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ABSTRACT & COMMENTARY

Carbohydrates, Insulin, and Obesity

By Joseph E. Scherger, MD, MPH

Vice President, Primary Care, Eisenhower Medical Center; Clinical Professor, Keck School of Medicine, University of Southern California, Los Angeles

Dr. Scherger reports no financial relationships relevant to this field of study.

SYNOPSIS: Carbohydrate intake stimulates insulin secretion, which is the primary driver of weight gain. Besides driving glucose into cells, insulin causes fat storage, increases hunger, and lowers energy expenditure. High insulin blood levels lead to obesity with some genetic variation.

SOURCE: Astley CM, Todd JN, Salem RM, et al. Genetic evidence that carbohydrate-stimulated insulin secretion leads to obesity. *Clin Chem* 2018:64:192-200.

Astley et al used several large databases and meta-analyses to estimate the causal relationship between insulin secretion and body mass index (BMI). The data sources included summary results from the largest published studies of people from a predominately European ancestry for insulin secretion. Data also were drawn from the Cardiology and Metabolic Patient Cohort study at Massachusetts General Hospital to validate genetic associations with insulin secretion and to test the observational association of insulin with BMI.

Genetics is a partial determinant of insulin concentration in the blood 30 minutes after oral glucose, known as the insulin-30 index. In their research, Astley et al discovered that higher genetically determined insulin-30 was associated strongly with higher BMI consistent with a causal role in obesity.

■ COMMENTARY

Clinicians learn in medical school that the role of insulin is to drive glucose into cells so that it can be used for energy. That fundamental role is highlighted by the pathophysiology of type 1 diabetes. There are other important metabolic roles for insulin that become important in obesity and type 2 diabetes. Insulin causes fat storage (lipogenesis) and blocks the burning of fat (lipolysis). Insulin also increases hunger and lowers energy expenditure.[1]

Insulin causes the human body to burn glucose rather than fat. Any circulating glucose not needed for energy

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becomes fat through lipogenesis. High insulin blood levels reflect a stress to metabolism to burn glucose for energy rather than fat. High insulin levels also cause inflammation. When insulin levels become low, the body will burn fat for energy, resulting in ketosis. Researchers have demonstrated that burning fat to a degree that causes ketosis does not happen unless the fasting insulin level is less than 10 mcIU/mL.[2]

Ludwig, one of the authors of the study reviewed here, has conducted considerable research on the carbohydrate-insulin model of obesity and how excess high glycemic carbohydrates cause hunger, obesity, and type 2 diabetes.[1,3] Despite opposition from the food industry, for whom refined carbohydrates are highly profitable, there is a clear path available to clinicians to combat obesity through low-carbohydrate nutrition augmented by intermittent fasting.[2] ■

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ABSTRACT & COMMENTARY

Can Hormone Therapy Prevent the Development of a 'Dowager's Hump'?

By Jeffrey T. Jensen, MD, MPH

Leon Speroff Professor and Vice Chair for Research, Department of Obstetrics and Gynecology, Oregon Health & Science University, Portland

Dr. Jensen reports that he is a consultant for and receives grant/research support from Bayer, Merck, ContraMed, and FHI360; he receives grant/research support from Abbvie, HRA Pharma, Medicines 360, and Conrad; and he is a consultant for the Population Council.

SYNOPSIS: Postmenopausal hormone therapy may reduce the risk of developing age-related hyperkyphosis, commonly known as a "Dowager's hump." Such therapy may provide long-term benefits.

SOURCE: Woods GN, Huang MH, Cawthon PM, et al. Patterns of menopausal hormone therapy use and hyperkyphosis in older women. *Menopause* 2018;25:738-743.

The abnormal exaggerated curvature of the dorsal spine with compensatory cervical lordosis that commonly occurs in elderly postmenopausal women is referred to colloquially as a "Dowager's hump." Medically, it is known as hyperkyphosis. Women with hyperkyphosis are at risk for other fragility health concerns, including poor physical function, falls, fractures, and early mortality. The risk factors for hyperkyphosis include low bone mineral density (BMD), bone loss, and vertebral fractures. Since menopausal hormone therapy (HT) reverses bone loss and prevents vertebral fractures, Woods et al hypothesized that use of HT would reduce the risk for developing hyperkyphosis. As an initial step to evaluate this hypothesis, they used data available from the Study of Osteoporotic Fractures (SOF), a longitudinal, multicenter, observational study of 9,704 community-dwelling ambulatory women ≥ 65 years of age recruited between 1986 and 1988 from four clinics in Baltimore; Minneapolis; Monongahela Valley, PA; and Portland, OR. Of these 9,704 women, the authors selected a random group of 1,063 women from a subset of participants with longitudinal follow-up (seven study visits) that detailed HT use spanning an average of 15 years and adequate spinal radiographs at baseline and at year 15 suitable for determination of a modified Cobb angle of kyphosis. The modified Cobb angle uses the anchors of T4 and T12 to measure the angle in lateral spine radiographs instead of T1 to T3, as

the higher thoracic vertebral bodies typically are not well visualized on lateral X-rays (available in the SOF). Readers of the films were blinded to HT status.

Investigators relied on self-report during the study period to classify HT: continuous (current use reported at six or more of seven visits), 12% of sample; intermittent (current use reported at between one and five of seven visits), 17%; remote past (reported past use at study baseline but no current use at any visit), 24%; or never, 46%. Evaluation of the demographic characteristics of participants revealed no clinically important or statistically significant differences between HT pattern groups and age (overall mean at follow-up, 83.7 years), body weight, or family history of hyperkyphosis (26%).

Compared to never users (52.6°), continuous HT users had the smallest mean Cobb angle (48.9°), followed by remote past (49.9°) and intermittent use (51.5°). Consistent with this effect, users of continuous HT also had higher BMD (0.805 g/cm^2) compared to never use (0.704 g/cm^2), with a dose effect observed with intermittent (0.733 g/cm^2) and remote past (0.715 g/cm^2) use. The authors did not report statistical significance.

The differences in the Cobb angle with continuous and remote past use of HT were statistically significant in the age- and clinic-adjusted model (P = 0.01). In the fully adjusted model, which also included the number of prevalent vertebral fractures, family history of hyperkyphosis, the presence of degenerative disc disease, total hip BMD, and body weight, the strength of association decreased and became nonsignificant (only -2.8°; P = 0.06) for continuous use. Of interest, this full adjustment did not attenuate the beneficial association seen with remote past use (-2.8°; P = 0.02). The authors concluded that these results support a role for postmenopausal HT in the prevention of age-related hyperkyphosis.

■ COMMENTARY

At first glance, these results seem obvious. We know that low BMD, bone loss, and vertebral fractures are predictable consequences of menopause, and also are independent risk factors for hyperkyphosis. We also know that HT prevents postmenopausal bone loss, maintains or improves BMD, and prevents fracture.[1,2] However, no one has evaluated whether HT can reduce the risk of developing hyperkyphosis.

Why study this question? The fact that we have a colloquial expression, "Dowager's hump," for the physical changes of spinal compression fractures and short stature that develop in elderly women reveals the ubiquity of the condition. But we also recognize hyperkyphosis as a fragility sign. While we cannot stop the aging process, I have not met any patient looking forward to the development of this physical change of fragility.

The results of this paper provide additional information useful in the counseling of perimenopausal and early postmenopausal women regarding HT. We now have evidence that the use of HT can reduce the risk of developing a Dowager's hump. This may motivate some women to consider HT more carefully.

The cross-sectional design, simple cohort analysis, and lack of detail on type or dose of HT represent major weaknesses that must be considered in evaluating this research. However, notable strengths include the large sample size and prospective follow-up over 15 years. We see biologic plausibility in the results. Continuous use of HT resulted in the greatest reduction in Cobb angle (almost 4°). I am not bothered that this benefit attenuated and was no longer statistically significant after full adjustment. The full adjustment model included BMD and the presence of degenerative disk disease (DDD). Not surprising, continuous HT users had the highest BMD and the lowest rate of DDD, as HT also improved both findings. Thus, these characteristics are not confounders of the association of benefit of HT on the reduced Cobb angle. HT improves BMD and prevents DDD. We should expect correlation with the benefit through a causal relationship. Also, we should expect that adjusting for these factors would tend to attenuate the overall beneficial effect seen with respect to the Cobb angle.

I am intrigued by the fact that remote past users also showed a significant reduction in the Cobb angle, and that this benefit remained significant even after complete adjustment. The absence in change in the effect supports my previous comment that adjusting for the benefit in BMD diluted the effect seen with continuous use. In contrast to continuous users, the BMD of remote past users was similar to that of never users. Remote past users stopped HT prior to enrolling in the study (mean age, 68 years). This suggests that initiation of HT and strong protection against bone loss in the early postmenopausal years might provide lasting benefit, even if bone loss eventually catches up.

These results may provide clinicians with an additional counseling point to encourage healthy perimenopausal and postmenopausal women to consider initiation of HT as an early intervention. If a patient has reservations about the potential benefits of HT, perhaps these new results will push her over the "hump." ■

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ABSTRACT & COMMENTARY

Coffee Consumption and Mortality

By Allison Becker, ND, LAc

Naturopathic Doctor, Acupuncturist in private practice in Evansville, WI

Dr. Becker reports no financial relationships relevant to this field of study.

SYNOPSIS: After rigorous evaluation using multiple statistics, an inverse relationship between coffee intake and all-cause mortality was demonstrated consistently across the racial/ethnic groups examined.

SOURCES: Gullar E, Blasco-Colmenares E, Arking DE, Zhao D. Moderate coffee intake can be part of a healthy diet. *Ann Intern Med* 2017;167:283-284.

Park SY, Freedman ND, Haiman CA, et al. Association of coffee consumption with total and cause-specific mortality among nonwhite populations. *Ann Intern Med* 2017;167:228-235.

Gunter MJ, Murphy N, Cross AJ, et al. Coffee drinking and mortality in 10 European countries: A multinational cohort study. *Ann Intern Med* 2017;167:236-247.

Travel throughout the world and one will find coffee to be one of the most popular drinks consumed. In the United States alone, about three-quarters of adults drink coffee and nearly half drink it daily.[1] One also will find coffee bean preparations to vary tremendously depending on the coffee culture. From drip coffee to espresso, from light roast to dark, techniques vary widely and affect both the caffeine and antioxidant content of the beans. Frequently, coffee is consumed with added cream, milk, and/or sugar, which increase the caloric content significantly. Considering the quantity of coffee consumed worldwide, it is important for healthcare providers to study closely the potential health benefits of drinking coffee across culture and race.

Two large prospective cohort studies, the European Prospective Investigation into Cancer and Nutrition (EPIC) and the Multiethnic Cohort Study of Diet and Cancer (MEC), yielded data useful in analyzing the potential health benefits of coffee consumption. Uncontrolled confounding variables, such as smoking, pre-existing illness, alcohol intake, body mass index, and exercise, make it difficult to generalize the health benefits of coffee consumption. The authors of the EPIC and MEC trials attempted to control for confounding variables using multiple statistical methods.

EUROPEAN PROSPECTIVE INVESTIGATION INTO CANCER AND NUTRITION

The EPIC study included 521,330 people ≥ 35 years of age from 10 European countries. The intent was to evaluate whether coffee consumption was associated with all-cause and cause-specific mortality. The authors of this large study generated baseline data and followed up with participants an average of 16.4 years. Only two data points were generated: coffee consumption at baseline and 16.4 years later. Data generated included coffee consumption but also data for a subcohort including biomarkers for liver function, metabolism, and inflammation (ALT, AST, GGT, Alk Phos, C-reactive protein [CRP], high-density lipoprotein, lipoprotein (a), and hemoglobin A1c [HbA1c]). The researchers found that participants in the highest quartile of coffee consumption had a statistically significant lower risk of dying. This inverse association applied to both men and women.

How coffee is prepared before consumption varies widely in these European countries. For example, espresso is small in quantity but concentrated in phytochemicals. One serving of Italian espresso is not the same as one cup of coffee in the United Kingdom. Special statistics were used to account for these differences, using country-specific quartiles and looking at trends across exposure groups. Four quartiles of consumption were generated (low, medium-low, medium-high, and high). The authors analyzed the volume of coffee consumed (zero cups, less than one cup, one to less than two cups, two to less than three cups, more than three cups per day) with one cup = 237 mL coffee. Participants in the highest quartile of coffee consumption had a lower risk of death from all causes. Similar inverse associations and linear trends were found with caffeinated and decaffeinated coffee.

Multivariable models adjusted for body mass index, physical activity, smoking status (type, frequency, duration), education, menopausal status, use of oral contraceptives or hormone replacement therapy, alcohol consumption, total caloric intake per day, consumption of red and processed meats, and consumption of fruits and vegetables. When the data were adjusted for these variables, there continued to be an inverse association between mortality and coffee consumption.

All-cause mortality was recorded. Both men and women in the highest quartile of coffee consumption had a statistically significant decreased risk of dying from all

gastrointestinal diseases (*P* trend < 0.001; hazard ratio [HR], 0.41 for men; HR, 0.60 for women). The gastrointestinal (GI) disease category included diseases of the oral cavity, esophagus, stomach, pancreas, gall bladder, liver, and intestines. More than one-third of the deaths from GI disease were from liver disease. GI disease was broken down further into liver disease and non-liver GI disease. Daily, frequent coffee drinking was associated with a decreased risk of dying from liver disease (sexes combined HR, 0.20; 95% confidence interval [CI], 0.13-0.29), cirrhosis (HR, 0.21; 95% CI, 0.13-0.34), and liver cancer, whereas coffee consumption did not decrease the risk of death from non-liver digestive diseases (HR, 0.81) conclusively. Interestingly, in the subcohort, liver function biomarkers (ALP, ALT, AST, and GGT) were significantly lower in people who drank coffee regularly compared with those who rarely or never drank coffee. In women only, higher coffee consumption was associated with lower CRP, HbA1c, lipoprotein (a), and higher high-density lipoprotein. This may account for the decreased risk of dying from heart disease in women who drank more coffee (HR, 0.70; 95% CI, 0.55-0.90). Finally, women who frequently drank coffee were at an increased risk of dying from ovarian cancer (HR, 1.31; 95% CI, 1.07-1.61) when compared to women who did not drink coffee.

MULTIETHNIC COHORT STUDY OF DIET AND CANCER

Until the MEC study, data in non-white populations evaluating coffee consumption and risk for total and cause-specific mortality were sparse. This study included 185,855 African-Americans, Native Hawaiians, Japanese-Americans, Latinos, and whites 45-75 years of age and living in the United States at the time of recruitment. Investigators followed these participants for an average of 16.2 years and assessed coffee intake with a food-frequency questionnaire. Like the EPIC study, the MEC study also featured only two data points: the baseline and the single follow-up. Coffee intake was reported in six categories: none, one to three cups per month, one to six cups per week, one cup per day, two to three cups per day, and more than four cups per day. Drinking coffee decreased the risk of dying across ethnic groups analyzed, even after adjustment for confounding variables: one cup per day (HR, 0.88; 95% CI, 0.85-0.91), two to three cups per day (HR, 0.82; 95% CI, 0.79-0.86), and more than four cups per day (HR, 0.82; 95% CI, 0.78-0.87). Decaffeinated and caffeinated coffee appear to produce similar benefits.

This study was analyzed to control for confounding variables and tease out the specific effect of coffee consumption on mortality. Those in the group of highest consumption of coffee (more than four cups per day) also tended to smoke cigarettes, creating a significant confounding variable in this analysis. Subgroup analyses were conducted for smoking, age, education level, pre-existing heart disease, and pre-existing cancer. A statistically significant inverse association with coffee consumption and mortality was found across these analyses. The association of coffee consumption and mortality was examined across five ethnic groups. An inverse association between coffee consumption and mortality was found with all groups. Statistical significance was reached in all populations except Native Hawaiians.

Total mortality and cause-specific mortality were analyzed in this cohort. After adjustment for confounders, there was a significant inverse association between increasing coffee consumption and all-cause mortality. The HR decreased as coffee consumption increased. The HR for death was 1.00 for one to three cups of coffee per month. In those who consumed one to six cups per week, the HR was 0.97. The lowest HR was 0.82 (95% CI, 0.78-0.87) for two groups: those who consume two to three cups per day and four or more cups of coffee per day. Consumption of both decaffeinated (P trend = 0.008) and caffeinated (*P* trend < 0.001) coffee decreased the risk of death. This association was similar in both women and men.

To determine if coffee consumption decreased the risk of death from specific causes, the authors analyzed the 10 leading causes of death in the United States. They found a statistically significant inverse association with coffee consumption and cardiovascular disease (*P* trend < 0.001), cancer (*P* trend = 0.023), chronic lower respiratory disease (*P* trend 0.015), stroke (*P* trend < 0.001), diabetes (*P* trend = 0.009), and kidney disease (*P* trend < 0.001). There was no significant association between coffee drinking and death from influenza, pneumonia, Alzheimer's disease, accidents, and intentional self-harm.

■ COMMENTARY

Is coffee an elixir of life? These two studies seem to answer with a resounding "yes." Although the authors generated compelling data and did their best to control for multiple confounding variables, there is not enough cross-cultural data to say definitively that coffee consumption benefits everyone all the time. In each study, only two coffee consumption data points, based on surveys, were generated over nearly 16.5 years. We do not know if coffee was consumed steadily for 16 years, just that it was at the beginning and at the end of the studies. To better assess the frequency and quantity of coffee consumption, multiple data points over several years would strengthen the argument that drinking coffee decreases the risk of death.

In addition, coffee is a popular beverage in many other countries that were not included in the study. According to the International Coffee Organization, the people of Finland consume more coffee per capita than other countries, but this was not included in the European

study.[2] All the participants in the NEC cohort were from the United States, which ranks 26th in coffee consumption per capita worldwide. Future studies generating data from the countries with higher coffee consumption would provide better data to evaluate the relationship of coffee to mortality more completely.

Previous studies have linked coffee with significant health benefits.[3,4] Coffee consumption has been shown to reduce insulin resistance and inflammation, lowering the risk for developing diabetes, metabolic syndrome, heart disease, and cancer. The EPIC researchers found that coffee improved liver function biomarkers and reduced the risk of dying from liver disease.

The health benefits of coffee can be attributed to the many phytochemicals naturally present in coffee.[5] These include antioxidants, chlorogenic acid, and caffeic acid. Caffeic acid has been shown to reduce inflammation, induce apoptosis, and produce an anticancer effect. Kahweol and cafestol activate enzymes that alter carcinogens and render them harmless. Coffee also is a source of lignans, compounds that cell culture and animal studies suggest may optimize estrogen metabolism, decrease cancer cell growth, and promote apoptosis of cancer cells.[6] The phytochemical content of coffee varies depending on where the beans are grown and how they are prepared for consumption. Laboratory studies show instant coffee may be lower in antioxidants than brewed coffee,[7] although more research is needed. Future investigation is needed to learn where the beans richest in these phytochemicals grow and what production methods favor high levels of phytochemicals. In a recent study on healthy adults, drinking up to five cups of coffee per day was not associated with acute toxicity or adverse cardiovascular, behavioral, bone, calcium, or developmental and reproductive effects.[8] For now, clinicians can be confident that patients who drink moderate amounts of coffee (up to four cups) daily are not harming themselves and, in fact, likely are benefiting their health and decreasing their risk of death. However, people with a tendency to anxiety, insomnia, and diarrhea need to be careful with coffee, as the stimulant and laxative effect of coffee can exacerbate these conditions. ■

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BRIEF REPORT

Poor Sleep Can Lead to Accelerated Atherosclerosis

By Alan Z. Segal, MD

Associate Professor of Clinical Neurology, Weill Cornell Medical College

Dr. Segal reports no financial relationships relevant to this field of study.

SOURCE: Dominguez Rodriguez F, Fernandez Alvira JM, Fernandez Friera L, et al. Association of actigraphy-measured sleep parameters and subclinical atherosclerotic burden: The PESA study. *Eur Heart J* 2018;39(Suppl 1):P2466.

Insufficient and poor quality sleep can lead to significant medical complications including atherosclerotic disease. Dominguez Rodriguez et al studied 2,974 patients in the Progression and Early Detection of Subclinical Atherosclerosis (PESA) cohort. Subjects were screened using 2D/3D ultrasound in the carotid, abdominal aorta, and iliofemoral arteries. A coronary artery calcium score on CT also was calculated. Movement sensors (actigraphy) were used to measure sleep duration during a one-week period. Actigraphy is a useful surrogate for more invasive types of sleep monitoring such as polysomnography. Subjects were stratified into four groups: markedly short sleep (< 6 hours), short sleep (6-7 hours), average reference (7-8 hours), and long sleep (> 8 hours). Sleep duration of less than six hours was associated with a mildly increased odds of atherosclerosis on ultrasound, although not on cardiac calcium (odds ratio [OR],

1.27; 95% CI, 1.06-1.52). Subjects with the most fragmented sleep (bottom 20%) had an increased risk of atherosclerosis as well (OR, 1.35; 95% CI, 1.05-1.65). The diagnosis of metabolic syndrome also was made more frequently in the subjects with short or disrupted sleep. This research corroborates prior data, although some previous studies have suggested a more complex U-shaped curve, putting both short sleepers and excessively long sleepers at risk for atherosclerotic disease. Regardless, these data provide further support for the importance of sleep in the optimization of medical outcomes. ■

PHARMACOLOGY UPDATE

Migalastat (Galafold) Capsules

By William Elliott, MD, FACP, and James Chan, PharmD, PhD

Dr. Elliott is Assistant Clinical Professor of Medicine, University of California, San Francisco.
Dr. Chan is Associate Clinical Professor, School of Pharmacy, University of California, San Francisco.

Drs. Elliott and Chan report no financial relationships relevant to this field of study.

The FDA has approved the first oral drug for the treatment of adults with Fabry disease. Migalastat is a pharmacological chaperone, or pharmacoperone, that binds to some forms of faulty alpha-galactosidase A (alpha-Gal A), restoring enzymatic function.[1] Migalastat received an accelerated approval and orphan status. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.[1] It will be marketed as Galafold.

INDICATIONS

Migalastat is indicated for the treatment of adults with confirmed diagnosis of Fabry disease and an amenable galactosidase alpha gene (GLA) variant based on in vitro assay data.[1]

DOSAGE

The recommended dose is one capsule (123 mg) orally once every other day at the same time of day.[1] The capsules should be swallowed whole and on an empty stomach (i.e., no food at least two hours before and two hours after). Migalastat is available as 123 mg capsules.

POTENTIAL ADVANTAGES

Migalastat provides the first oral option for the treatment of Fabry disease, which generally requires intravenous enzyme replacement therapy (ERT) infusion, usually for life.[2]

POTENTIAL DISADVANTAGES

Migalastat was not effective in subjects with nonamenable GLA variants. Common (> 10%) adverse events (vs. placebo) include headache (35% vs. 21%), nasopharyngitis (18% vs. 6%), urinary tract infections (15% vs. 0%), nausea (12% vs. 6%), and pyrexia (12% vs. 3%).[1]

COMMENTS

Pharmacological chaperones are small molecules that cross into cells and target proteins within the cells.[3] Fabry disease is an X-linked lysosomal storage disorder caused by a mutation in the GLA gene, resulting in functional deficiency of lysosomal alpha-galactosidase activity. Some variants are folded abnormally and/or are less stable but retain enzymatic activity.[1] Migalastat binds reversibly to the active side of alpha-galactosidase of these mutations (amenable variants), acting as molecular scaffolding, stabilizing and "restoring" some of its enzyme function. The efficacy of migalastat was evaluated in 67 adult subjects with Fabry disease and 45 with amenable mutations. These patients had histological data at baseline and at six months.[1,4] The primary efficacy endpoints were the proportion of subjects with ≥ 50% reduction from baseline in the average number of globotriaosylceramide (GL-3) inclusions per kidney interstitial capillary assessed by renal biopsy after six months and the median change from baseline in the average number of GL-3 inclusions. Fifty-two percent of patients on migalastat showed ≥ 50% reduction compared to 45% for placebo (not statistically significant). Subjects with baseline GL-3 ≥ 0.3 demonstrated a higher median change from baseline (-0.91 vs. -0.02), with 78% showing ≥ 50% reduction vs. 25% with ≥ 50% reduction for placebo.[1] In 56% of subjects who reported diarrhea symptoms at baseline, clinically meaningful improvement was reported with migalastat. Meanwhile, diarrhea worsened in the placebo group.[5] Subjects with nonamenable GLA variants showed no change from baseline in GL-3 inclusions.[1] In an 18-month study, subjects treated previously with ERT (n = 57) were randomized to migalastat or remained on ERT (agalsidase alfa or beta).[6] Annualized glomerular filtration rates from baseline to 18 months were comparable. Left ventricular mass index decreased significantly in favor of migalastat. Plasma globotriaosylsphingosine remained low and stable after switching to migalastat.

CLINICAL IMPLICATIONS

Fabry disease is a rare, progressive, life-threatening, X-linked lysosomal storage disorder. The estimated prevalence of classic (severe) disease is 1:40,000 in males,[7] although both males and females can be

affected. Mutations of the GLA gene result in deficiency of alpha-galactosidase A, leading to accumulation of glycosphingolipids, which is followed by development of progressive renal failure, cardiac hypertrophy, arrhythmias, stroke, and early death.[3] Standard therapy is ERT. There are more than 1,000 known GLA mutations. Approximately 35-50% may have amenable mutations.[8] These may be stabilized by migalastat, providing an alternative to the traditional ERT. The annual cost for migalastat is $315,250, compared to $306,488 for agalsidase beta (Fabrazyme) for a 70 kg adult. ■

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CME QUESTIONS

1. What macronutrient and hormone combination is most associated with obesity?
a. Fat and insulin
b. Fat and thyroid
c. Carbohydrate and thyroid
d. Carbohydrate and insulin

2. In the study evaluating hyperkyphosis, Woods et al noted that women who reported continuous use of hormonal therapy during 15 years of follow-up showed which of the following?
a. A reduction in nonvertebral and vertebral fractures compared to intermittent users
b. A reduction in the Cobb angle, a marker of kyphosis, compared to never users
c. A decrease in bone mineral density compared to remote past users
d. A reduction in weight compared to all reference groups

3. What statement is true regarding coffee consumption?
a. Coffee consumption increases all-cause mortality.
b. Coffee consumption negatively increases risk of death from digestive disease.
c. Drinking coffee daily decreases liver function biomarkers.
d. All of the above

4. Chronic sleep disorders are a risk factor for the development of atherosclerosis.
a. True
b. False

CME OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- describe new findings in the differential diagnosis and treatment of various diseases;
- describe the advantages, disadvantages, and controversies surrounding the latest advances in the diagnosis and treatment of disease;
- identify cost-effective treatment regimens;
- explain the advantages and disadvantages of new disease screening procedures.