



4-8-2019

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Running head: BENEFITS OF A PLANT BASED DIET, CHOLECYSTITIS

Benefits of a Plant Based Diet For Prevention of Cholecystitis

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PERMISSION

Title The Benefits of a Plant Based Diet of Prevention of Cholecystitis

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Degree Master of Science

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Abstract

Cholelithiasis, or the formation of gallstones, is a worldwide problem, but much more common in the Western and European countries. 90-95% of gallstones are composed of cholesterol. This case study reviews a 47 year old that presents to the clinic for evaluation of right upper quadrant and epigastric pain that radiates to the back. The patient has many risk factors for cholelithiasis including type 2 diabetes mellitus, poorly controlled hypertension, obesity, and regular alcohol consumption of at least two drinks daily. Literature review largely agrees that the traditional “Western” diet that favors increased caloric intake, increased cholesterol, increased sugar, fatty acids, meat and carbohydrates is a more favorable predictor of gallstone disease while diets that are high in unsaturated fat, fiber, and fresh fruits and vegetables have been linked to reduced risk of gallstones. More notably, a higher intake of fibers and polyphenols, or compounds commonly found in plants, has been linked to a rightful balance in the gut microbiota, which lessens the risk of gallstone formation, while diets high in fat cause increased secretion of bile, which has an antimicrobial affect on the normal microbiota of the bowel. Ultimately, increased consumption of fruits and vegetables in the diet lessens the likelihood of gallstone formation and supports the normal balance of gut microbiota.

Background

This case study reviews a 47-year-old patient who is presenting to the clinic for the chief complaint of right upper quadrant pain and epigastric pain that radiates to the right back, as well as right shoulder pain. The patient has a history of type 2 diabetes mellitus, poorly controlled hypertension, obesity, and regular

alcohol consumption of at least two drinks daily. On exam, the patient is noted to have right upper quadrant tenderness and a positive Murphy's sign.

While gallstone disease is considered a worldwide disease, its incidence is far higher in Western and European countries than in other countries of the world, affecting about 10-15% of adults. Acute cholecystitis is caused by gallbladder stones in 90-95% of cases (Yokoe, et al., 2017). These stones may lead to the obstruction of the cystic duct, which based on duration, lead to far more serious complications if not attended to swiftly. Gallstones are classified according to what they are composed of. Following cholecystectomy, nearly 90% of gallstones are typically found to be of the cholesterol type (Qihan Wang, et al. 2017).

The following case study and literature review will address the impact of a plant-based diet on the prevention of cholecystitis. It is well established that plant-based diets have been linked with lower total cholesterol levels and lower low-density lipoprotein (LDL) levels (Chang, et al., 2019). But what is the impact of a plant based diet on the occurrence of cholelithiasis?

Case Report

Chief Complaint: Abdominal Pain

History of Present Illness

This very pleasant 47-year-old female presents to the clinic today for the chief complaint of abdominal pain with an onset of last evening following her evening meal, about 12 hours ago. The patient describes the location of the pain as being epigastric and in the right upper quadrant. The pain has been ongoing since last night and progressively worsening. The patient describes the pain as being dull

in nature, about and 8-9/10 on the pain scale. The patient reports that sitting “hunched over” or lying on her side seems to alleviate some of the pain, while movement and lying supine aggravates the pain. The patient states that the pain radiates around to the back, with pain in the right shoulder. The patient reports a food like emesis, followed by two bilious emeses since last evening. The patient reports a subjective fever. The patient states that she has had similar episodes in the past following meals, but these have resolved within several hours.

Allergies: NKDA

Medical History: Diabetes mellitus type 2, hypertension, and obesity

Surgical History: None

Medications: Losartan 50mg daily, Metformin 1000 mg daily

Social History: Works as a financial consultant, lives at home with her husband, drinks 1-2 glasses of wine at dinner nightly. Negative history of drug or tobacco use. The patient states that she does not exercise. Diet consists of “what the kids like to eat – mac 'n' cheese, spaghetti and meatballs – comfort food like that”.

Family History: Father died of a stroke when he was 65. Mother has history of gallstones.

Review of systems revealed a normal appetite up until the event of onset, as well as a subjective fever, nausea, vomiting, and right upper quadrant and epigastric pain. The patient denied any change in stool color or blood in the stool. The patient denied any urinary symptoms.

Physical exam revealed active bowel sounds in all four quadrants and tenderness to palpation of the right upper quadrant, as well as a positive Murphy's sign. Tenderness to palpation of the right flank was noted.

Vital signs

Temp: 99.5°F **BP:** 186/100 **HR:** 102 **Resp:** 20 **BMI:** 30 kg/m²

Assessment: Right upper quadrant pain

Plan:

Diagnostic studies ordered included an ultrasound of the abdomen (positive for gallstone disease, negative for pancreatitis), Alkaline phosphatase, GGT, total and direct bilirubin (all were elevated with this patient), AST and ALT (both elevated), a CBC (WBC elevation), an amylase and lipase (WNL), a comprehensive metabolic panel (WNL), and an ERCP (positive for gallstones at the bile duct).

Diagnosis: Acute cholecystitis

General surgery was consulted with the above findings, as they were suspicious of cholecystitis. Following consultation, the patient was scheduled to have a laparoscopic cholecystectomy that same evening. In follow-up, careful emphasis was placed on monitoring the patient's blood pressure over the course of 7 days. If the blood pressure average had not decreased at that time, the plan would be to initiate an increase in the patient's dose of losartan, from 50 mg to 100 mg daily. Consultation with a dietician would be initiated, as well as immediate lifestyle modification suggestions for diet consisting of the DASH diet and exercise of 150 minutes weekly as recommended by the Centers for Disease Control and Prevention.

Literature Review

Numerous databases were searched, including CINAHL, Clinical Key, and COCHRANE, with the results narrowed to focus articles and research within the past 5 years using the following terms: cholelithiasis, cholelithiasis + diet, gallstones, cholecystitis, gut microbiota.

Cholecystitis is defined as the acute or chronic infection of the gallbladder. It is often associated with cholelithiasis, or formation of gallstones. Cholelithiasis is considered a worldwide disease, its incidence far higher in Western and European countries than in other countries of the world, affecting about 10-15% of adults in those countries. There are many risk factors that can contribute to gallstone disease including being of the female sex, increasing age, an increased body mass index, hyperlipidemia, alcohol consumption, and diabetes mellitus (Chang, et al., 2019). In the case study presented above, the patient was found to have many of these risk factors.

Cholelithiasis is not the only complication of gallstones. Serious complications can arise when the gallstones block the common biliary duct through which bile flows. When this duct is blocked bile and pancreatic enzymes are not able to flow well into the intestines leading to pancreatitis and damage to the liver. The inflammation caused by gallstones is thought to be a major cause of gallbladder cancer in the United States every year.

Acute cholecystitis is caused by gallbladder stones in 90-95% of cases (Yokoe, et al., 2017). These stones may lead to the obstruction of the cystic duct, which based on duration, lead to far more serious complications if not attended to

swiftly. Many people are unaware that they have gallstones, as often they cause no symptoms. In fact, up to 80% of people with gallstones never know that they have them (Kenney, 2018). However, for those that experience symptoms of gallstone pain, the treatment is most often the surgical removal of the gallbladder or a cholecystectomy. Cholelithiasis has become so prominent in our society that the most common elective abdominal procedure performed in the United States is now the cholecystectomy, with approximately 750,000 performed annually (Kenney, 2018).

Type of Stones

Gallstones are classified according to what they are composed of. Following cholecystectomy, nearly 90% of gallstones are typically found to be of the cholesterol type in the United States (Qihan Wang, et al. 2017). The remaining types of gallstones are composed mainly of calcium salts of bile pigments or activated by parasitic infection.

The exact factors that contribute to the formation of cholesterol gallstones are not well identified, but genetics, increased secretion of cholesterol from the liver, bile super saturated with cholesterol, and a slow-moving gallbladder caused by crystals made of precipitating cholesterol all have been found to contribute to this type of gallstone (Chang, et al., 2019). Thus it is logical to look to the impact of blood cholesterol levels on gallstone development. It is well established that plant based diets have been linked with lower total cholesterol levels and lower low-density lipoprotein (LDL) levels as well as decreased incidence of hypertension,

metabolic syndrome, diabetes mellitus, ischemic heart disease, diverticular disease, and colorectal cancer (Chang, et al., 2019).

Fundamentally, cholesterol type gallstones are the result of one fact: the bile is supersaturated with cholesterol. Because cholesterol is composed of lipids, it dissolves inadequately in water. It is the role of bile to keep cholesterol from precipitating by providing emulsification. Gallstones are prevented as the bile softens or emulsifies the cholesterol. If there is not a good balance or a good ratio between bile and cholesterol, cholesterol starts to form crystals that eventually form sludge. As the crystals in this sludge grow larger they have potential to develop into gallstones. Thus, when the cholesterol content increases and the bile acid decreases, the ratio is disturbed and the risk of that cholesterol forming a precipitate, and then gallstones, increases (Kenney, 2018). Multiple risk factors for this phenomenon exist including obesity, dyslipidemia, type 2 diabetes, non-alcoholic fatty liver disease, advanced age, female sex, pregnancy, rapid weight loss, and increased intestinal absorption of cholesterol (Nissinen, et al., 2017). A higher intake of animal products that have increased saturated fats and cholesterol increase the ratio of cholesterol to bile and subsequently gallstone formation. In comparison, statin drugs reduce the production of cholesterol by the liver ultimately reducing the risk of gallstone formation (Kenney, 2018).

Impact of Diet on Cholelithiasis

For decades, there has been research concerning the prevalence of gallstone formation in developing countries of the world whose primary diets have progressively become more “Westernized”. East Asia populations have seen a

significant rise in the percentage of cholesterol rich gallstones, and a very steady decline in other type of gallstones, as the diet of the population has become more and more similar to Western society. The country of Saudi Arabia has an even more dramatic story to tell. In the 1950-1960's it was not uncommon for the largest hospital in the country to not remove a single gallbladder in an entire year. Between 1977 and 1988 there was a tremendous escalation in a more Western civilization diet including dietary fat, cholesterol, sugar, and calorie intake all increasing significantly, while the intake of whole grains and fiber declined by 75% (Kenney, 2018). By the 1990's, cases of cholecystectomies had increased by 978% (Bertola Compagnucci, et al., 2016). Similar findings have been observed in India, where a case-control study found that increased caloric intake was a risk factor for gallstone development, with fat intake a risk factor found only related to men. In Japan, an increase in gallstones has been noted over the last 50 years, during which there has been a significant increase in fat intake and decrease in vegetables and fruit consumption. In contrast, Iran has historically been noted to have a decreased prevalence of gallstone development, which has been linked to a diet that is high in vegetables, fruit, dairy, and grains, and otherwise lacking meat (Bertola Compagnucci, et al., 2016).

The diet of Western society tends to favor increased caloric intake, increased cholesterol, increased sugar content, fatty acids, and carbohydrates. Both Kenney (2018) and Bertola Compagnucci et al. (2016) emphasize that these factors significantly contribute to increased risk for gallstone formation. In comparison, those diets that are high in levels of fiber, ascorbic acid, unsaturated fat, vegetables,

protein, nuts, whole grains, and calcium reduce this risk (Bertola Compagnucci, et al., 2016). Pak & Lindseth support this theory, stating that diets high in unsaturated fat, coffee, fiber, ascorbic acid, calcium, fish oil, and fresh fruits and vegetables have been found to reduce the risk of gallstones (2016). As mentioned above, obesity is a common risk factor for developing gallstones. However, in 2018, Kenney cautioned against rapid weight loss using diet shakes, extremely low caloric diet, or bariatric surgery as all of these factors were found to lead to a high risk of forming gallstones. Kenney recommended that weight loss that is done slowly on a “healthful, minimally-processed, plant-rich diet” reduces the risk of gallstones forming” (2018).

Not all studies came up with these similar findings. Chang et al. reports that, while some literature has proposed that increased fruit and vegetable consumption in women reduces the risk of having a cholecystectomy, the results of a European EPIC-Oxford study showed that a total vegetarian diet was actually a risk factor for symptomatic gallstone disease (2019). In 2016, McConnell supported this risk factor, reporting that there was a small increase in the likelihood that vegetarians would develop gallstones versus non-vegetarians. This did take into account the fact that a higher BMI can contribute to a higher incidence of gallstone disease as well. Another consideration was the increased consumption of starches that may lead to increased prevalence of gallstones in vegetarians.

While there have been consistent links between increased prevalence of gallbladder disease and higher intake of calories and fat, Chang et al. reports that a vegetarian diet lessens symptomatic gallstone disease by directly lowering the cholesterol level (2019). In a study examining the risk of symptomatic gallstone

disease in Taiwanese vegetarians and nonvegetarians, they found that a vegetarian diet was correlated with decreased risk of symptomatic gallstone disease in women, but not in men. Ultimately, this study indicated that a vegetarian diet in women could powerfully protect against gallstone formation in those women with normal cholesterol levels, but not in men of the same status (Chang et al., 2019).

Biliary Microbiota

Another factor that is demanding more presence in literature is the abundance of gut microbiota, or normal flora found in the digestive system, during the process of gallstone formation (Qihan Wang, 2017). The significant increase of gut microbiota contributes to metabolic imbalance of cholesterol and bile acid (Shabanzadeh et al., 2017). Patients who develop gallstones typically consume more potatoes and lesser intake of other vegetables. This results with less folate, calcium, magnesium, and vitamin C in the diet. These patients are found to have increased abundance of *Bacteroidaceae*, *Chitinophagaceae*, *Propionibacteraceae*, *Bacteroides*, and *Escherichia-Shigella*. Gutiérrez-Díaz, I., et al. found that these factors show links between dietary intake, biliary microbiota, and cholelithiasis (2018).

A common factor in the occurrence of cholelithiasis across many studies is the lower intake of vegetables. Historically, the intake of fruits and vegetables has been considered protective in preventing gallstones due to the increased content of insoluble fiber. However, in 2018, Gutiérrez-Díaz, et al. found that the intake of increased fibers and polyphenols (compounds commonly found in plants), was also found to have a positive impact on the gut microbiota. Thus the historical attribution of fruits and vegetables to the prevention of cholelithiasis could actually

be more accurately linked to the role that the microbiota play. For example, *Prevotellaceae*, *Bacteroidaceae*, *Chitinophagaceae*, *Fusobacteria*, and *Bacteroides* were all found to be elevated in those suffering from gallstones or sclerosing cholangitis while *Xanthomonadaceae* and *Propionibacteraceae* were found to be reduced in those with cholelithiasis versus a healthy liver after donation (Gutiérrez-Díaz, et al., 2018). High fat diets yield increased amounts of bile, which has a robust antimicrobial affect on the normal microbiota of the bowels. This explains the lower levels of *Xanthomonadaceae* and *Propionibacteraceae* found in those with cholelithiasis. In contrast, certain bacteria are overgrown such as *Haemophilus*, whose elevation is consistently linked with the intake of seafood, meat, cholesterol, and fatty acids.

In conclusion, approximately 90-95% of gallstones evaluated after a cholecystectomy are made of cholesterol. Diets exempt of, or with decreased intake of, meat and higher intake of fiber, fruits, and vegetables results in lower cholesterol levels and thus lower incidence of cholesterol type gallstones. Diets high in fruits and vegetables increase or decrease certain key gut microbiota leading to a healthier amount of flora and subsequently a decreased incidence of cholelithiasis. Diets high in fat cause increased secretion of bile, which has an antimicrobial affect on the normal microbiota of the bowel. Diets that are lower in fat result in less bile secretion and a better balance of gut microbiota.

Learning Points

- 90-95% of gallstones evaluated after a cholecystectomy are made of cholesterol.
- Diets exempt of, or with decreased intake of, meat and higher intake of fiber, fruits, and vegetables results in lower cholesterol levels and thus lower incidence of cholesterol type gallstones.
- Diets high in fruits and vegetables increase or decrease certain key gut microbiota leading to a healthier amount of flora and subsequently a decreased incidence of cholelithiasis.
- Diets high in fat cause increased secretion of bile, which has an antimicrobial affect on the normal microbiota of the bowel.
- Diets lower in fat result in less bile secretion and a better balance of gut microbiota.

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