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Available Online: <http://jceg.edwiserinternational.com>***Biliary Dyskinesia: An Overlooked Disorder****Heather Elmore¹, Dina Avery¹, Floyd Josephat¹, Joe Garner¹, Kathy Nugent¹ and M. Tino Unlap^{2*}*¹Department of Clinical and Diagnostic Sciences, University of Alabama at Birmingham, USA²Department of Clinical and Diagnostic Sciences and Biochemistry and Molecular Genetics, University of Alabama at Birmingham, USA

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Abstract

Biliary Dyskinesia (BD) is a disorder of the gallbladder that is characterized by inflammation, abnormal contraction and emptying of the gallbladder, and failure of proper movement of the Sphincter of Oddi, which results in reduced emptying of the gallbladder. Symptoms include nausea, vomiting, upper right quadrant pain, and lower abdominal cramping. Because these symptoms are common among a number of disorders, proper diagnosis is difficult, and diagnosis becomes even more difficult since the two diagnostic tests that can detect BD can only be administered upon a physician's suspicion.

Methods: *Therefore, this study was conducted to survey BD sufferers in order to identify common symptoms, age of onset, and efficacy of treatment. The survey was administered in person and respondents were informed that the results would be compiled, analysed and submitted for publication.*

Results: *Our study showed that the average age of onset is 15 and that patients suffered an average of 4 years before a proper diagnosis was rendered. BD sufferers shared common symptoms which consisted of nausea, lower abdominal cramping, upper quadrant pain, loss of appetite, bloating, and extreme pain after eating. BD was often misdiagnosed or overlooked, and the only test that provided the correct diagnosis in each case was the CCK-HIDA test. The most common prescribed treatment was cholecystectomy and it only provided partial relief.*

Conclusion: *Thus, a teenager that complains about nausea, lower abdominal cramping, upper quadrant pain, loss of appetite, bloating and extreme pain after eating should first be tested with the CCK-HIDA test in order to rule out BD and to avoid years of needless pain.*

Keywords: *Biliary dyskinesia; Cholecystectomy; CCK-HIDA; Gallbladder; Sphincter of Oddi; Nausea; Bloating*

Introduction

The gallbladder serves a critical role in the digestion of fats in the digestive system. This is accomplished by releasing bile salts which combine with triglycerides to form complexes which are soluble in the aqueous environment of the gastrointestinal tract, thus making them accessible to lipases in the small intestine.

Digestion of triglycerides by lipases is necessary for the fatty acids and glycerol components to be absorbed into the brush border cells of the intestinal wall. In addition to making fats accessible to lipases, bile salts also increase the absorption of fat-soluble molecules like vitamins A, D, E and K by the brush border cells of the

intestinal wall. Therefore, bile salts are critical for the absorption of fats and fat-soluble molecules [1,2].

Biliary dyskinesia is a general description that is given to a disorder of the gallbladder that does not involve gallstones but consists of inflammation, reduced contraction, and abnormal emptying of the gall bladder [2-4]. Biliary dyskinesia symptoms consist of chronic upper right quadrant abdominal pain, nausea, cramping after eating, bloating, and loss of appetite [3]. Diagnosis can be extremely difficult since the symptoms are common among many disorders. Diagnosis is by CCK-HIDA (cholecystokinin-hepatoiminodiacetic acid) test [2] and hepatobiliary function scintigraphy (HBFS) [5] which demonstrate whether the gallbladder is filling, contracting, and emptying normally. These two tests must be requested specifically and upon suspicion of the physician that the disorder might be biliary dyskinesia.

Treatment is by cholecystectomy [6-8], the most common surgery in North America, and can be done by minimal invasion via laparoscopy or by the normal open method. Studies demonstrate that while cholecystectomy provides total relief in over 90% of people with gallstones, this surgery provides only partial relief from the symptoms of biliary dyskinesia in majority of the patients [6].

Because BD is often mis-diagnosed, and the present treatment paradigm is not very efficient, this study was conducted in order to determine if BD has unique features that can be exploited in diagnostic tests, which can then lead to proper treatments for this debilitating disorder.

Methods

Survey Form

A survey form was generated to assess a number of parameters that would allow the testing of the hypothesis that BD has unique features that can be exploited in diagnostic tests that can lead to proper treatments for this debilitating disorder. This survey included the following inclusion criteria: male or female, 13 years or older, suffers from undiagnosed gall bladder pain for a number of years before being diagnosed and treated properly.

Age of onset: Sufferers of non-gallstone related gallbladder problems often experience problems as they enter their teens. Including the age of onset in the survey enabled us to determine if BD begins at a certain age.

Age of diagnosis: Sufferers of BD often go years without a proper diagnosis. This parameter allowed us

to determine, on average, how long a sufferer goes without receiving the correct diagnosis.

Sex: Most sufferers of gallbladder problems that are not gallstone related are females. This survey tested if BD predominantly occurs in females than males.

Symptoms: Sufferers of BD have many of the same symptoms. Comparing the symptoms among all the respondents allowed us to determine if there are common symptoms that are shared among sufferers of BD.

Other diagnoses before receiving the proper diagnosis: Once a teenager complains about abdominal pain, nausea, bloating and panic attacks, a physician often prescribes a number of tests in order to arrive at a diagnosis for the underlying problem. Using the wrong test often leads to wrong diagnoses. Having this on the survey allowed us to determine what some of the wrong diagnoses are.

Tests performed: Many sufferers with BD will undergo many diagnostic tests that may or may not help in finding the proper diagnosis. Including this question on the survey allowed us to determine all the tests performed and compared them with what test or tests that were responsible for obtaining the proper diagnosis.

Test that diagnosed BD: Sufferers with BD are usually diagnosed using the same tests. Including this on the survey enabled us to determine what those tests are.

Treatment: Patients diagnosed with BD usually undergo cholecystectomy. This allowed us to determine if this is the only treatment available or if other treatments exist for BD.

Efficacy of treatment: Most patients that received a cholecystectomy still experience symptoms of BD. Including the efficacy of treatment allowed us to assess if cholecystectomy resolved the symptoms of BD.

Administration of Survey

The seven subjects were interviewed in person. Prior to the administration of the survey, each subject was informed that the survey was strictly voluntary and that they had every right to terminate the survey at any time. In addition, the subjects were given a consent form detailing the purpose of the survey and the manner in which the data would be used.

Selection of Survey Subjects

Only those who had been diagnosed with BD or who had complained of symptoms characteristic of BD were

chosen to participate in the survey. Respondents were friends, family members and neighbours.

Analysis of Survey

The results of the survey were tabulated and analysed for significance using one-way Analysis of Variance (ANOVA).

Results

Survey

Our survey showed some very interesting common parameters among all the respondents:

Age of onset: Symptoms for BD first appeared during the early teen years and continued even after cholecystectomy.

Age of diagnosis: In some respondents, diagnosis was rendered immediately after the onset of symptoms. In some, however, diagnosis was not rendered until years later.

Sex: All of the respondents, who suffered from BD were females.

Symptoms: Sufferers of BD shared symptoms which included nausea, lower abdominal cramping, upper quadrant pain, loss of appetite, bloating and extreme pain after eating.

Other diagnoses before receiving the proper diagnosis: Although physicians are often suspicious when encountered with BD symptoms which often leads them to ascribe symptoms to other diseases, none of the seven respondents were diagnosed with other diseases.

Tests Performed: A number of tests were prescribed in response to the onset of symptoms which included blood tests, ultrasound, colonoscopy, and CCK-HIDA.

Test that diagnosed BD: In every case where BD was correctly diagnosed, the CCK-HIDA test was used.

Treatment: The treatment paradigm was surgical removal of the gallbladder.

Efficacy of treatment: Surgical removal of the gallbladder attenuated the symptoms but did not completely abrogate the symptoms.

Administration of Survey

The method by which the surveys were administered, in person, was very efficient and reliable and required little effort, manpower and cost.

Selection of Participants

Selection of the participants was strictly random and was based on whether or not individuals have had gallbladder related problems.

Discussion

Biliary dyskinesia is attributed to abnormal emptying of the gall bladder. In majority of individuals diagnosed with biliary dyskinesia, the ejection fraction is significantly less than 50% [9-12]. Studies also showed that a small number of individuals suffering from biliary dyskinesia demonstrated ejection fraction that was greater than 50% [9-12]. It was difficult to determine the ejection fraction for each of the respondents since none of them had their test records with them during the interviews. However, it was not difficult to imagine that majority of them probably had ejection fractions that were significantly less than 50%.

Studies also showed that biliary dyskinesia patients that demonstrated ejection fractions less than 50% had a greater than 90% prognosis to have their symptoms reduced significantly after cholecystectomy [9-12], the most often prescribed treatment for biliary dyskinesia. Six of the seven survey respondents showed that the symptoms that were extremely severe prior to surgery were significantly attenuated after gallbladder surgery (Tables 1-8).

Table 1: Survey is of a 16-year old female patient who complained of gallbladder-related problems with symptoms which consisted of burning pain in stomach, loss of appetite and nausea after eating. The patient was administered the HIDA scan and blood tests prior to the prescription of cholecystectomy for treatment. The HIDA Scan correctly diagnosed the problem and cholecystectomy did not completely abolish the symptoms.

| Parameters | Data |
|---------------------------|--|
| Age of onset of symptoms | 16 |
| Age diagnosed | 16 |
| Sex | Female |
| Symptoms before treatment | Burning pain in stomach under chest, loss of appetite, nausea after eating |

| | |
|--|--|
| Other diagnoses before correct diagnosis | None |
| Diagnostic tests performed | HIDA Scan, Blood Tests |
| Diagnostic test that correctly diagnosed problem | HIDA Scan |
| Prescribed treatment | Cholecystectomy |
| Effectiveness of prescribed treatment | Most symptoms are gone but continues to feel burning pain in stomach |

Table 2: Survey is of a 12-year old female patient who complained of gallbladder-related problems with symptoms which consisted of stomach virus type of symptoms after eating certain foods and waking up in the middle of the night with acute attacks. The patient suffered these symptoms for seven years before the prior diagnosis could be rendered. The patient was administered the HIDA scan, endoscopy and blood tests prior to the prescription of cholecystectomy for treatment. The HIDA Scan correctly diagnosed the problem and cholecystectomy did not completely abolish the symptoms.

| Parameters | Data |
|--|---|
| Age of onset of symptoms | 12 |
| Age diagnosed | 19 |
| Sex | Female |
| Symptoms before treatment | Stomach virus symptoms after eating certain foods; wake up in the middle of the night with symptoms followed by attacks |
| Other diagnoses before correct diagnosis | None |
| Diagnostic tests performed | Ultrasound, Blood Tests, Endoscopy, and HIDA Scan |
| Diagnostic test that correctly diagnosed problem | HIDA Scan |
| Prescribed treatment | Medicine, diet and cholecystectomy |
| Effectiveness of prescribed treatment | Most symptoms are gone but can't hold down foods, lost 15 lbs, stomach virus symptoms persist and ribs feel like they're collapsing after a night's sleep |

Table 3: Survey is of an 18-year old female patient who complained of gallbladder-related problems with symptoms which consisted of burning pains and difficulty sitting up straight. The patient suffered these symptoms for one year before the prior diagnosis could be rendered. The patient was administered the HIDA scan, ultrasound and blood tests prior to the prescription of cholecystectomy for treatment. The HIDA Scan correctly diagnosed the problem and cholecystectomy did not completely abolish the symptoms.

| Parameters | Data |
|--|---|
| Age of onset of symptoms | 18 |
| Age diagnosed | 19 |
| Sex | Female |
| Symptoms before treatment | Burning pain and had difficulty sitting up and felt like breath had been knocked out |
| Other diagnoses before correct diagnosis | None |
| Diagnostic tests performed | Ultrasound, Blood Tests, and HIDA Scan |
| Diagnostic test that correctly diagnosed problem | HIDA Scan |
| Prescribed treatment | Cholecystectomy |
| Effectiveness of prescribed treatment | Symptoms persisted but the duration of occurrence was longer, started having panic attacks and having problems holding down foods |

Table 4: Survey is of a 20-year old female patient who complained of gallbladder-related problems with symptoms which consisted of nausea, vomiting, acid reflux and extreme pain in the upper right quadrant. The patient suffered these symptoms for one year before the prior diagnosis could be rendered. The patient was administered the HIDA scan and ultrasound tests prior to the prescription of cholecystectomy for treatment. The HIDA Scan correctly diagnosed the problem and cholecystectomy did not completely abolish the symptoms.

| Parameters | Data |
|--|---|
| Age of onset of symptoms | 20 |
| Age diagnosed | 20 |
| Sex | Female |
| Symptoms before treatment | Nausea, vomiting, acid reflux, pain in upper right quadrant |
| Other diagnoses before correct diagnosis | None |
| Diagnostic tests performed | Ultrasound and HIDA Scan |
| Diagnostic test that correctly diagnosed problem | HIDA Scan |
| Prescribed treatment | Reglan and Nexium before Cholecystectomy |
| Effectiveness of prescribed treatment | Some symptoms persist but not as severe if eat fatty or spicy foods |

Table 5: Survey is of a 15-year old female patient who complained of gallbladder-related problems with symptoms which consisted of nausea, lower abdominal cramping, loss of appetite, bloating and severe pain after eating. The patient suffered these symptoms for six years before the prior diagnosis could be rendered. The patient was administered the HIDA scan, blood tests, endoscopy and ultrasound tests prior to the prescription of cholecystectomy for treatment. The HIDA Scan correctly diagnosed the problem and cholecystectomy did not completely abolish the symptoms.

| Parameters | Data |
|--|--|
| Age of onset of symptoms | 15 |
| Age diagnosed | 21 |
| Sex | Female |
| Symptoms before treatment | Extreme nausea and lower abdominal cramping, loss of appetite, bloating, severe pain after eating |
| Other diagnoses before correct diagnosis | None |
| Diagnostic tests performed | HIDA Scan, Endoscopy, Colonoscopy, Blood Tests |
| Diagnostic test that correctly diagnosed problem | HIDA Scan |
| Prescribed treatment | Cholecystectomy |
| Effectiveness of prescribed treatment | Symptoms not as severe nor frequent, panic attack after eating, slight pressure on abdomen lead to lightheadedness |

Table 6: Survey is of a 13-year old female patient who complained of gallbladder-related problems with symptoms which consisted of nausea, abdominal pain, upper right quadrant pain, loss of appetite and bloating. The patient suffered these symptoms for one year before the prior diagnosis could be rendered. The patient was administered the HIDA scan, blood tests and ultrasound tests prior to the prescription of cholecystectomy for treatment. The HIDA Scan correctly diagnosed the problem and cholecystectomy did not completely abolish the symptoms.

| Parameters | Data |
|--------------------------|--------|
| Age of onset of symptoms | 13 |
| Age diagnosed | 14 |
| Sex | Female |

| | |
|--|---|
| Symptoms before treatment | Extreme nausea, abdominal pain, upper right quadrant pain, loss of appetite, bloating |
| Other diagnoses before correct diagnosis | None |
| Diagnostic tests performed | HIDA Scan, Blood Tests and Ultrasound |
| Diagnostic test that correctly diagnosed problem | HIDA Scan |
| Prescribed treatment | Cholecystectomy |
| Effectiveness of prescribed treatment | Symptoms subsided but not completely abolished |

Table 7: Survey is of an 11-year old female patient who complained of gallbladder-related problems with symptoms which consisted of nausea, loss of appetite, severe pain after eating, bloating, and upper right quadrant pain. The patient suffered these symptoms for fourteen years before the prior diagnosis could be rendered. The patient was administered the HIDA scan and blood tests for diagnosis. The HIDA Scan correctly diagnosed the problem and no treatment has been prescribed in this case.

| Parameters | Data |
|--|--|
| Age of onset of symptoms | 11 |
| Age diagnosed | 25 |
| Sex | Female |
| Symptoms before treatment | Moderate nausea, loss of appetite, severe pain after eating, bloating, upper right quadrant pain |
| Other diagnoses before correct diagnosis | None |
| Diagnostic tests performed | HIDA Scan, Blood Tests |
| Diagnostic test that correctly diagnosed problem | HIDA Scan |
| Prescribed treatment | None |
| Effectiveness of prescribed treatment | N/A |

Table 8: Common parameters from seven surveys which showed that sufferers of BD began to experience symptoms at 15 years of age and usually suffered these symptoms for an average of four years prior to the correct diagnosis. They are all females and shared symptoms which consisted of nausea, lower abdominal cramps, upper quadrant pain, loss of appetite, bloating and extreme pain associated with eating. Patients were administered the HIDA Scan, blood tests, endoscopy and ultrasound for diagnosis. The HIDA Scan was the test that correctly identified the problem and once identified cholecystectomy was the treatment of choice. This treatment paradigm did not abolish the symptoms associated with BD.

| Parameters | Data |
|--|---|
| Age of onset of symptoms | 15 |
| Age diagnosed | 19 |
| Sex | Female |
| Symptoms before treatment | Nausea, lower abdominal cramps, upper quadrant pain, loss of appetite, bloating and extreme pain after eating |
| Other diagnoses before correct diagnosis | None |
| Diagnostic tests performed | HIDA Scan, Blood Tests, Endoscopy, Ultrasound |
| Diagnostic test that correctly diagnosed problem | HIDA Scan |
| Prescribed treatment | Cholecystectomy |
| Effectiveness of prescribed treatment | Most symptoms are gone but continues to feel burning pain in stomach |

This seems to support the idea that most, if not all of these six subjects, likely demonstrated less than 50% ejection fraction on their CCK-HIDA scans (Tables 1-8).

Our study indicates that there are common symptoms that are shared by sufferers of biliary dyskinesia. These symptoms range from mild flu like symptoms (Table 2) to severe nausea and abdominal cramps (Tables 5 and 7) with a range of symptoms in between (Tables 1, 3, 4 and 6). Upon consolidating the findings of the study, we found that there were common symptoms among the respondents. These include nausea, lower abdominal cramps, upper quadrant pain, loss of appetite, bloating (feeling full after a small amount of food intake) and extreme pain after eating (Table 8). Previous studies have not identified common symptoms of biliary dyskinesia [9,13,14]. Thus, our study demonstrates an important finding that anyone complaining of persistent symptoms that include nausea, lower abdominal cramps, upper quadrant pain, loss of appetite, bloating and extreme pain after eating should be immediately considered as a prime candidate for biliary dyskinesia.

In addition to all of the common symptoms, our study also showed two interesting patterns. All seven of the respondents were females (Tables 1-8) with an average age of 15. Previous studies have not shown if this disorder is more common in one gender than another and whether or not this disorder affects individuals in a certain age range. Therefore, our findings demonstrate that preteen females that complain of nausea, lower abdominal cramps, upper quadrant pain, loss of appetite, bloating and extreme pain after eating should be checked immediately for biliary dyskinesia before being considered for other disorders.

Finally, our study shows that the CCK-HIDA scan is the most effective way of determining if an individual suffers from biliary dyskinesia (Table 8). While other tests were often employed in the diagnosis of biliary dyskinesia including blood tests, ultrasound, and endoscopy, these tests simply served to prevent the correct diagnosis and often lead to an average of four years of needless suffering from this debilitating disease before the proper diagnosis was rendered. Once the proper diagnosis was rendered, studies showed that the most common treatment was gall bladder surgery [3,4,8,14], a treatment that diminished the symptoms but did not completely cure the problem.

Conclusion

While surgery is considered the primary treatment for biliary dyskinesia which has marginal success even in the seven cases that we studied (Table 8) other treatment

paradigms must be explored. One nonsurgical treatment that needs to be seriously considered is the use of the drug tiotropium [13], an antispasmodic drug which has shown to restore normal emptying function to a compromised gallbladder.

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Conflict of Interest

None declared.

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