

The unexpected truth about dates and hypoglycemia

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ABSTRACT

Background: Dates are a concentrated source of essential nutrients, vitamins, minerals, and carbohydrates (CHOs), which are necessary for the maintenance of optimum health. Most of the CHOs in dates come from sugars including glucose and fructose. Dates are commonly consumed in Saudi Arabia, particularly at the time of breaking the fast to provide instant energy and maintain blood sugar level. However, dates may cause hypoglycemia in a rare condition named as heredity fructose intolerance (HFI), and a few families have been to see us with a history of that nature. This is to report the preliminary results of an on-going study of a group of patients who get symptoms of hypoglycemia following the ingestion of dates and have suffered for years without an accurate diagnosis. **Methodology:** This report is based on three patients, from the same family, living in a date growing region of the Kingdom of Saudi Arabia (KSA). The patients had been to several medical centers without getting any definite answers or diagnosis until they were referred to the Gastroenterology Clinic of King Fahd Hospital of the University, Al-Khobar, KSA. The data were obtained by careful history and laboratory investigations, and a final diagnosis of HFI made on fructose intolerance test (FIT). **Results:** The patients reported that they had avoided eating dates because of various symptoms, such as bloating, nausea, and even hypoglycemia when larger amounts were consumed. Their other symptoms included sleepiness, sweating, and shivering. After full examinations and necessary laboratory tests based on the above symptoms, FIT was performed and the patients were diagnosed with HFI. They were referred to a dietitian who advised a fructose-free diet. They felt well and were free of symptoms. **Conclusion:** HFI may remain undiagnosed until adulthood and may lead to disastrous complications and even death. The diagnosis can only be suspected after a careful dietary history is taken supported by FIT. This can prevent serious complications. Restricting dietary fructose may give relief from symptoms in a high proportion of patients with this disorder.

Key words: Dates, heredity fructose intolerance, hypoglycemia

INTRODUCTION

The date fruit is one of the oldest cultivated trees, numerous varieties of which are widely grown in Saudi Arabia. In many ways, dates may be considered as an ideal food to provide a wide range of essential nutrients and potential health benefits.^[1]

Antioxidant and anti-inflammatory assays confirm bioactive compounds in Ajwa dates.^[2] Their content of

natural sugars depends on the variety. As the date fruit dries, the sugar becomes concentrated. Total sugar may be about 70%, mainly in the form of glucose and fructose with small fractions of maltose and sucrose. Chemical composition of different types of dates is shown in Table 1.^[3] In patients with heredity fructose intolerance (HFI) which is a rare hereditary disorder, the presence of significant amount of fructose in dates can lead to symptoms and complications. Table 2 provides a list of other foods (including honey) which have high content of fructose.^[4]

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Table 1: Chemical Composition of various types of dates in Saudi Arabia

| Contents (%) | Types of dates | | | | |
|------------------|----------------|-------|----------|--------|------------------|
| | Fara'd | Lulu | Bo Ma'an | Dabbas | Khalas |
| Moisture | 13.20 | 14.40 | 14.81 | 12.89 | 16.13 |
| Crude fiber | 2.64 | 1.84 | 2.58 | 2.36 | 2.50 |
| Fat | 0.12 | 0.15 | 0.06 | 0.15 | 0.12 |
| Nitrogen | 0.186 | 0.240 | 0.224 | 0.259 | 0.191 |
| Protein | 1.162 | 1.498 | 1.399 | 1.622 | 1.192 |
| Fructose | 33.25 | 31.64 | 32.51 | 28.55 | 32.36 |
| Glucose | 35.73 | 36.25 | 36.29 | 37.08 | 36.47 |
| Sucrose | 0.91 | 1.07 | 0.16 | 2.26 | BLD ^b |
| TRS ^a | 68.98 | 67.89 | 68.80 | 65.63 | 68.83 |

^aTRS: Total reducing sugars, ^bBLD: Below limit of detection

Table 2: Some foods with high fructose content

| Food | Fructose (g/100 g) | Glucose (g/100 g) |
|---------------------------------|--------------------|-------------------|
| Sucrose (for reference) | 50 | 50 |
| Apples | 5.9 | 2.4 |
| Pears | 6.2 | 2.8 |
| Fruit juice e.g., apples, pears | 5-7 | |
| Watermelon | 3.4 | 1.6 |
| Raisins | 29.8 | 27.8 |
| Honey | 40.9 | 35.7 |
| High fructose corn syrup | 42-55 | 45-58 |
| Mango | 4.68 | 2.01 |
| Agave nectar | 55.6 | 12.43 |

The term of fructose intolerance is a general term that describes two possible conditions.

Hereditary fructose intolerance

This is a rare autosomal recessive genetic disorder that results from a deficiency of fructose-1-phosphate aldolase in the liver, intestines, and kidneys. The estimated incidence is one in 20,000 live births,^[5] but the prevalence of HFI in adults is difficult to estimate since the majority of patients are asymptomatic and affected people may simply avoid the ingestion of most or all sweets.

The clinical symptoms were first described by Chambers and Pratt in 1956.^[6] Affected individuals fail to metabolize fructose completely in the liver, kidney, and intestines because of aldolase enzyme deficiency, and the ingestion of fructose causes symptoms such as abdominal pain and vomiting with hypoglycemia. In the early and mid-20th century, death from fructose infusion was frequently reported in Europe in this group of population.^[7] If fructose intake is restricted and its intravenous (IV) administration is strictly avoided, serious life-threatening complications can be prevented. Continuous use of oral fructose intake may lead to renal failure and liver cirrhosis.^[8,9]

Fructose malabsorption

Patients have difficulty in absorbing fructose because of the deficiency of co-transporters in the small intestine. This is a less serious disorder because it does not result in liver or kidney damage but can cause abdominal pain, bloating, gas, and diarrhea. Fructose malabsorption (FM) is not a rare condition and is found in up to 30% of the population.^[10,11]

Because of the similarity of symptoms between HFI and FM and the similar type of diets causing the problems, HFI may be confused with FM. An easy way to differentiate the two is by performing fructose intolerance test (FIT) and fructose breath test (FBT). FIT is positive in HFI while positive FBT indicates FM. Other diagnostic tests include intestinal, kidney, or liver biopsy to assess aldolase enzyme deficiency and DNA analysis for mutated gene in suspected cases for the confirmation of HFI.^[12,13]

METHODOLOGY

This report is based on three patients, from the same family, who live in a date growing region of the Kingdom of Saudi Arabia (KSA). The patients had visited several medical centers without any definite answer or diagnosis being made. These patients were then referred to the Gastroenterology Clinic of the King Fahd Hospital of the University, Al-Khobar, KSA. The data were obtained by taking careful history and laboratory investigations, and a final diagnosis of HFI was made after an FIT.

RESULTS

The first patient was a 32-year-old male who was a well-educated government employee from the eastern region of KSA. He was also known to have ulcerative colitis and was well controlled on treatment. He was referred to the Gastroenterology Clinic of the King Fahd Hospital of the University, Al-Khobar, KSA, for the evaluation of episodic nonspecific abdominal pain with easy fatigability and sweating. He reported that his symptoms were associated with possible ingestion of dates but had no problem with the usual amounts of dairy products. He also mentioned that he is allergic to honey which makes him slow, tired, shivery, and sleepy (symptoms of hypoglycemia). He could not recall if his parents had any similar problem. The other two patients were the younger sisters of this patient, who also suffered from similar problems after the intake of dates and honey. They had made frequent visits to many peripheral clinics. Unfortunately, only one of the sisters was able to take the test.

They neither had any abnormal physical finding nor suffered from anemia, kidney, or liver problem. Thyroid function

test and insulin level were reported normal. Repeated stool analysis, percutaneous abdominal ultrasound, and upper gastrointestinal endoscopy were performed, and all were normal.

Hydrogen breath test for fructose malabsorption did not show any positive results. During repeated follow-up visits, they always referred again and again to their experiences with the intake of dates and the symptoms of hypoglycemia. A question of adult HFI was, therefore, raised. They were offered fructose infusion test; however, after they were given detailed descriptions of the test, they refused IV fructose infusion. However, they agreed to take the FIT, one of the diagnostic tests for HFI that required the ingestion of a specific amount of fructose followed by periodic measurements of sugar levels in the blood.

They were given 1 g of fructose of per kg body weight. The tests revealed gradual decrease in the blood glucose levels, from about 100 mg/dl to about 60 mg/dl at 150 min [Table 3]. The patients also developed significant hypoglycemic symptoms which were controlled with dextrose infusion after completion of the test. The patients were discharged after being stabilized. Based on the results of FIT and aforementioned symptoms, the patients were diagnosed as adult HFI. They were referred to a dietitian who advised fructose-free diet. The patients felt well and were free of symptoms.

DISCUSSION

Fructose is a sugar found naturally in many fruits (including dates) and honey. It is absorbed from the small intestine by active transport, metabolized primarily in the liver and kidney and partially in the small intestine and adipose tissue.^[8,12]

Deficiency in aldolase B in the above-mentioned areas causes fructose intolerance.^[14,15] After ingestion, fructose rapidly enters the hepatocytes where fructose is phosphorylated to fructose-1-phosphate. Because of the deficiency of enzyme fructose-1-phosphate

aldolase in HFI, which splits fructose-1-phosphate into glyceraldehydes and dihydroxy-acetones-phosphate, the accumulation of fructose-1-phosphate results in the inhibition of other enzymes namely phosphorylase, liver fructose 1–6 bisphosphate aldolase, and fructose kinase. This results in impaired glycogenolysis and gluconeogenesis and induced hypoglycemia,^[15,16] which can lead to further life-threatening complications such as hepatorenal damage and death.^[9,17,18] Further, a series of cases of fatalities due to intravenous fructose infusion has been reported in some European hospitals.^[5,13,14] The cause of severe hepatic dysfunction remains unknown but may be a manifestation of focal cytoplasmic degeneration and cellular fructose toxicity. Hypoglycemia and acidosis may act together to cause organ damage, shock, or coma. Mortality may result from any or all of the above conditions.^[7,15,19]

Fortunately, most of the patients start gradually avoiding diets that contain fructose due to the previous undesirable experiences so are saved from severe complications and side effects as was mentioned in an earlier case report of a 50-year-old German woman.^[13] Definitive therapy simply consists of avoidance of fructose-containing diet. Continuous intake of fructose in the diet can lead to complications. Eliminating fructose early in the course of the disease totally restores the affected child's health. The prognosis is excellent for infants who are rapidly diagnosed and are fructose-containing diet avoided sooner. In such individuals, life expectancy remains normal.

CONCLUSION

Dates contain high amounts of sugar. So it's unusual to lead to hypoglycemia. But If incase that happens, one should consider a rare condition i.e., hereditary fructose intolerance.

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Conflicts of interest

There are no conflicts of interest.

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Table 3: Results of oral fructose intolerance test (1 g of fructose of per kg body weight)

| | Blood glucose patient 1 (%mg) | Blood glucose patient 2 (%mg) |
|--------------------------------|-------------------------------|-------------------------------|
| Blood glucose before ingestion | 100 | 95 |
| 30 min after ingestion | 95 | 88 |
| 1 h after ingestion | 85 | 80 |
| 90 min after ingestion | 75 | 70 |
| 2 h after ingestion | 65 | 65 |
| 150 min after ingestion | 60 | 62 |

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