

Pediatric Gastroesophageal Reflux Disease

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Abstract

This objective of this review is to present the known data in regards to Gastroesophageal Reflux Disease (GERD) in infants. Articles with relevant definitions, diagnosis and treatment options were evaluated. It is evident that much controversy exists in the diagnosis and treatment of this disease, and there is the question as whether this disease can be called GERD. Current ability to attribute the symptoms infants present with the disease is still difficult to clarify, despite the fact that as many as 60% of infants show symptoms of this disease. The current testing options have proven to be insufficient in concretely diagnosing infants. Treatment for GERD has proven to be controversial as well. The medications for acid suppression are not a guaranteed cure and are being proven to have a lack of efficacy, show adverse effects and other negative aspects. The invasive options are not always ideal either. Altering changes in lifestyle helps, but is usually not the cause or cure when it comes to infants. Research is being done to come up with a test that is a definitive diagnosis, as well as a treatment option that is completely effective. Research has shown that despite the fact that acid suppression therapy is the most common answer by physicians today, it does not effectively work to eliminate all the symptoms. This does suggest that either GERD is not the condition, or that modern therapies and treatments for reflux are not effective. Further research is needed on the subject.

Introduction

Does Pediatric Gastroesophageal Reflux Disease (GERD), also known as acid reflux, exist? GERD is a condition in which over 60 million Americans suffer from at least once a month (Maddox 2012); this condition is commonly called heartburn. Acid reflux is not the typical pain felt after eating a heavy meal or the wrong kinds of foods. It is a much stronger and severe condition. Reflux is defined as the passage of gastric contents into the esophagus and is a physiologic process. (Vandenplas, et al. 2009) Doctors have questioned whether it is a possibility for infants and children to suffer from such a condition, which is often believed to come with age or bad eating habits. The NIH and many other prestigious organizations and hospitals in the United States and around the world are doing extensive research on this condition (Nelson, et al. 1997). This review will attempt to present the known research on the acid reflux-like symptoms in infants and children and what evidence there is to prove if it is indeed pediatric GERD, as well as present the possible medical ways of alleviating their suffering.

Methods

General websites like NIH.gov, and Webmd.com, with definitions of what GERD is were accessed first and reviewed to gain a general knowledge about GERD. The NIH's scholarly website, Pubmed, with original research and review articles from all types of medical and research journals was accessed. Information about GERD in infants was evaluated. General data regarding GERD, GERD in infants and any diagnostic testing and treatment of the disease were researched and evaluated for relevant information. In Touro College's library, the Touro Ebsco search engine was accessed and utilized to locate useful articles and original research papers as well.

Discussion

Many people feel the sensation of food "coming up" on them after eating heavy foods. This sensation may indeed be food escaping the lower esophageal sphincter and rising upward into the esophagus (fig.1). There is no cause for alarm when the person does not feel any troubling symptoms as a result of this; at this stage the condition is not called GERD and is not labeled a disease (Rudolph, et al., 2001). It is simply called GER, Gastroesophageal Reflux. Once the condition crosses over to the point of symptoms with major side effects, it is called GERD, Gastroesophageal Reflux Disease. The same parameters of diagnosis are applied for infants. When a child is thriving and growing healthily, despite showing symptoms for GERD, it is not regarded as a disease (Vandenplas, et al. 2009). The symptoms for this condition in infants include spitting up, vomiting, refusal to eat, feeding difficulties, colic, incessant crying, arching the back and neck, hoarseness and cough (Brodsky, et al. 2000). Some say that there are even a wide range of respiratory problems as a result of acid reflux as well. The problem with

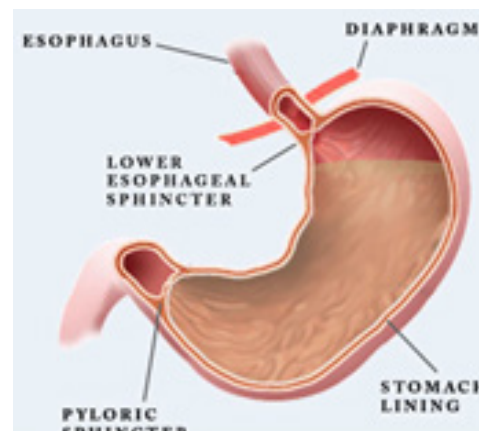


Figure 1
Reflux Defense 2009

diagnosing GERD based solely on an infant's symptoms is that these are symptoms for many other conditions as well (Ghezzi, et al. 2010). Guaranteeing that they are a result of reflux is very hard to prove.

Many infants may show signs for some or all of these symptoms. When it comes to diagnosing adults, doctors can rely on asking the patient about the symptoms they feel. The patient would be able to describe when, how, what time of day, before or after or even during meals, what specifically they feel regarding their symptoms. However, it is

very different with an infant. They do not have the ability to specifically communicate what they are feeling. Infants have one means of communication for all of their necessities and issues, good or bad. Infants cry as their means of indicating something is not right with them. Parents are asked many questions to help doctors understand what exactly their child may be feeling and what symptoms they may have (Deal, et al. 2005). Figures 2 and Table 1 have a list of some of the questions a doctor might ask the parents. Doctors have to rely on the parents of the infants to relate what they presume is going on with their child. This hinders the ability to properly diagnose the disease tremendously.

Site No.	Patient No.	Patient Initials □□□	Visit ID		
Date Completed □□ □□ □□ □□ D D M M M Y Y					
Relationship to Patient <input type="checkbox"/> Mother <input type="checkbox"/> Step Mother <input type="checkbox"/> Grandmother <input type="checkbox"/> Guardian <input type="checkbox"/> Father <input type="checkbox"/> Step Father <input type="checkbox"/> Grandfather <input type="checkbox"/> Other, specify _____					
<u>SYMPTOMS</u>			<u>QUESTION A</u> How many times did each symptom occur in the past 7 days? (such as 0, 1, 2, 3, etc)		
1. VOMITING / REGURGITATION Throwing-up / swallowing food, or liquids that have come back up into the infant's mouth.			□□□ Times in the past 7 days (Do not leave blank)		
2. CHOKING / GAGGING			□□□ Times in the past 7 days (Do not leave blank)		
3. ARCHING BACK			□□□ Times in the past 7 days (Do not leave blank)		
4. IRRITABILITY / FUSSINESS Episodes of crying during feeding or inconsolable.			□□□ Times in the past 7 days (Do not leave blank)		
5. REFUSAL TO FEED			□□□ Times in the past 7 days (Do not leave blank)		
TOTAL			□□□ Total should be > 16		

Figure 2
Cohn, et al. 1996

GERD is considered a very complicated disease to diagnose. As of now there is no one test that has received the “gold star” as the perfect test to diagnose the disease. (Arko, et al. 2009) When it comes to children, the process of diagnosing is even harder. Much of the research on the subject begun because of parents coming forward with their infants because they did not understand what is wrong with their children. Parents have come forward when a child refuses to eat as an infant (from as early as four weeks old.) Other parents came forward because of incessant vomiting; the infant would not stop vomiting and presented no signs of infection or virus (Omari, et al. 2002). These are just two of the more common symptoms that cause parents to approach a doctor about their child’s issue. Without parents taking the initiative to ask the doctor what issue their child has, research may not exist.

One wonders if the parents themselves are a blind spot in the diagnosis. If the parents have GERD themselves, it may hinder their ability to objectively see what is going on with their child and relay all pertinent information to the doctor. Another aspect that may need to be brought for further research is whether there is a genetic component to GERD. If the parents have it as adults, could their children have it as infants? Do doctors and researchers need to take this into account when setting up parameters for diagnosis and treatment?

There exists a few means of testing patients for GERD. The problem with many of them is that they are not perfect and by no means perfect for infants. Another issue that arises is that many doctors suspect that reflux is just a cover for a real condition that is going on in the body, like anatomical abnormalities or hernias, for example (Rudolph, et al., 2001). The doctors questioned whether they should begin invasive testing for severe conditions and possible surgeries, or to first try out the known protocols for testing for reflux and the treatments done on adults. As many of these doctors do not believe reflux exists in infants, they begin intense procedures to discover what is really wrong with the child. One theory was that the H. Pylori bacteria was causing over production of acid in infants. This theory was soon dismissed as eradicating the bacteria made no change in the patients’ condition (Maris, et al. 2013). Other doctors who do not believe it exists either, take the approach of ignoring the matter and waiting until the child outgrows the condition, which is often the case with infants (Carroll, et al. 2002). Most research indicates that infants do outgrow this condition by 24 months of age. A third approach is to follow the protocol done on an adult, with the future risks to the infant still unknown.

Testing

The first test commonly done when reflux is suspected is called the Barium Study Swallow Test. (Arko, et al. 2009). This test is considered to be the least invasive test of all the reflux diagnostic tests. This test is done to determine if there are any blockages in

Figure 3: Questionnaire

1.a	1	*Does your child vomit or regurgitate > 1x / day
1.b	2	*Does your child vomit or regurgitate > 3x / day
1.c	3	*Does your child vomit or regurgitate > 5x / day
2.a	4	*Is the mean volume > 1 coffee spoon?
2.b	5	*Is the mean more than 1 soup spoon?
2.c	6	*Is the mean more than 3 soup spoons?
	7	Is the vomit/regurgitation projectile (with force)?
3	8	*Is the regurgitation painful?
4	9	*Does your child, according to your opinion, cry “too much”?
5.a	10	*Does your child cry more than 1 hour a day?
5.b	11	*Does your child cry more than 3 hours a day?
6	12	*Does your child cry during and after feeding?
7	13	*Does your child refuse feeding even when hungry?
	14	Does your child burp difficulty?
8	15	*Is the weight gain OK?
	16	Does respiration make a lot of noise?
9.a	17	†Did your child have an apnea with cyanosis?
9.b	18	†Did your child have an apnea with “tossing”?
9.c	19	†Did your child have an apnea with cyanosis and tossing?
	20	Did your child have a pneumonia?
	21	Did your child have a bronchitis?
	22	Does your child have chronic coughing?
10	23	*Does your child have hiccups more frequently than normal?
	24	Does your child have hiccups more than once a day?
	25	Does your child have hiccups more than 5 min a day?
	26	Are the stools normal?
	27	Does your child suffer “chronic diarrhea”?
	28	Does your child have “chronic constipation”?
	29	Does your child not have daily stools?
	30	Is there more than 2 days between 2 defecations?
	31	Is there a reflux pathology in your family?
	32	Do you have other children?
	33	Did a brother/sister have a reflux pathology?
	34	Is there allergy in your family?
	35	Do you think your baby has a reflux pathology?

Figure 3
Hauser, et al. 2005

the anatomy of the patient or anomalies or conditions that do not belong there. The infant is given Barium Sulfate, a white substance, to drink; Barium Sulfate is opaque to x-rays causing a contrast in the body. X-rays are taken immediately and during swallowing of the liquid to highlight the upper gastrointestinal tract and show if anything is out of the ordinary. This test does not indicate any form of acid levels in the body or if reflux is the diagnosis. It simply rules out other issues like pyloric stenosis, tracheoesophageal fistulae as well as other abnormalities associated with the upper gastrointestinal tract.

Endoscopy with pH probe testing is another means of testing for GERD. This method was the focus of testing for many years. This method looks to see what the acid levels within the infant are and shows any signs of damage to the esophagus (Hauser, Novario, Salvatore, Vandemaele, & Vandenplas, 2005). Research indicates

that when the pH testing showed the child having an esophageal pH of less than 4, reflux was the main cause. This test uses an endoscope probe that has a camera attached at the end, as well as an LED light to aid in visualization. It is inserted down the patient's throat (some up the nose and down the throat) and lowered down the esophagus. (Ferreira, et al. 2012) This test is considered invasive for infants and children and does require general anesthesia. The pH probe is attached to the endoscope, so both are lowered down the esophagus together.

If the readings of the pH levels indicate lower than 4, acid is present and reflux is suspected. The endoscope will indicate how much damage has been done to the esophagus, if any. Most children did have less damage to the esophagus when the symptoms they experienced did start to get alleviated. This test is not considered perfect because many times the lower esophageal sphincter may have just opened and released a little acid into the esophagus, altering the validity of the pH probe's results (Ferreira, et al. 2012). Another issue is that the pH probe missed acid levels in some children who showed signs of severe esophageal damage, which clearly indicated that acid was present. The endoscopy test also is not a clear indicator for acid reflux. Infants/Children may have damage to their esophagus for other reasons, and not everyone with GERD has damage to their esophagus. Both of these indicated that the means of diagnosing at that time was terribly insufficient. The logical conclusion is that further research was needed to come up with a new, more accurate test. (Badriul, et al. 2004)

Another option for diagnosis is to do pH-probe tests over an extended 24-hour period. This tested for pH dropping to levels below 4 and infants having the symptoms during or after the drop. This test data did show that some patients have a correlation between reflux like symptoms and the test scores. However, the research tests do not show a big difference in acid reflux levels between those undergoing the 24-hour test and those being evaluated for reflux-like symptoms. (Badriul, et al. 2004). This has to mean that the test is not perfect as well.

The next test available is called the pH-MII test, Multichannel Intraluminal Impedance Test. It is similar to the pH probe. It also goes through the nose and down the throat to the esophagus where it stays for 24 hours. This test measures acid levels, esophageal flow and bolus presence. It has small detection devices at 6 levels along the catheter within the esophagus. It can test for acid or non-acid reflux and whether it is liquid or gas. When researchers define non-acid reflux, as having a pH of greater than 4, this test was able to detect reflux in infants, that the standard pH test missed 89% of the time. (Omari, et al. 2002)

This test helps infants that were being diagnosed simply by evaluation of symptoms. If the patient was treated solely based on symptoms, they might have been misdiagnosed. This test shows

that the regurgitation may have nothing to do with pH levels. It greatly proved that the old pH test was not enough. The need to come up with a better means of diagnosis was clearly evident. The pH-MII test does provide more accuracy. However, it also causes more questions. Even if the pH is less than 4, and is recorded by the probe, how close in time does the reflux event need to happen next to the appearance of a symptom to be considered associated? And how many events and symptoms need to occur together in a day, for example, for it to be considered problematic and relevant for diagnostic purposes? Another question is why is there a correlation between the non-acid reflux and symptoms? If it is all an indication of the presence of acid in the infant's esophagus, how could the test show that acid levels were above pH of 4, and yet there was a bolus present at the same time as the symptoms? One has to wonder if there is a third entirely different option going on that just has not been recognized yet.

The pH-MII test was good for eliminating GERD as a diagnosis in some patients, however, for those that didn't fit into the category, all it did was raise more questions. Another study questioned if raising the pH level to between 4.5-5.5 in different positions was the answer. (Chiou, et al. 2011) Many more infants were diagnosed with GERD when this was the new parameter for acid reflux. Parents that need some reprieve were provided with an answer and some form of treatment. Indeed, many did respond to treatment. As of yet this is the best test there is. It is not perfect but it does provide some answers.

Treatment

An interesting factor in treatment for GERD is that it can also be diagnostic. If the patient gets better with the treatment, doctors presume they had the disease. When it comes to infants, the first treatment tried is called nonpharmacological therapies (Carroll, et al. 2002). This includes positioning the infant differently, thickening the child's formula, changing the formula and modifying how many times a day the infant has a meal. The positioning changes only worked on some patients and only in some positions. Thickening the formula helped with caloric intake, but it did not reduce the symptoms or reflux episodes in infants. (Khoshoo, et al. 2000) Changing the formula from a milk protein to a different amino acid basis did help some of the symptoms. Symptoms of milk allergy or intolerance are very similar to reflux (for example: regurgitation, fussiness, colic, etc.); however the research doesn't show that it limited reflux episodes (Nielsen, et al. 2004). Infants that did show improvement with the switched formula usually did so as a result of not having reflux to begin with. Their symptoms were mistaken for reflux because the symptoms of a milk allergy or intolerance do overlap with reflux in many areas. Research indicates that these therapies of altered lifestyle tend to help a little, but most do not last very long.

The most common treatment done for infants with reflux is acid suppression. This is done through medications. They are divided into histamine 2 (H2) antagonists and proton pump inhibitors. (Bachmaier, et al. 2014) Both of these reduce gastric acidity and help heal damage to the esophagus. Very often the medication is prescribed without doing a test like an endoscopy or pH probe. So there is no way of knowing what caused the symptoms to be alleviated or if the acid content and production in the stomach was ever there. (Comer, et al. 2010)

H2 blockers work by decreasing the amount of acid produced by the stomach. Brand name examples of these medications are Pepcid AC, Tagament and Zantac. The symptoms in infants did tend to improve. However, a double blind research study indicated that infants with the medication did not show improvement in symptoms greater than those with the placebo (Comer, et al., 2010). So the question remains, what made the child get better and why isn't another child getting better? Figure 4 shows a list of common H2 receptor drugs as well as proton pump inhibitor drugs.

Proton Pump Inhibitors work by suppressing acid production as well. However, the mechanism is different and they target different types of acid and different means of acid production. They seemed to work a little better than H2 antagonists for those with more severe GERD symptoms. The issue arises though, that with both

types of medication acid is being minimized in the gastric area. The infants do become more prone to GI tract and pulmonary infections. The question remains, what is worse- reflux or infection? Many doctors will not give medication for those infants who seem to be growing well, despite the other symptoms. There have been some adverse effects by some of these medications too. One has been removed from the market because of the possible neurological damage as a side effect (Chen, et al. 2012). Despite all this, medication does seem to be the most common form of treatment for infants with GERD.

One other means of treatment is surgical; the most common being inserting a feeding tube. (Kuwata, et al. 2013) This did alleviate the symptoms to a great extent, however at a great price. These children did tend to develop issues with eating orally later on; they had trouble with chewing, swallowing and sensory issues, to name a few. The children needed physical and occupational therapy to help them learn how to properly eat, chew and not have an aversion to the different textures of their food. Most physicians deem this option to be a last resort because of the developmental issues that can arise later on, as well as the invasiveness of the procedure. Doctors generally have seen that infants do outgrow the condition with age. When evaluating treatment options, this fact has to be taken into account.

Type of medication	Recommended oral dosage	Adverse effects/precautions
Histamine₂ receptor antagonists		
Cimetidine	40mg/kg/day divided TID or QID (adult dose: 800–1200 mg/dose BID or TID)	rash, bradycardia, dizziness, nausea, vomiting, hypotension, gynecomastia, reduces hepatic metabolism of theophylline and other medications, neutropenia, thrombocytopenia, agranulocytosis, doses should be decreased with renal insufficiency
Nizatidine	10 mg/kg/day divided BID. (adult dose: 150 mg BID or 300 mg qhs)	headaches, dizziness, constipation, diarrhea, nausea, anemia, urticaria, doses should be decreased with renal insufficiency
Ranitidine	5 to 10 mg/kg/day divided TID (Adult dose: 300mg BID)	headache, dizziness, fatigue, irritability, rash, constipation, diarrhea, thrombocytopenia, elevated transaminases, doses should be decreased with renal insufficiency
Famotidine	1 mg/kg/day divided BID (adult dose: 20 mg BID)	headaches, dizziness, constipation, diarrhea, nausea, doses should be decrease with renal insufficiency
Proton pump inhibitors		
Omeprazole	1.0 mg/kg/day divided qd or BID (adult dose 20 mg qd)	headache, diarrhea, abdominal pain, nausea, rash, constipation, vitamin B12 deficiency
Lanzoprazole	No pediatric dose available (adult dose: 15–30 mg qd)	headache, diarrhea, abdominal pain, nausea, elevated transaminase, proteinuria, angina, hypotension
Pantoprazole	No pediatric dose available. (adult dose: 40 mg qd)	headache, diarrhea, abdominal pain, nausea
Rabeprazole	No pediatric dose available (adult dose: 20 mg qd)	headache, diarrhea, abdominal pain, nausea
Prokinetic		
Cisapride	0.8 mg/kg/day divided QID. (adult dose: 10–20 mg QID)	rare cases of serious cardiac arrhythmia (FDA recommends ECG before administration) beware of drug interactions do not use in patients with liver, cardiac or electrolyte abnormalities (FDA recommends K ⁺ , Ca ⁺⁺ , Mg ⁺⁺ and creatinine before administration)

Figure 4:

Drugs demonstrated to be effective in gastroesophageal reflux disease (Rudolph, et al. 2001)

Conclusion

As of yet there is no way to conclude with absolute certainty that GERD exists in infants. All the evidence linking the two is not definite. Most infants did tend to get better over time as they aged, or with symptom alleviation due to one form of treatment or another. (Or unfortunately death caused the subject to no longer be in the research data.) None of these indicate with absolute certainty that the GERD was ever there to begin with. Thorough evaluations are needed to properly diagnose GERD in infants. Further research is needed in order to come up with a diagnostic test that clearly identifies GERD as the condition. Physicians should take a conservative approach in treating patients whom they suspect have this condition, because more damage than good can be done to these infants in the process of trying to alleviate their symptoms.

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