Biliary Dyskinesia in Pediatrics

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Biliary dyskinesia is a potential cause for acalculous biliary colic in pediatric patients. A triad of symptoms and signs, consisting of abdominal pain (with or without associated nausea or fatty food intolerance), absence of gallstones, and an abnormally low cholecystokinin-stimulated gallbladder ejection fraction is used to diagnose the disorder. In several small pediatric case series, cholecystectomy resulted in symptomatic improvement in a majority of patients with biliary dyskinesia. However, the diagnosis of biliary dyskinesia and appropriate management remain controversial. This review discusses the purported pathophysiology of biliary dyskinesia and the data available regarding diagnosis and treatment of this entity in the pediatric population.

Introduction
Biliary dyskinesia is defined as a disorder of the gallbladder and biliary tract that presents with abdominal pain, without sonographically apparent gallstones, and with an abnormal cholecystokinin (CCK)-stimulated gallbladder ejection fraction with a lack of any other clear cause for symptoms [1•]. The descriptive nature of the definition makes it difficult to compare the available studies. Currently there are no universally accepted clinical findings that serve as an indication for scintigraphic studies of the gallbladder. The protocols used when performing pediatric CCK-stimulated gallbladder ejection studies are also variable, and the reference range for gallbladder emptying is poorly defined in pediatric patients. Thus, there is little consensus regarding the criteria for diagnosis of biliary dyskinesia in pediatric patients [1•,2•−5•,6,7].

Physiologic Regulation of Bile Duct Motility
Cholecystokinin is the principal factor controlling postprandial gallbladder contraction, but several other hormones, including VIP (vasoactive intestinal peptide), somatostatin, and substance P, influence gallbladder motility or modulate the effect of CCK. In physiologic doses CCK causes gallbladder contraction and relaxation of the sphincter of Oddi; however, administration of high-dose CCK can cause paradoxical contraction of the sphincter of Oddi. This effect can lead to false-positive results in gallbladder ejection fraction studies [8•]. Because the infusion doses to achieve physiologic concentrations of CCK in children are not well established at different ages and weights, this paradoxical response to CCK may be more problematic in pediatric patients.

Pathophysiology of Biliary Dyskinesia
Biliary dyskinesia is hypothesized to result from partial cystic duct obstruction with pain occurring from exaggerated gallbladder contractions that are required to overcome the obstruction. Various explanations for the cystic duct obstruction have been suggested, including chronic inflammation causing stenosis of the cystic duct [9] and spasm of the cystic duct or gallbladder neck occurring at the time of contraction of the fundus of the gallbladder [8•]. Similar clinical presentation can occur with spasm of Oddi dysfunction because this may also impede bile flow [10].

Abnormal biliary motility may be a primary disorder in which impairment of the motility of the bile ducts results from the process intrinsic to the bile duct muscle or can be secondary to a variety of other disorders. These disorders should be taken into consideration during the diagnostic workup of possible biliary dyskinesia (Table 1) [8•]. Primary dyskinesia may result from decreased gallbladder activity due to chronic acalculous cholecystitis or from a deficiency of CCK receptors [11]. Dyscoordinated gallbladder or cystic duct contractions could also impair gallbladder emptying into the common bile duct.

In adults, scintigraphic protocols have been used to differentiate between cystic duct malfunction and sphincter of Oddi dysfunction. The utility of these protocols has not been tested in pediatric patients [12].

Other disorders may alter gallbladder emptying, including celiac disease, parenteral nutrition, starvation, elevations in VIP or somatostatin, and diabetes mellitus [8•]. The effect of stress on gallbladder emptying is not well studied, but stress is known to alter gastric emptying [13]. Stress may have a significant impact upon mea-
Table 1. Classification of biliary motility disorders

<table>
<thead>
<tr>
<th>Primary dyskinesia</th>
<th>Secondary forms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased gallbladder contractility</td>
<td>Celiac disease</td>
</tr>
<tr>
<td>Chronic acalculous cholecystitis</td>
<td>Parenteral nutrition</td>
</tr>
<tr>
<td>CCK receptor deficiency</td>
<td>Starvation</td>
</tr>
<tr>
<td>Dyscoordinated gallbladder/cystic duct contractility</td>
<td>Billroth II gastric resection</td>
</tr>
<tr>
<td>Cystic duct syndrome</td>
<td>VIP-oma, somatostatinoma</td>
</tr>
<tr>
<td>Sphincter of Oddi dysfunction</td>
<td>Administration of octreotide or somatoctatin</td>
</tr>
<tr>
<td></td>
<td>Diabetes mellitus</td>
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</tbody>
</table>

CCK—cholecystokinin; VIP—vasoactive intestinal peptide. Adapted from Lonovics et al. [8•].

measurement of gallbladder emptying in children, in whom testing can promote substantial stress.

Clinical Presentation

No good data are available on the prevalence of biliary dyskinesia in childhood. More importantly, we have no data on the likelihood of a particular symptom or symptom pattern predicting disorders of gallbladder motility in children. It is much more difficult to obtain accurate symptom descriptions in children than in adults. Biliary dyskinesia classically presents with chronic right upper quadrant abdominal pain, vomiting, nausea, or fatty-food intolerance. However, in the case series reported in children the pain described by patients is often poorly localized [1,2•–5•]. This common, relatively nonspecific symptom is the most frequent indication cited for evaluation of possible biliary dyskinesia, but the presentation overlaps with other more common pediatric disorders, including functional abdominal pain [14].

There are no good data on the prevalence of biliary dyskinesia in childhood. More importantly, we have no data on the likelihood of a particular symptom or symptom pattern predicting disorders of gallbladder motility in children. It is much more difficult to obtain accurate symptom descriptions in children than in adults, with vague poorly localized pain occurring in common disorders such as esophagitis [15], gastritis, eosinophilic gastroenteritis, peptic ulcer disease, and celiac disease [14], which further complicates diagnosis. Most of these more common disorders need to be considered before children undergo scintigraphic studies for possible biliary dyskinesia.

No epidemiologic studies describing symptoms and natural history of the biliary motility disorders in pediatric patients have been published to date. Because disorders of biliary motility in children are thought to be rare, frequent screening for biliary dyskinesia based upon poorly defined symptoms that are present in other common pediatric disorders may result in a high rate of false-positive results and unnecessary cholecystectomy being performed in children. The six published pediatric case series (Tables 2 and 3) give some useful insight into clinical presentation of biliary dyskinesia in pediatric patients, but these reports should be interpreted with caution because all the studies come from tertiary care institutions and are subject to significant referral bias. Data were not reported for all symptoms in all case series.

Diagnostic Evaluation

No established paradigm is available for cost-effective workup of pediatric patients with suspected biliary pain. Based on history and clinical examination it may be difficult to differentiate among biliary pain, dyspeptic pain, or functional pain in children. As detailed previously, symptoms of right upper quadrant pain or fatty-food intolerance, which are considered suggestive of biliary pain, are not universally present in pediatric patients diagnosed with biliary dyskinesia. Diffuse or poorly localized abdominal pain is common in other disorders. Therefore, more common disorders must be ruled out prior to consideration of biliary dyskinesia as a likely diagnosis. Laboratory workup should include complete blood counts, liver function tests, amylase, lipase, urea nitrogen, electrolytes, and urinalysis. Radiologic studies must include an abdominal ultrasound to rule out gallstones or other structural disorders of the gallbladder and biliary tract and an upper gastrointestinal study to rule out disorders such as intestinal malrotation, which can present with similar symptoms. In patients with less specific symptoms that overlap with dyspepsia, a trial of proton pump inhibitors and/or upper endoscopy with biopsy is usually indicated. Other causes of right upper quadrant pain should also be considered [14]. Painful rib syndrome is characterized by pain in the upper abdomen or lower chest, a tender spot on the costal margin, and reproduction of pain with pressure on the tender spot or trigger point [16]. Pneumonia, pleurisy, shingles, muscle strains, congenital or incisional hernias, persistent omphalomesenteric duct, intestinal duplications, chronic appendicitis or Meckel’s diverticulum, and urinary tract abnormalities may all present with localized upper abdominal pain.

If gallbladder ultrasound does not reveal stones and other causes of pain are not identified, the diagnosis of biliary dyskinesia is entirely dependent upon CCK-