SICKLY SWEET: THE DEVELOPMENT OF A STANDARDIZED METHOD FOR TESTING LACTOSE AND FRUCTOSE INTOLERANCE AND MALABSORPTION

by

Taylor Lawless

A Senior Honors Project Presented to the

Honors College

East Carolina University

In Partial Fulfillment of the

Requirements for

Graduation with Honors

by

Taylor Lawless

Greenville, NC

May 2014

Approved by:

Faculty Mentor (signature required):

Dr. Kimberly B. Myers

Sickly Sweet: The Development of a Standardized Method for Testing Lactose and Fructose Intolerance and Malabsorption

Student: Taylor Lawless

Mentor: Dr. Kimberly Myers

Abstract

Lactose intolerance has been a known cause of gastrointestinal distress for many years. Recently, it has come to attention that fructose intolerance elicits many of the same symptoms as lactose intolerance. The consumption of fructose has more than doubled in the past twenty years; conversely, the instances of fructose intolerance have also increased. Fructose and lactose intolerance are measured using similar methods. While there are common practices and guidelines used when testing fructose and lactose intolerance and malabsorptive issues, there is no official standard method including precise practices for before, during, and after the test. Therefore a standard system was created by comparing methods used in previous studies. If used on a wide scale, the standard system will enable researchers to compare results of different studies. Ultimately, this would enable researchers to gain a better understanding of lactose and fructose intolerance and malabsorptive issues in order to develop improved treatments and potential cures.

Introduction

Lactose intolerance has been a popular nutrition topic for many years. Many suffer from Irritable Bowel Syndrome (IBS) due to the milk or dairy sugar lactose. Interestingly, as fructose has become more prevalent in the human diets, people have begun suffering similar malabsorpitve effects.

Lactose intolerance can cause an array of painful and irritating symptoms such as gas, bloating, diarrhea, vomiting and nausea[1]. These same symptoms have been observed in those with fructose intolerance[2]. This has caused people to ask questions regarding the relationship between the type of sugars individuals are consuming and the way the sugars are metabolized.

Fructose consumption has more than doubled in the past 20 years[2]. While the full effect of this increase is not yet know, more instances of fructose malabsorption are being noticed. Some attribute this malabsorption to the metabolic pathway of fructose. It has been speculated that fructose is absorbed by facilitated diffusion or that fructose can only be absorbed with glucose[3]. While the absorption of fructose is still being studied, it is know that lactase breaks lactose into galactose and glucose in the human body[4].

While the causes of sugar malabsorption are unknown, there is research being done on the different types of sugar malabsorption and intolerance. Malabsorption refers to when sugar is not properly broken down in the body[5] and intolerance implies that the body is incapable of breaking down the sugar[3].

Fructose and lactose malabsorption and intolerance can tremendously impact the life of an individual. Similarly, misdiagnosis of such conditions can also have negative implications. If a person is incorrectly diagnosed with and intolerance, the individual may eliminate the sugar from the diet unnecessarily[1,6]. That is particularly concerning with lactose as restriction of lactose can lead to calcium deficiencies. A diagnosis implying the person is not intolerant when the person is can be dangerous as well because the person will continue to consume the sugar and experience the discomfort[7].

Hydrogen breath tests are the primary tool used to measure fructose and lactose malabsorption and intolerances. The inconsistencies associated with conducting such tests have left people questioning the validity of the results[7]. Testing differences also make it difficult for scientists to compare results. For these reasons, a standard system of measurement has been created to alleviate the ambiguity of current testing systems.

<u>Discussion</u>

Before deciding which practices were the best, a literary view was conducted on studies about fructose and lactose malabsorption. The literary review was conducted using articles regarding fructose and lactose malabsorption and intolerance in order to build a knowledge foundation about common practices. The primary focus of the review was the methods used and the results yielded. The methods used often affected the results which is why both methods and results were reviewed together.

While a case study of an Italian family genetics can be a factor in the absorption of sugars[8], some speculate that age could be a factor as well. “Effect of Age on Fructose Malabsorption in Children Presenting With Gastrointestinal Symptoms” was a study conducted by Hilary Jones that was published in 2011. The patients had been referred to the study because of presenting signs and symptoms of carbohydrate malabsorption. Prior to the test the patients were asked to fast for eight hours or more, if possible. If the child was younger than half a year only a six hour fast was required. The last meal before the fast was requested to be low in fiber. Patients were not permitted to smoke or exercise prior to the test[9]. Fasting and abstaining from exercise and smoking prior to the test are two very important practices that will be seen in many of the studies reviewed.

The dose of sugar given to patients was 0.5 grams of fructose per kilogram of body weight. The fructose was administered in 100 mL of water to those older than six months and in 80 mL for those younger. Lactose was administered in the dosage of 2 grams per kilogram of body weight.

All of the patients were under the age of 15 years and were given hydrogen breath test for fructose. Of the 1093 children tested, 50% had a positive breath test. For this study a positive test constituted a greater than or equal to 10 ppm increase in two successive measurement periods. Jones found that younger children had a higher frequency of fructose intolerance than older children.

Jones also investigated using lactose breath tests. These were conducted on 3073 patients, where slightly less than 40% had a positive result. Jones found that lactose test results were not significantly affected by age[9]. These results suggested that there could be a correlation between an increase in age and ability to absorb fructose. The results also suggested that there isn't a relationship between having lactose malabsorpition issues and age.

Also interested in the effects of fructose intolerance on children, Robert Gomara conducted a research project to learn more. The study entitled "Fructose Intolerance in Children Presenting with Abdominal Pain" was published in 2008. The objective of the study of Gomara was to measure how prevalent fructose malabsorption was in pediatric patients who had experienced discomfort in the abdominal cavity due to bowel irritation. The questions asked by the authors were what symptoms do the patients suffer and how badly, and does the dosage of fructose have any effect.

To test the hypotheses, the authors conducted the trials with 16 boys and 16 girls between the ages of 7 and 17 years. All of the patients suffered regular, long-term abdomen discomfort. Before conducting the study, patients were tested for any other malignity that could be attributed for their irritable bowel syndrome or nausea. For example, those who had bacterial infections or any other malabsorptive syndrome were not included.

After the sample was gathered the patients underwent a series of tests. The patients began the trial by avoiding foods containing large concentrations of fat, fructose or lactose and fasting in the evening. Upon arrival at the clinic, patients were asked to complete a survey ranking 9 bowel symptoms on a scale of 0 to 3. Next, baseline hydrogen breath test samples were taken. If the hydrogen levels increased by 20 ppm over baseline during the trial then they had a positive result. Following the baseline test the patients were randomly administer a random dose of fructose with 1 gram, 15 grams, or 45 grams in 240 mL of water[3]. The 45 gram dose was used for comparison by an earlier study by Choi whose work will be reviewed in this paper[2]. Over the next 3 hours breath samples were taken every 30 minutes and symptoms suffered during that time. Symptoms for some were so severe that a few patients needed to drop out of the study[3].

The results of this data were analyzed using a chi squared analysis and had a p value of less than .05. Just over 30% of patients had a positive fructose breath test. 13 patients received the large dose of fructose, 10 patients received the medium dose and 9 patients received the small test. The percentage of patients with a positive test result directly correlated with the size of the dose received. The patients with the highest dose had 61% positive breath tests and the patients receiving the smallest dose had no positive breath tests. The number and severity of symptoms also directly correlated with the dosage. The author concluded that their study showed that fructose restriction can reduce irritable bowel syndrome in pediatric patients. This result is justifiable because none of the patients in the low dose group suffered symptom whereas over 60% in the high dosage group did suffer.

Patients who had positive test results were given guidance on avoiding fructose containing foods. Those who avoided such foods had a decrease in symptoms. One limit of the study was that patients were only given instruction if they had a positive breath test. Another concern was the small sample size and the uneven number of patients in each test group[3]. As will be mentioned later, compiling information regarding treatment methods and the effectiveness of the methods from many studies, and could result in an effective treatment for intolerances and malabsorption could be created.

In addition to age and genetics, dietary influences could play a role in sugar absorption. In 2009 an article called “Dietary fructose, fruits, fruit juices and glucose tolerance status in Japanese-Brazilians” was published in Elsevier. The purpose of the study was to investigate the effects that fructose has on glucose absorption within the specific population of Japanese-Brazilians. There were 1054 subjects in the study. A questionnaire was used to assess how the participant lived and the medical history of the participant. Anthropometric measures of the participants were also taken. To gather a more accurate idea of fructose intake a food frequency questionnaire was distributed to determine the quantity and sources of fructose were consumed in the diet of the participant.

Next, the blood glucose was analyzed after a 10 hour fast. The data was analyzed using chi squared tests, ANOVA and logistic regression models. The results showed that the greater the intake of fruit juices, the more likely the participant was to have impaired glucose tolerance. Therefore the consumption of fructose can affect the absorption of glucose[10]. This is significant as consumption of fructose has tremendously increased in a short period of time[2].

Fructose intolerance can cause great discomfort. Therefore, Young Choi conducted a study called “Fructose Intolerance in IBS and Utility of Fructose Restricted Diet.” The study published in 2008 study was important because it helped to determine whether or not fructose intolerance is a cause of IBS. The objective of the study was to determine how common fructose intolerance was in the sample and to see if lifestyle changes regarding fructose intake would have an effect on IBS experienced by the patients. The researchers questioned how effective the fructose restricted diets would be for limiting IBS.

Participants in the study were referred to a tertiary care center with which the researchers worked. All of the patients presented similar symptoms including discomfort in the abdominal cavity with an unknown cause and potential IBS. Patients were not included in the study if abnormal test results for stool samples were found, if an endoscopy had been received, if the patient had been a part of hematologic or biochemical studies, or if the patient had had anything in the abdomen removed or tampered with excluding the appendix or uterus.

Initially the study had 209 patients; however 129 of the patients could not be included as they had other diagnosed causes of gastrointestinal discomfort. The final sample included 26 men and 54 women with a mean age of 42 years.

The day prior to the test fructose, lactose and high fat foods were supposed to be avoided. The night before starting the study the patients fasted. The next morning they took a fructose breath test and filled out a survey questionnaire on the type of gastrointestinal symptoms suffered as well as the severity of those symptoms. A positive fructose was achieved if the patient had a baseline hydrogen reading of 20ppm and experienced an increase of greater than or equal to 5ppm of hydrogen and or methane at least three times in a row when measured every 30 minutes for 5 hours. Those with a positive test result were deemed fructose intolerant. The patients that received a positive breath test were then given a kit that contained information regarding a fructose restricted diet.

After one year patients were asked to return and repeat the same tests and surveys. In addition, the patients were asked to answer questions regarding how strictly the diet was followed according to the guidelines and how much time was spent following the guidelines[2]. Such procedures were mirrored in the study by Gomara that was mentioned earlier[3].

The results showed that of the 80 participants, 31 had a positive fructose breath test. Greater than 90% of those with a positive test claimed that the test caused the usual gastrointestinal discomfort symptoms, which have been attributed to fructose intolerance. The patients reported that the lifestyle changes had a 2.93 out of 5 effect on their lifestyle. This denotes a mild to moderate effect. Averages were most often used to show the results. The researcher concluded that there was a correlation between the lifestyle changes and the symptoms of those in the positive test group.

A possible limitation of the study included the fact that all of the patients were referred to the researchers. In addition, of the fructose intolerant patients 46% reported not complying with the diet restrictions. Those patients also did not show improvement of symptoms after the year was up[2].

While lactose and fructose malabsorption are not the same and are often studied separately, they share many similarities, especially the symptoms produced. The next study examines the malabsorption of both sugars. CFM Gijsbers conducted research that was published in Acta Paediatrica in 2012 under the title "Lactose and fructose malabsorption in children with recurrent abdominal pain: results of double-blinded testing." The study was conducted to determine if fructose or lactose malabsorption could be the cause of recurrent abdominal pain in children.

There were 220 patients at the beginning of the study, 128 of which were female. In order to test lactose and or fructose malabsorption, patients were randomly assigned solutions of fructose or lactose by the hospital pharmacist. Doses contained 2 grams of the sugar per kilogram of body weight. The experiment was double blind meaning that neither the patient nor the person collecting data knew which sugar was consumed. If the patient had a positive hydrogen breath test meaning there was a 30 ppm over baseline increase, then they were given more fructose and lactose solutions to be consumed at home. The patients were to consume one container of solution at a time. If the solution gave the patient symptoms, the patients were to wait until symptoms were completely gone before the next day that a solution was consumed. The absence of symptoms of abdominal pain after the removal of fructose and lactose from the diet was considered indicative of fructose and or lactose malabsorption.

The lactose test was successfully completed with 210 of the 220 patients and the fructose test was successfully completed in 121 of 134 patients. The study was of value because it helped to determine that fructose and lactose malabsorption can be the cause of recurrent abdominal pain and that removing the malabsorbed sugar from the diet of the patient can help alleviate the symptoms[3]. Similar results were found in the studies by Choi and Gomara[2,3].

The previous study examined children; however the flowing study examined the elderly population. In the article “Malabsorption may contribute to malnutrition in the elderly” Terry Bolin explores the reasons for malnutrition amongst the elderly. The population from which the sample was selected consisted of elderly people recommended for rehabilitation due to malnutrition. The study suggested that a cause of malnutrition was that the bodies of the elderly did not properly absorb the nutrients from the foods consumed. 48 people participated in the study. The average age of the participants was 83.7 years with a standard deviation of 6.1 years. The majority of participants, 67%, were male and the average BMI of those in the study was 21.8 kg/m^2 with a standard deviation of 3.9. Lactulose, which will be discussed later, was used for the sugar absorption portion of the study[6].

More on the metabolism of sugars was examined in the next study. “Habitual Intake of dairy products influences serum 1,5-anhydrolglucitol levels independently of plasma glucose” is an article that describes a study conducted by Masafumi Koga that was published in the Diabetes Research and Clinical Practice in 2010. The study looked at the relationship between the intake of dairy products and serum 1,5-anhydroglucitol levels. 1,5-anhydroglucitol levels were measured in addition to blood glucose and several other measures. In addition, the subjects completed a questionnaire about eating habits.

The patients were all from the Kinki Central Hospital. Between July and August 2008 558 patients from the hospital were given a glucose tolerance test in which the patient ingested 75 g of glucose. If the patient had a normal test result, meaning that the blood glucose level test result was less than or equal to 140 mg/dL after ingestion, the patient was asked to participate in the study. The final study had 330 participants.

The study showed that there was a correlation between what the subjects typically consumed and the results of the different tests run on the patients. For instance the serum 1,5-anhydroglucitol levels were lower if the subject regularly consumed dairy products.

One limitation of the study is that eating habits were self-reported. Self-reported habits can be less accurate. Further studies were recommended as the serum 1,5-anhydroglucitol levels vary from person to person[4].

Earlier in the discussion, dietary and hereditary causes of fructose malabsorption were mentioned. The following study looked at the dietary, regional and heredity causes of lactose malabsorption through a comparison of two regions of India. In 2010 Janaki Babu had an article entitled “Frequency of lactose malabsorption among healthy southern and northern Indian populations by genetic analysis and lactose hydrogen breath and tolerance tests” published in the American Journal of Clinical Nutrition. The subjects of the study were 153 volunteers. The tests were conducted during the first 6 months of 2008.

Lactose tolerance tests, hydrogen breath tests and genetic sequencing were all used to collect data. The day before the test subjects were asked to refrain from eating starchy carbohydrates and fiber. Overnight fasting and avoidance of exercise and smoking two hours prior to the test were also avoided. Before breath hydrogen values were taken, patients were required to brush their teeth and use antiseptic mouthwash. 25 g of lactose in 100mL of water was the standard dosage. An increase in breath hydrogen of 20 ppm over baseline was considered a positive result. The researchers concluded from the data that there lactose malabsorption is more common in the southern region of India nearly 80% has a positive test as opposed to the northern region where about 57% had a positive result[11]. Further studies could be conducted to figure out why that was the case.

A major concern of lactose malabsorption is that essential minerals will not be absorbed. In a study by da Silva Mederios called “Lactose Malabsorption, Calcium Intake, and Bone Mass in Children and Adolescents” the relationship between bone mass and calcium intake was compared to lactose absorption. This study was completed in Sao Paulo, Brazil and looked at a convenience sample of children and adolescents. There were five criteria for those participating in the study. These included being five years of age or older, no diarrhea in the past 28 days, lack of antibiotic use, lack of laxative or enema product usage in the past month, abstinence from medicines that alter bone or calcium in the body, and parental consent.

Firstly the children were measured for anthropometric data such as height and weight. This data was analyzed using the EpiInfo program, version 3.4.3. The children were then given a hydrogen breath test which was used to determine whether or not they were an absorber of calcium or malabsorber. The night before, they were asked to eat white rice with chicken and not to eat after the meal. Before the breath tests the parents were asked to fill out a symptom form for their child. This is a potential source of bias as the parents cannot feel what their children do. The children washed their mouth with antiseptic mouthwash prior to the test.

In addition to the breath test a 24 hour recall was conducted for a weekday and a second for a weekend. This data was evaluated using System from Nutritional Decision, version 1.5. Lastly the bone density of the subjects was measured using the facility of Image Diagnostics Center of the Oncology Pediatric Institute and the DPX-IQ Lunar equipment. Tests for the entire study used chi squared and the Fisher exact test to make comparisons. In addition to the aforementioned EpiInfo analysis, Jandel Sigma Stat 3.5 was used.

Out of the 86 subjects who met the requirements, 76 were used in the study. The remaining 10 subjects were excluded to issues that could have compromised the validity of the study. The subjects included in the study were between the ages of 5 and 12 years. Approximately 67% were white and 33% were mixed. The study showed that 29 of the 76 participants could readily absorb lactose and 47 of the 76 participants had difficulty absorbing the sugar. The bone in the absorbers and malabsorbers showed little physical or chemical difference. Nine samples were collected during the 80 minute period. Two grams of lactose per kilogram of body weight were provided.

Most of the studies on calcium absorption focus on adult populations, however, this study was one of the few that looks at the younger population. While some studies ace found that the calcium intake was much lower among the lactose intolerant, this study did not support that theory. The statistics collected in this study also did not show a difference in bone density between the two groups[1].

Many researchers are concerned about the discomfort caused by lactose malabsorption, particularly with regards to children. In 2012 an article called “Short- and long-term effects of a lactose-restricted diet and probiotics in children with chronic abdominal pain: A retrospective study" was published in Complementary Therapies in Clinical Practice. The lead researcher was L.E. Ockeloen. The study was conducted to determine the short and long term effects of limiting lactose intake on children with chronic abdominal pain.

This study was retrospective and was conducted using a database of 91 children between the ages of 1 year and 18 years. The researchers examined the symptoms recorded and followed the various treatments for the abdominal pains cause by the ailments lactose intolerance and or SIBO. The treatment charts were used to collect the data that was used in the study. The data was evaluated with the McNemar test. Just over 40% of the children had a positive hydrogen breath test. About 60% of children showed improvement of symptoms following treatment. The results of the study imply that restricting lactose from the diets of children with chronic abdominal pain decreases the symptoms suffered[12]. That information is valuable as it suggested that by limiting lactose in the diet, the pain suffered by afflicted children could be reduced.

Diet can be a great way to regulate the negative effects of lactose intolerance; however, there can be negative consequences when a person has self-perceived lactose intolerance and cuts important foods from a diet. Theresa Nicklas conducted a study that published in the American Journal of Clinical Nutrition in 2011. The article describing the study was entitled "Self-perceived lactose intolerance results in lower intakes of calcium and dairy foods and is associated with hypertension and diabetes in adults." The study was based on the idea that when people have the belief of suffering from lactose intolerance people were more likely to exclude dairy from the diet. Avoidance of dairy products could result in insufficient intake of calcium in the diet, as well as increased body weight and likelihood of having diabetes, colon cancer and elevated blood pressure.

The study was conducted using a variation of the Nominal Group Technique meeting. Participants were selected based on race and ethnicity because diverse population was desired for the study. The questionnaire survey was distributed via telephone. Interviewers were trained to do the interviews and were systematically monitored during the study. Phone calls took less than 15 minutes on average and were conducted between January and October 2009. The interviewers called potential participants up to 15 times. Overall the response rate of those called to participate in the study was 25%. Despite the low response rate, the sample size could still be used because it was so large.

The sample from which results were drawn consisted of 3,452 people. The sample was slightly over 30% male and slightly less than 70% female. The sample was 47.74% non-Hispanic white, 27.75% non-Hispanic black and 24.51% Hispanic. The data concerning demographics and self-perceived lactose intolerance was analyzed using chi squared tests. Other regression models were used to look at the relationships between calcium intake and other variables.

The study showed that those who thought they were lactose intolerant avoided dairy foods more frequently. In addition, women were more likely to think that they were lactose intolerant than men. About 50% of those with self-perceived lactose intolerance were non-Hispanic blacks as opposed to the 30% of non-Hispanic whites and 20% of Hispanics[13].

Other researchers were also interested in the effects of self-perceived lactose intolerance. A study by Leann Matlik published in 2007 called "Perceived Milk Intolerance Is Related to Bone Mineral Content in 10- to 13- Year-Old Female Adolescents" examined the relationship between mineral content in the bones of adolescent female and perceived milk intolerance.

230 girls received breath-hydrogen tests for lactose. The girls were required to fast for 12 hours prior to the test and were provided a low fiber, lactose free dinner the night before the test. The dose of lactose was. 35 g per kilogram of bodyweight and hydrogen samples were taken at 30 minutes after consumption for baseline and every hour for three hours.

The heights and weights of the girls were measured and then the BMI of each girl was calculated. The volume of lactose received during the test was based on the weight of the girl. The girls were asked to self-assess their pubic hair and breast development stage using diagrams provided by the researchers. Bone mineral composition density and body composition were both measured using phantom scans. These results were analyzed in a double blind setting to reduce bias. Girls also completed a perceived milk intolerance questionnaire to determine whether or not it was believed that milk intolerance was present. Food frequency questionnaires were distributed in order to deduce how often dairy was consumed.

The researchers used SPSS for Windows 12.0 to analyze the data. Out of the 246 completed surveys, 47 surveys were completed by girls with perceived lactose intolerance. The girls with perceived milk intolerance consumed considerably less dairy products. Similarly, the girls with perceived milk intolerance lower body mass compositions. The effect of perception varied with regards to the densities of different bones.

Girls that had perceived milk intolerance consumed less calcium. The researchers concluded that it is important for long term bone health that sufficient calcium intake happens during the adolescent years. For that reason the researchers were of the opinion that proper education regarding calcium intake and proper diagnosis of lactose intolerance would benefit bone health[14].

Overall, diet can be a great way to control lactose intolerance. "Systematic Review: Effective Management Strategies for Lactose Intolerance" is an article that was published in Annals of Internal Medicine in 2010. The goal of the study by Aasma Shaukat was to determine the "maximum tolerable dose of lactose" and then study management strategies that allow the patient to consume more than the maximum dose. The subjects were either lactose intolerant or lactose malabsorbers. Data was selected, extracted and assessed by three investigators.

Series of studies were reviewed to collect data. Therefore the researchers retrieved their data from previous studies and compiled it for the use of the study being conducted. The data was then combined and used answer the initial questions of the study. Only studies where lactose was consumed without other nutrients were included because the other nutrients can affect the absorption.

The researchers believed that one of the greatest limitations of the study was that the participants were most often lactose malabsorbers, not lactose intolerant. The researchers think that more studies should be conducted and that a standard form of assessment should be adopted[15].

As it was frequently mentioned in the studies above, it is clear that hydrogen breath tests are common in the analysis of fructose and lactose malabsorption and intolerance. In 2009 a very insightful research article by John Bate was published. "Benefits of breath hydrogen testing after lactulose administration in analyzing carbohydrate malabsorption" made several great suggestions that could behoove the hydrogen breath test as a whole. Bate suggested the use of lactulose. Lactulose consists of fructose and galactose and is made by man. Since it is unnatural and the body does not have a predetermined way to break it down, hydrogen is always produced as it is fermented in the small intestine. This offers as a great benchmark level of hydrogen production due to the fact that it is not absorbed. The hydrogen breath test conducted using lactulose can be used as a baseline for hydrogen breath tests using other sugars such as fructose or lactose. The results from the lactulose offer a more personalized and accurate baseline for comparison because everyone has different metabolic rates and individual baselines help to acknowledge that and therefore collect more accurate data.

The population used in the study with lactulose was 200 patients from the Gastrointestinal Physiology Service of Box Hill Hospital. Two separate days of trials were conducted. On the first, the patient was given a hydrogen breath test using lactulose. On the next trial day fructose or lactose was used. Patients were not allowed to consume fermentable substrates an entire day before the test. They were required to fast overnight. Doses varied between sugars but were all administered in 200 mL of water. 15g of lactulose, 35g of fructose and 50g of lactose were the standards. Readings were taken every 15 minutes for 2 or more hours. Fisher's exact test and Mann-Whitney U test were used to assess the data. The test results from the lactulose were related to those of the fructose and lactose tests[16].

Materials and Methods

After reviewing the literature the procedures from eight studies published between 2008 and 2012 were used to create the standard method. Compiling data was also done in the study by Ockeloen[12]. The methods were compiled into Table 1. Common trends were observed and the most effective methods were determined. Once the best practices were selected the compilation in the creation of a standardized tool.

Results

The standardized tool can be seen in Figure 1. The standardized tool is actually a form with guidelines that are to be followed and that is meant to be filled out by the physician or researcher. Optimally, the test form will be electronic. Each patient will be given an ID number so that their information is confidential. If electronic, the form can be submitted to a database where all of the results can be compiled. This compilation will allow researchers to analyze data and observe trends. Such trends can be used to better understand malabsorption and intolerance. This process could be facilitated by creating an app. The app would contain the meal choices, the test form and the procedure instructions. During the test the physician could enter the patient data directly into the app form which would be loaded on to an icloud database. By creating a database via the icloud all physicians would have access to the data, allowing them to compare results. Patient identities would remain confidential as each patient would be assigned an identification number known only to the physician providing analysis.

It was common in the studies reviewed for the subjects to be asked to avoid high fat meals and foods containing fructose and lactose the day before testing (Table 1). The purpose of the request is to avoid results being skewed from hydrogen production from the breakdown of the meals of the previous day. In the study of children in San Paulo, Brazil Lilian da Silva Medeiros requested that children eat white rice with ground chicken that had been fried or roasted as the last meal before the test. The simplicity of that meal made it easy to obtain. The meal is also low fat and does not contain lactose[1]. The fact that all of the patients have the same last meal adds to the consistency of the study.

In order to increase consistency and decrease stress to the patients trying to follow the dietary guidelines on the day before the test prepackaged meals should be provided**.** Three square meals and optional snacks shall be given to the patient to consume on the day before the test. The meals will be prescribed by the physician and will be low fat and lactose free. There shall be a list of meal options from which the patients can select meals. The meals will be known to the physician and the nutrient content will be easily accessible. The patient will not be required to consume the entire meal as the meals are only to ensure that the low fat, lactose free guidelines are followed.

The compilation of fructose recipes and appendices from *The Sugar Fix* would be a great reference to provide patients for the day before the test and for a fructose free diet. *The Sugar Fix* by medical doctor Richard J. Johnson is a book describing the negative influence of fructose has on the human body[17]. The recipes that have lactose or that are high fiber should be excluded or the ingredient should be substituted.

The meals consumed should be recorded. Notes may be added regarding how much of the food was consumed, but it is not necessary. If high fat foods or foods containing lactose were consumed, the patient must come back for testing another day having followed the procedures properly. The form has a specific box asking if the patient has followed the dietary restrictions.

The patients should fast from 10:00pm. The studies suggested different times, such as after last meal or from midnight (Table 1). 10:00pm has been selected as it allows those who eat late to have dinner while still allowing ample fasting time, but pinpoints a standard time for patients to stop eating.

Smoking and exercising are prohibited from bedtime. This was consistent in many of the studies because the aforementioned activities effect the volume of hydrogen produces, excess hydrogen can skew the results.

The sex of each patient should be recorded as should the height, weight and waist circumference for comparative analysis. Fasting blood glucose and iron levels should be measured as well because the tests are easy to preform and may prove useful in later studies.

Recording those measures for later analysis is not time consuming or expensive. Trends relating iron and glucose levels to intolerance may be observed if they are regularly recorded.

As shown done in several of the studies, the mouths of the patient should be sanitized in order to prevent the bacteria in the mouth from affecting the results. Teeth should be thoroughly brushed and antiseptic mouthwash should be generously used. The form provides a safeguard to ensure this is done.

The majority of studies conducted research using solutions of fructose or lactose in water. Several studies used lactulose as a constant as it is always malabsorbed. The sugar solutions posed an issue in some studies when patients refused to drink the solution. In order to combat that issue and to more accurately reflect the ways the sugars are found in nature, it was suggested that real food should be used in the tests. For example, raisins would be used to measure fructose intolerance and milk could be used to measure lactose intolerance. The sugar solutions are highly concentrated and do not reflect their naturally found counterparts. However, using real foods would pose many issues like making sure the same concentration of sugar was in each dose and the other component of the real food ma effect the result. Therefore even though using actual food with predetermined sugar values would be more appealing to the patient and more reflective of actual sugar intake, the sugar solution will still be used.

Several of the studies assigned sugar intake based on mass in kilograms. The most common assignments were 0.5 g per kg of body weight for fructose and 2 g of lactose per kilogram of bodyweight. While this is consistent with mass, it is not reflective of actual intake because a 45 kg person is going to eat one serving of something with a certain amount of sugar just as a 60 kg person. For that reason a set amount of sugar was assigned.

Baseline will be measured at 0 minutes and breath hydrogen will be measured every 30 minutes for three hours. An increase of 20 ppm over baseline constitutes a positive result. All data collected should be entered into the form provided. This form shall be completed electronically so that it can be saved by the doctor and submitted to a database.

Conclusion

All things considered, there have been significant advances in the acknowledgment and study of sugar malabsorption and intolerance issues. While more studies have been conducted on lactose, fructose related issues are becoming more prevalent. The increased prevalence is like due to the increase of fructose consumption[2]. While there are no apparent problems with not consuming fructose, several of the lactose studies suggested that calcium deficiencies could result in the avoidance of dairy[13,14].

A standard test for lactose and fructose intolerance and malabsorption should be adopted. The test should begin with a night of fasting. A hydrogen breath test using lactulose should be conducted for continuity. The results of the test could be used as the baseline hydrogen values of the patient. A standard food frequency questionnaire should be distributed to gather data about the sources and quantities of fructose and lactose consumed. In addition, follow up hydrogen breath tests using fructose and lactose should be conducted.

By using a standard test, it would be easier to analyze and compare the results. In addition a standard diagnosis could be created. This would make it easier to determine the sugar absorption of an individual. After a standard is set, more studies on fructose and lactose could be conducted. If the causes of sugar malabsorption and intolerance are all determined, researchers could work towards a solution to avoid the negative effects produced by the malabsorption and intolerance.

This tool will be helpful in consistently determining cases of fructose and lactose intolerance and malabsorption. By adopting a standard procedure, people will be able to more easily understand tests and the results of the test[7]. This is especially important during this time where there has been an increase in cases of fructose intolerance.[2] The standardized method will be beneficial to those with lactose intolerance, too.

In order to be successful, this system must be adopted and used on a wide scale. This would begin by having an app created for physicians and researchers to use. This app would allow scientists to save data to the database and access information from other patients to compare and contrast. Due to the standardized protocol, results from all studies would be possible to accurately compare.

Hopefully, this database would provide information that would lead to further studies involving the control and treatment of fructose and lactose intolerance and malabsorptive issues. The overall quality of life of those who have such issues would be improved as symptoms such as symptoms such as gas, bloating, diarrhea, vomiting and nausea[1,2] would decrease or be alleviated all together. By standardizing the testing procedures, scientists will be one step closer to being able to treat lactose and fructose intolerance and malabsorption.

Figure 1

Fructose and Lactose Malabsortpion and Intolerance Test Sheet

Patient ID:________________________ Patient DOB:____________________________ ☐male ☐female

Height:_______feet __________inches Weight:_______pounds Waist circumference:_________inches

Signs and symptoms: (check all that apply)

☐Bloating ☐Constipation ☐Diarrhea ☐Gas ☐Headache ☐Indigestion

☐Nausea ☐Vomiting ☐Other (please describe)____

Has the patient smoked since waking up? ☐yes ☐no (if yes please ask the patient to return another day for testing)

Has the patient exercised since waking up? ☐yes ☐no (if yes please ask the patient to return another day for testing)

Has the patient followed the dietary guidelines? ☐yes ☐no (if no please ask the patient to return another day for testing)

Please select the ID numbers of the meals consumed:____

____

Fasting blood glucose:_____________________mg/dL Hemoglobin:_____________________________g/dL

Has the patient thoroughly brushed their teeth and sanitized their mouth using antiseptic mouth wash? ☐yes ☐no (if no, have the patient do so now)

Sugar being tested: ☐fructose ☐lactose ☐lactulose

	Reading ppm	Notes (signs and symptoms)
0 minutes (baseline)		
Has the patient consumed 25g of the sugar mixed with 200mL of water? ☐yes ☐no (if no, have the patient do so now)		
15 minutes		
30 minutes		
45 minutes		
60 minutes		
75 minutes		
90 minutes		
105 minutes		
120 minutes		
135 minutes		
150 minutes		
165 minutes		
180 minutes		

If there was an increase of at least 20ppm over the baseline the test is positive.

Did the patient have a reading with a 20ppm increase over baseline? ☐yes ☐no

Will the patient be tested for or have they been tested using other sugars? Check all that apply:

Have been tested using: ☐fructose ☐lactose ☐lactulose

Will be tested using: ☐fructose ☐lactose ☐lactulose

Table 1

Primary researcher, year	Sugar Tested	Subjects	Pre-Test	During Test	Results
Gomara, 2008	fructose	32 (50/50 male/female) subjects with IBS, functional dyspepsia, or functional abdominal pain syndrome between 7 to 17 years	avoid foods with high fat content, lactose or fructose for 24 hours post test. Fast from midnight before test. Complete bowel symptom survey. Take base breath hydrogen	1g fructose (control) 15g fructose (juice dose) 45g fructose (comp to previous study) Report symptoms, measure breath hydrogen (>20ppm over baseline is positive)	33% had positive test overall; 0 positive 1g; 33% (3/10) positive 15g; 61% (8/13) positive for 45g +more frequent symptoms
Bate, 2010	lactulose, fructose and/or lactose	200 subjects (150 females, 50 males); 5-88 years range, mean 39; 69IBS, 16 functional bloating, functional 7 constipation, 5 functional diarrhea, 11 unspecified bowel disorder, ...	avoidance of fermentable substrates 24hours pre test. Fast overnight. Baseline breath hydrogen.	in 200mL water: 15g lactulose then 35g fructose and/ or 50g lactose at least two days apart. Measure breath hydrogen every 15 minutes for at least two hours.	52% definite or borderline FM; 36% definite or borderline LM; 15% both definite; 38%neither
Ockeloen, 2011	lactose	91 database subjects age 1-18years		2g lactose; breath hydrogen measured at intervals for 3 hours; 20ppm over baseline+symptoms is positive lactose intolerance	37 children (41%) abnormal test result used in study; 5 incomplete data or lost; 18 lactose intolerance; 10 SIBO; 4 SIBO and intolerance; 4 lactase deficiency
CFM Gijsbers, 2012	lactose or fructose	220 subjects (128 female, 92 male), 4.1-16 years, RAP (recurrent abdominal pain)	baseline breath hydrogen	breath test with 20ppm over baseline is positive; 2 doses of 25g or fructose or lactose were taken home and patients were to take them one at a time. Consumption of second was to occur after stop of symptoms from the first.	210/220 completed lactose tests; 121/134 completed fructose tests (some refused to drink)
Choi, 2008	fructose	229 subjects, became 80 after exclusions; 26 male, 54 female; 20-76years, mean 42years	no high fat, lactose, or fructose containing foods for day before test, fast from midnight, no smoking, baseline breath hydrogen	25g fructose in 250mL water; breath hydrogen measured every 30 minutes for five hours; increase of >/= 5ppm for three or more tests OR >20ppm over baseline =positive; symptoms recorded	33% positive tests
da Silva Medieros, 2012	lactose	76 subjects between 5 and 12 years	measure height and weight; white rice and ground fried or roasted chicken as meal night before test, fast after meal; oral hygiene conducted before test to prevent false data; baseline breath hydrogen; 2 24hour food recalls completed by parents	180 minutes with breath samples every 15minutes (9 samples); lactose after baseline was given in dose of 2g/kg body weight with 50g max; lactose malabsorption is positive if >20ppm over baseline increase	61% (47/76) showed lactose malabsorption; median consumed less than AI calcium in all age groups
Babu, 2010	lactose	153 volunteers from India (76 south, 77 north)	carbs and fiber avoided for last meal before overnight fast; no smoking or exercise two hours pretest; brush teeth and rinse mouth to avoid incorrect baseline; avg of four readings taken for baseline	25g lactose in 100mL water; breath hydrogen every 15minutes for three hours; rise of 20ppm over baseline for two readings =abnormal result	60/76 south (78.9%) and 44/77 north (57.1% had lactose malabsorption
Jones, 2011	fructose and lactose	1093 fructose subjects, 3073 lactose subjects	low fiber evening meal, at least an 8 hour fast; no smoking or exercising morning of	.5gfructose/1kg body weight up to 10g fructose in 100mL water or 80mL for children less than 6months; 2glactose/kg body weight up to 20g lactose; breath collected every 30 minutes for 150minutes; positive fructose malabsorption increase of 10ppm for two consecutive readings or final reading >10ppm over lowest value before 60 minutes	50% fructose tests positive for malabsorption; 39.3% lactose tests were positive

Works Cited

1. da Silva Mederios, Lillian C., et al. "Lactose Malabsorption, Calcium Intake, and Bone Mass in Children and Adolescents." *Journal of Pediatric Gastroenterology and Nutrition* 54.2 (2012): 204-09. Web. 2013.
2. Choi, Young K., et al. "Fructose Intolerance in IBS and Utility Fructose-Restricted Diet." *J Clin Gastroenterol* 42.3 (2008): 233-38. Web. 2013.
3. Gomara, Robert E., et al. "Fructose Intolerance in Children Presenting With Abdominal Pain." *Journal of Pediatric Gastroenterology and Nutrition* (2008): 303-08. Web. 2013.
4. Koga, M., Murai, J., Saito, H., Mukai, M., & Kasayama, S. (2010, July 14). Habitual intake of dairy products influences serum 1,5-anhydroglucitol levels independently of plasma glucose. *Diabetes Research and Clinical Practice*, 122-125. Retrieved 2013.
5. Gijsbers, CFM., Et al. "Lactose and fructose malabsorption in children with recurrent abdominal pain: results of a double blind test." *ACTA Pediatica* (2012): e411-15. Web. 2013.
6. Bolin, T., et al. (2010). Malabsorption may contribute to malnutrition in the elderly. *Nutrition*, *26*, 852-853. doi:10.1016/j.nut2009.11.016
7. Barrett, J. S., & Gibson, P. R. (2012, May). Fructose and lactose testing. *Australian Family Physician*, *40*(5), 293-296. Retrieved September, 2013
8. Caciotti, Anna, et al. "Different genotypes in a large Italian family with recurrent hereditary fructose intolerance." *European Journal of Gastroenterology & Hepatology* (2008): 118-21. Web. 2013
9. Jones, H. F., et al. (2011, May). Effect of Age on Fructose Malabsorption in Children Presenting With Gastrointestinal Symptoms. *JPNG*, *52*(5), 581-584. doi:10.1097/MPG.0b013e3181fd1315

10. Sartorelli, D., et al. (2008). Dietary Fructose, fruits, fruit juices and glucose tolerance status in Japanese-Brazilians. *Elsevier*, 77-83. doi:10.1016/j.numecd.2008.04.004

11. Babu, J., et al, (2010). Frequency of lactose malabsorption among healthy southern and northern Indian populations by genetic analysis and lactose hydrogen breath and tolerance tests. *American Journal of Clinical Nutrition*, *91*, 140-146. doi:10.3945/ajcn.2009.27946

12. Ockeloen, L., & Deckers-Kocken, J. Short- and long-term effects of a lactose-restricted diet and probiotics in children with chronic abdominal pain: A retrospective study. *Complementary Therapies in Clinical Practice*, *18*, 81-84. doi:10.1016/j.ctcp.2011.11.002

13. Nicklas, Theresa A., Et al. "Self-perceived lactose intolerance results in lower intakes of calcium and dairy foods and is associated with hypertension and diabetes in adults." *The American Journal of Clinical Nutrition* (2011): 191-98. Web. 2013.

14. Matlik, L., Savaiano, D., McCabe, G., VanLoan, M., Blue, C. L., & Boushey, C. J. (2007, September). Perceived Milk Intolerance Is Related to Bone Mineral Content in 10- to 13-Year-Old Female Adolescents. *Pediatrics*, *120*(3), e669-e677. doi:10.1542/peds.2006-1240

15. Shaukat, A., et al. (2010, June 15). Systematic Review: Effective Management Strategies for Lactose Intolerance. *Annals of Internal Medicine*, *152*(12), 797-803. Retrieved 2013.

16. Bate, J. P., et al. (2010). Benefits of breath hydrogen testing after lactulose administration in analyzing carbohydrate malabsorption. *European Journal of Gastroenterology & Hepatology*, *22*, 318-326. doi:10.1097/MEG.0b013e32832b20e8

17. Johnson, R. J., & Gower, T. (2008). *The Sugar Fix*. New York, NY: Pocket Books.