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Pediatric Biliary Dyskinesia and Sphincter of Oddi Dysfunction



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Biliary dyskinesia is a gall bladder disorder in the setting of a normal biliary tree. Adult gastroenterologists consider it a functional disorder, but this is not the case in pediatrics, as it is amongst the most common reasons for laparoscopic cholecystectomies. Sphincter of Oddi dysfunction is a motility disorder in the contraction of the sphincter leading to obstruction of the bile or pancreatic juice.¹ New research has opened the door for Type 3 sphincter of Oddi dysfunction to be considered as a functional disorder in adult gastroenterology. Pediatric gastroenterologists should follow the lead of our adult colleagues and consider the reclassification of biliary dyskinesia and sphincter of Oddi dysfunction type 3 as functional disorders.

INTRODUCTION

Pediatric Biliary Dyskinesia

Biliary Dyskinesia (BD) is a gall bladder disorder in the setting of an anatomically normal biliary tree. The clinical manifestations include episodic colicky right upper quadrant pain or epigastric pain triggered by food, associated with nausea and vomiting in the absence of cholelithiasis. The pain is thought to be caused by contraction of the sphincter of Oddi at the

time of gall bladder relaxation. The most commonly affected tend to be female patients and/or overweight patients.^{2,3}

Pediatrics often takes its cues from the adult world in terms of diagnosis and treatments so as to mitigate any potential risks for our society's most vulnerable citizens. Biliary dyskinesia (BD) is an example of a disorder first described in adults and treated operatively with subsequent practice adoption in pediatrics.⁴ BD is considered a functional disorder according to Rome III,⁵ but it is not recognized as a childhood functional disorder.⁶ Despite BD being classified as an adult functional disorder, laparoscopic cholecystectomy has been relied on as the final therapeutic solution.⁷

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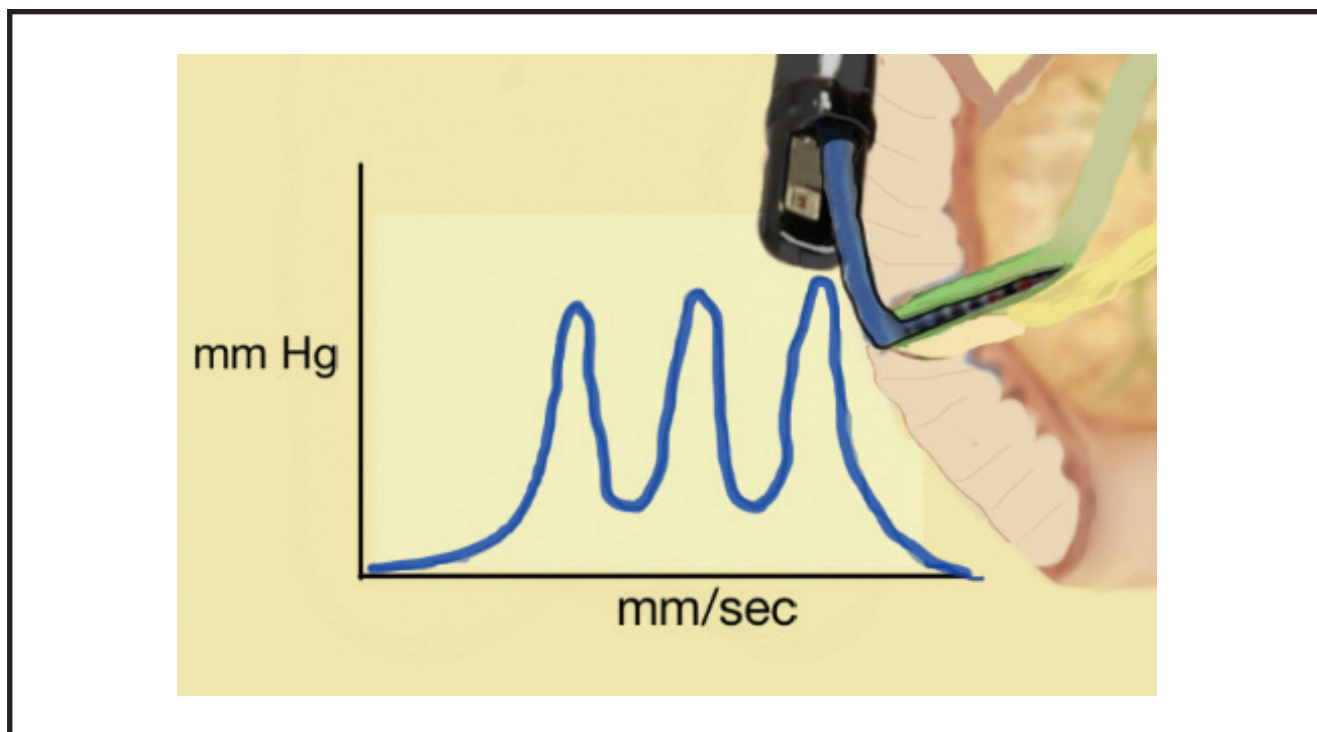


Figure 1. A duodenoscope is shown cannulating the sphincter of Oddi with a pressure sensing catheter for manometry. The catheter is within the common bile duct and a schematic representation demonstrates the pressure tracing. Note there is a baseline tonic sphincter pressure and in addition there are superimposed phasic contractions that can be appreciated.

Diagnostically, a Hepatobiliary Iminodiacetic Acid (HIDA) scan along with an injection of cholecystikinin (CCK) is used to assess gall bladder function by evaluating bile excretion, accumulation, and ejection from the gall bladder. Gallbladder emptying less than 35% along with typical symptoms established by the Rome III Criteria establish the diagnosis of BD.⁵ One study found problems with solely using a HIDA scan to make a diagnosis of BD. Some children who had abnormal ejection fractions on their first scans, later had normal ejection fractions.⁸ Caution must be taken regarding opiate pain medication in the background at the time of the abnormal HIDA scan. This is one example of the problems encountered with extrapolating adult data to fit the needs of pediatric patients. The clinical response to cholecystectomy is subsequently used to confirm the diagnosis of BD if there is no recurrence of pain for 12 months.⁵ HIDA scans and Ejection Fractions should be considered as only one aspect in the decision making process.

The diagnosis of BD has been on the rise and this is seen in the steady rise of laparoscopic cholecystectomy. Mehta et al. describe the trend of cholecystectomies at

one of the countries largest children's hospitals in which from the years 1980-1996, there were no documented cases of BD, but from the years 2005-2008, there were 64 cases, making it the third most common indication for a cholecystectomy, behind complicated obstructive disease, and symptomatic cholelithiasis.²

Their study, much like those of others, demonstrated that histologically, the gall bladder had features of chronic cholecystitis.⁸⁻¹⁰ Friesen et al. demonstrated that patients with BD had an increase in mast cell density, which parallels other functional disorders.⁸ When comparing the differences between patients who underwent a cholecystectomy secondary to stones vs. BD, patients with BD had more mast cells in the lamina propria. Mast cell degranulation and the high levels of mast cells within the lamina propria, however, did not correlate with the ejection fraction.

What has been lacking in BD research is randomized control trials with larger groups for analysis. The research data for the diagnosis and treatment is based on retrospective studies with small number sizes. Time of response to surgery has also been limited and mostly to only a few months after surgery. Few studies have

Table 1. Pediatric Functional Disorders

Infant/Toddler		Child/Adolescent	
Vomiting and Aerophagia		Abdominal Pain-Related Functional GI Disorders	Constipation and Incontinence
Infant Regurgitation	Adolescent Rumination Syndrome	Functional Dyspepsia	Functional Constipation
Infant Rumination Syndrome	Cyclic Vomiting Syndrome	Irritable Bowel Syndrome	Non-retentive Fecal Incontinence
Cyclic Vomiting Syndrome	Aerophagia	Abdominal Migraine	
Infant Colic		Childhood Functional Abdominal Pain	
Functional Diarrhea		Childhood Functional Abdominal Pain Syndrome	
Infant Dyschezia			
Functional Constipation			

looked into long-term follow-up. One such study looked at 2.8 years after surgery³ and demonstrated that 44% of their cohort was symptom free after laposcopic cholecystectomy. Nelson, et al., evaluated 55 patients and compared cholecystectomy to children who did not undergo surgery, but instead were observed in the setting of BD.⁸ At the two-year follow up, 55% of the cholecystectomy group had complete resolution of pain and 55% of the observation group also had complete resolution of pain. Twenty-six percent of the cholecystectomy group and 20% of the observation group had partial resolution of pain. Two years after the original two-year follow-up, there were no differences in the rate of response to pain. This study used long term data to suggest that a non-operative approach may be just as effective as an operative one, which is consistent with the long-term outcome of functional disorders.

The relationship between pediatric functional disorders and gall bladder disease was explored by Chumpitazi et al.¹¹ They found that children with BD may also have concomitant gastroparesis, suggesting a neuroenteric abnormality affecting both biliary and gastric motility. Srinath et al. argue that BD is a safe diagnosis in children in that there are minimal associated complications. This should emphasize, according to them, the need to explore therapies used in treating BD as a functional disorder and there should be less reliance on the surgical routes of care for this disorder where there are complications from such interventions.¹²

Currently, there are no established biliary functional disorders in pediatrics (Table 1).¹³ More research for conservative management has begun to set the stage for Biliary Dyskinesia in Pediatrics to be managed like other functional disorders in Pediatrics—conservatively, medically, perhaps with combination therapy involving psychological aspects to treatment.¹²

Pediatric Sphincter of Oddi Dysfunction

The sphincter of oddi (SO) is located at the duodenal junction of the biliary and pancreatic ducts.⁵ Sphincter of oddi dysfunction (SOD) is a motility disorder manifested as an abnormality in the contraction of the sphincter of oddi (SO)¹⁴ that leads to an obstruction of bile or pancreatic juice.¹ Patients typically have biliary obstructive pain not relieved with cholecystectomy. There are three distinct types of SOD. Type 1 consists of patients with a dilated bile duct and abnormal liver labs. Type 2 consists of patients who have either a dilated bile duct or abnormal liver labs, but not both. Type 3 have neither a dilated duct nor abnormal labs.¹⁵

SOD can present with symptoms that include epigastric pain or right upper quadrant pain that radiates to the back or right shoulder in episodic fashion. It can present as idiopathic pancreatitis, biliary type pain with an intact gallbladder and no gallstone, and present after a cholecystectomy. In addition, SOD has been studied as a possible cause of recurrent abdominal pain

(continued on page 62)

(continued from page 60)

in children.¹⁶ Currently in the adult literature, SOD is regarded as a functional disorder,⁵ but not so in the pediatric literature.⁶ There is limited data in pediatrics in regards to the number of studies performed. All studies are retrospective chart reviews and the number of patients is small. Brown et al. and Lemmel et al. found 3 of 38 children and 7 of 29 children with SOD as the cause of recurrent pancreatitis, respectively.^{17,18} Varadarajulu et al. evaluated 6 patients, three type II, and three type III over a three year time period.¹ Cheng et al. as a part of a large ERCP series evaluated, six patients with SOD type II, 35 patients with SOD type III over a ten-year period. Chronic abdominal pain and recurrent pancreatitis were the two most common presentations. Post ERCP rates of pancreatitis in these patients ranged from 21-30%.¹⁹ Misra et al. performed a retrospective chart review with telephone follow up.¹⁶ Twelve patients, 9 of which had SOD Type III, underwent SO manometry and sphincterotomy for treatment. Of the twelve patients, three did not respond. Seven patients at the five-year follow up continued to be asymptomatic. Phone follow up, however, did not include a standardized pain scale assessment.

Sphincter of Oddi Dysfunction is first suspected with the above mentioned clinical presentation. To confirm the diagnosis, the ampulla of Vater is cannulated with an endoscopic retrograde cholangiopancreatography (ERCP). Sphincter of Oddi manometry is then performed with a low compliance infusion pump system (Figure 1). Basal sphincter of Oddi manometry pressure greater than 40 mm Hg or greater are considered abnormal and based on adult data.¹⁹ Treatment of the SOD consists of a sphincterotomy that is preformed on the biliary and/or pancreatic sphincter, depending on which one is above the adult based normal value. There are no pediatric manometrical based pressure values and therefore, adult values are used. Adult data demonstrates that SOD II is more likely to have manometric demonstrable SOD 55% of the time vs. 28 % of the time in SOD III.²⁰ These procedures are not without risk. Post ERCP pancreatitis rates in pediatrics has occurred in up to 13% of cases.²¹

Recently, Cotton et al. performed the first multicenter, sham-controlled, randomized control trial with a large patient volume involving 214 patients.¹⁵ The results of this study have shifted the dynamic of SOD III. Cotton et al. demonstrated that sphincterotomy was not more effective than a sham ERCP in post cholecystectomy patients with SOD type III.¹⁵ Furthermore, manometrical

findings, biliary or pancreatic pressures, were not associated with sphincterotomy outcomes. Given these results, treatment with sphincterotomy for patients with SOD III should be called into question because it was demonstrated that sphincterotomy, which is not without risk, is a procedure no better than placebo.

This recently published trial is being interpreted by adult gastroenterologists as moving SOD into a functional bowel disorder category such as irritable bowel syndrome. Hence, the stage invites SOD III in children to be considered a functional disease with therapy that at the very least should no longer involve an invasive approach. Further studies are needed to determine the pathophysiology of pain and a medical route of therapy. Like other pediatric functional disorders, and much like what is suggested for the treatment of biliary dyskinesia, a therapeutic combination that includes a non-invasive approach should be considered in the management of this disease. This combination of treatment should include psychological techniques to deal with anxiety and visceral sensitivity that are so often a part of pediatric functional abdominal pain.²² In the future we speculate that brain-gut modifying agents may be worthy of treatment trials, e.g. Tricyclics. In addition, treatment with cholinergic therapy addressing colon motility will have a role.

Diet could also be considered another form of therapy. There already is precedence for this kind of therapy in irritable bowel syndrome (IBS) with the FODMAPS diet. Much like the role of the intestinal microflora in IBS, perhaps it is also playing a role in SOD. Changing the intestinal microflora is one of many treatment possibilities for a disease whose current treatment should be further explored. ■

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19	E	I		20	E		21	L	E		22	I	T	E	M	23
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