Octreotide Use in Children With Gastrointestinal Disorders

Emmanuel Mas, Osvaldo Borrelli, Ilse Broekaert, J. Martin De-Carpi, Jernej Dolinsek, et al. Drugs in Focus: Octreotide Use in Children With Gastrointestinal Disorders. Journal of Pediatric Gastroenterology and Nutrition, Lippincott, Williams & Wilkins, 2021, 74 (1), pp.1–6.

Somatostatin, also known as growth hormone inhibiting hormone, has strong regulatory effects on various systems of the body. It inhibits gastrointestinal (GI), pancreatic, pituitary secretions. Octreotide the synthetic agonist of somatostatin has a longer half-life; has high resistance to degradation as compared to somatostatin and is used in treatment of various GI disorders such as bleeding, chylothorax, chylous ascites, primary intestinal lymphangiectasia, pancreatitis, intestinal dysmotility, and secretory diarrhoea. This paper is the literature search of past 21 years on the usage, mode of delivery and safety of octreotide.

1. Gastrointestinal Bleeding: Octreotide is very effective in controlling variceal as well as non-variceal GI bleed in children. For variceal bleeds it is given as 1–2 μg/kg bolus over 30 minutes followed by maintenance infusion of 2 μg/kg/hour and should be continued for 5 days after cessation of the bleeding. It has also been used as an adjunct to endoscopic therapy in variceal bleed where it is administered in a dose of 2 μg/kg/hour, one hour before the endoscopy and is continued for the next 2–3 days. It should be started in a child with variceal bleed before referral to endoscopic centre. One study reported administration of intramuscular long-acting octreotide in a dose of 2.5–20 mg once a month in children refractory to endoscopic therapy for varices, and a significant reduction in the bleeding episodes were observed.
2. Chylothorax and Chylous Ascites: Intravenous infusion of octreotide in a dose of 2–10 μg/kg/hour showed improvement in congenital as well as post cardiac surgery chylothorax and chylous ascites in
3. Primary Intestinal Lymphangiectasia: Octreotide can be used if the standard treatment with low fat diet with medium chain triglyceride and albumin infusion is not improving the ascites.
4. Pancreatitis: Octreotide decreases the pancreatic secretions, so it has been used in pancreatitis complicated by pseudocyst and ascites. In few studies, doses as high as 50 μg/hour have been more effective than the lower doses especially in predicted severe pancreatitis and for the prevention of acute pancreatitis following endoscopic retrograde cholangio-pancreatography.
5. Intractable secretory diarrhea: Octreotide has anti-diarrhoeal action which can be attributed to inhibition of GI motility, exocrine digestive secretions, and intestinal absorption. It has been found beneficial in intractable diarrhea due to epithelial dysplasia, diarrhea in short gut syndrome secondary to necrotising enterocolitis and chemotherapy induced diarrhea. In the first two conditions higher doses as 20 μg/kg/day three times daily and 4 μg/kg/day twice daily subcutaneously for 420 and 240 days, respectively was found to be effective.
6. Intestinal motility: In adult studies, octreotide has been found to stimulate intestinal motility in normal and in scleroderma patients. In children the efficacy of octreotide in improving intestinal dysmotility has been observed in some studies. However, it has not been proven to be beneficial in improving the colonic motility in chronic constipation.

3. Presentation and Outcomes of Infants With Idiopathic Cholestasis: A Multicenter Prospective Study

Hertel PM, Hawthorne K, Kim S, Finegold MJ, et al. Childhood Liver Disease Research Network (ChiLDReN). Presentation and Outcomes of Infants With Idiopathic Cholestasis: A Multicenter Prospective Study. J Pediatr Gastroenterol Nutr. 2021 Oct 1; 73(4):478–484. doi: 10.1097/MPG.0000000000003248. PMID: 34310436; PMCID: PMC8448404.

Idiopathic cholestasis (IC) in infants is the term assigned when the etiology of the cholestasis is not known and most of the times it resolves spontaneously. This paper describes the features of IC analysed in a multicentric, prospective longitudinal study of infants presenting with neonatal cholestasis at 15 clinical sites in the United States and Canada over an 11-year period. The outcome was classified as: complete resolution with total bilirubin (TB) <1 mg/dL and ALT <35 U/L within 2 years; partial resolution normalisation of TB but alanine aminotransferase (ALT) remained >35 U/L and third, 'exited healthy group' where complete biochemical resolution was not observed but clinically resolution of disease was declared. A total of 94 children were evaluated, youngest being 29 weeks of gestation. Following observations were made:

1. Stool colour: Almost one third of infants in the biochemical group as well as the exited healthy group had white or pale stools, but none in the partial resolution group reported depigmented stools. Thereby concluding that in children in whom biliary atresia has been ruled out, stool colour may not be associated with poor outcome.
2. Serum TB levels: The median TB was 7 mg/dL in all the groups at enrolment, and the level of <1 mg/dL was achieved in median 4.6 months and 5.2 months of age in the biochemical resolution group and partial resolution group respectively.
3. ALT levels: It was lower in the biochemical resolution group (95 U/L) than in other groups. It took a median of 7.6 months for the complete resolution group to reach ALT <35 U/L whereas it remained high in the partial resolution group until 2 years.
4. Gamma-glutamyl transferase (GGT) levels: Median baseline GGT remained lower in the biochemical resolution group (127 U/L). It went down to <100 U/L in the complete resolution group by 2 years.
5. Overall outcome: They had very good prognosis with 98% survival with native liver by 30 months of age.

4. Safety of Lubiprostone in Pediatric Patients With Functional Constipation: A Nonrandomized, Open-Label Trial

Hussain SZ, Labrum B, Mareya S, Stripling S, Clifford R. Safety of Lubiprostone in Pediatric Patients With Functional Constipation: A Nonrandomized, Open-Label Trial. J Pediatr Gastroenterol Nutr. 2021 Nov 1;73(5):572–578. doi: 10.1097/MPG.0000000000003280. PMID: 34387619; PMCID: PMC8528133.

Pediatric functional constipation (PFC) accounts for 95% of childhood constipation and still remains a challenge for pediatric gastroenterologist. Polyethylene glycol is the first line drug for PFC but recently few gastrointestinal and neuropsychiatric side effects have been reported with PEG. Lubiprostone, a locally acting chloride channel activator acts by promoting fluid secretion into the small bowel thereby accelerating colonic transit without altering serum electrolyte concentrations. It has been proven to be safe and effective in adult patients for constipation. This study was conducted with an aim to investigate the safety of lubiprostone in children and adolescents with PFC. This was a phase 3 multicentric trial in 87 children from 6–18 years of age who were diagnosed with PFC. Lubiprostone capsules in a dose of 12 and 24 mcg twice daily was administered in children with weight less than and more than 50 kg respectively, for 24 weeks. Few mild treatment related adverse effects were reported such as diarrhea, nausea, abdominal pain, and upper abdominal pain, dyspepsia, chest pain, headache etc. Adverse effects leading to the discontinuation of the drug were mainly gastrointestinal related predominantly abdominal pain, and were mild in intensity which resolved after discontinuation of the drug. The authors concluded that lubiprostone was very well tolerated in the pediatric population.

Compiled by **Dr Rimjhim Shrivastava**