Galactose promotes fat mobilization in obese lactating and nonlactating women[1–4]

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ABSTRACT

Background: Galactose consumption as the only carbohydrate source results in little increase in plasma glucose and insulin concentrations when compared with fasting. Lower insulin might promote endogenous lipolysis during meal absorption, which may facilitate fat loss.

Objective: The objective was to test the hypothesis that consumption of an isocaloric, isonitrogenous galactose drink will result in higher rates of lipolysis and fat oxidation than consumption of a glucose drink in obese lactating and nonlactating women.

Design: Seven healthy, obese, exclusively breastfeeding women and 7 healthy, obese, nonlactating women were studied on 2 occasions according to a randomized, crossover, single-blinded design. Subjects received drinks providing ≈70% of the daily estimated energy requirement, of which 60% was either glucose or galactose. The primary outcomes were the rate of appearance (Ra) of glycerol and palmitate, and the secondary outcomes were glucose Ra, milk production, energy expenditure, and substrate oxidation.

Results: Plasma glucose and insulin concentrations were lower ($P < 0.05$) and those of glycerol, palmitate, free fatty acids, and triglycerides were higher ($P < 0.05$) during galactose than during glucose feeding in both nonlactating and lactating women. During galactose feeding, glucose Ra was lower ($P < 0.01$) and glycerol, palmitate, and free fatty acid Ra were higher ($P < 0.01$) in both groups. During galactose feeding in all women combined, fat oxidation was higher ($P = 0.01$) and protein oxidation was lower ($P < 0.01$). Milk production, energy expenditure, and carbohydrate oxidation were similar between glucose and galactose feeding.

Conclusions: Galactose consumption is associated with higher endogenous fat mobilization and oxidation during meal absorption. Long-term studies are required to determine whether galactose as an exclusive carbohydrate source would promote body fat loss in obese subjects. *Am J Clin Nutr* 2011;93:374–81.

INTRODUCTION

Many lactating women are concerned about losing weight gained during pregnancy in the postpartum period without adversely affecting lactation. Weight gain during sequential pregnancies can lead to excessive weight gain and obesity. During pregnancy and the postpartum period, obesity is associated with short-term, but significant, adverse health effects, including hypertension, pre-eclampsia (1, 2), gestational diabetes (3, 4), thromboembolic events (3), cesarean delivery (5), and failure to initiate or sustain breastfeeding (6). Over the long term, obesity in these women increases their risk of type 2 diabetes (7) and other aspects of the metabolic syndrome (8).

A large number of dietary approaches have been proposed to facilitate weight loss in the general population (9–11). However, only a limited number of studies have dealt with weight loss among lactating women (12, 13). It is postulated that high-carbohydrate foods with a high glycemic index induce a rapid increase in blood glucose, which results in insulin release (14), which in turn inhibits endogenous fat mobilization (13, 15) and promotes the retention of body fat. On the other hand, diets that produce a low glycemic response may minimize postprandial insulin secretion, thus facilitating fat mobilization and loss. However, these premises remain largely unproven in clinical studies. Although returning to prepregnancy (or ideal) body weight after delivery should be the goal, extreme dietary programs could compromise milk production (16).

Oral galactose provides a nutrient substrate that is converted to glucose without significant increase in plasma glucose and insulin concentrations (17–19).Thus, galactose, a potential substrate for lactose synthesis (17), might also promote fat mobilization and oxidation. The present study was designed to determine whether an isocaloric, isonitrogenous drink of galactose as the sole carbohydrate source, when compared with an identical drink of glucose, will promote fat mobilization and oxidation in obese lactating and obese nonlactating nonpregnant women without adversely affecting milk production in lactating women.

SUBJECTS AND METHODS

Subjects

After approval by the Institutional Review Board for Human Subjects and the General Clinical Research Center (GCRC) Advisory Committee at Baylor College of Medicine, written

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consent was obtained from each subject. The initial recruitment started in September 2007. All subjects were determined to be healthy if they had normal results from a physical examination and liver function tests and normal fasting blood glucose, hemoglobin, and glycated hemoglobin concentrations. None of the women had a history of gestational diabetes or had children, parents, siblings, or grandparents with diabetes. Except for routine postpartum vitamin and mineral supplements prescribed by their physician, none of the subjects were taking any medications, including birth control pills. All women had a negative pregnancy test at the time of the study. To exclude any pregnancy-related changes in body composition and hormones and to ensure a stable physiologic model, all lactating women were studied between 6 and 12 wk postpartum. Nonlactating women were studied $\geq$1 y after their last delivery. No attempt was made to study the subjects at a specific time in their menstrual cycle or to select subjects on the basis of ethnicity. Seven obese, healthy, exclusively breastfeeding women [age: 26.6 $\pm$ 1.3 y; body mass index (in kg/m^2): 34.5 $\pm$ 1.7; height: 165.7 $\pm$ 3.0 cm; weight: 94.2 $\pm$ 3.6 kg; and total body fat (measured by dual-energy X-ray absorptiometry; QDR 11.2; Hologic, Bedford, MA): 42.0 $\pm$ 1.4%; 1 African American, 2 whites, and 4 Hispanic Americans] were recruited. The infants of the lactating women weighed 5.24 $\pm$ 0.22 kg, were 9.76 $\pm$ 0.56 wk of age, and were healthy at the time of the study. In addition, 7 obese, healthy, nonpregnant, nonlactating women (age: 29.7 $\pm$ 1.7 y; body mass index: 35.5 $\pm$ 1.4; height: 162.6 $\pm$ 1.4 cm; weight: 94.0 $\pm$ 4.6 kg; and total body fat: 42.5 $\pm$ 0.6%; 2 African Americans, 1 white, and 4 Hispanic Americans) were recruited as control subjects.

Protocol

The participants were studied on 2 occasions separated by 1–2 wk. They were instructed to consume a standardized mixed meal providing $\approx$15% protein, 50% carbohydrate, and 35% fat for the 3 d preceding admission to the GCRC. Lactating women were asked to bring 180–300 mL breast milk to supplement their infants' feedings should they have technical difficulty with breastfeeding and/or decreased milk production during the study.

On each study occasion, the women were admitted to the GCRC for 4 d and 3 nights. The women were randomly assigned to receive feedings (every 3 h) of a liquid, isocaloric drink containing either glucose or galactose (98% purity; Sigma-Aldrich, St Louis, MO). The sugars of the drinks provided $\approx$60% (325 $\pm$ 5 g/d) of the women's daily estimated energy requirement (EER). An additional $\approx$10% of their daily EER was provided as protein (38 $\pm$ 5 g/d, Beneprotein; Novartis, Minneapolis, MN) and essential fatty acids (13 $\pm$ 1 g safflower oil/d, >70% linoleic acid). Thus, the drink provided a total of 70% of the women's EER. Carbohydrate, protein, and fat provided 83%, 10%, and 7% of the calories in the drink, respectively. EER was calculated according to the Institute of Medicine for overweight and obese women $\geq$19 y of age (20):

$$\begin{aligned}\text{EER (kcal/d)} = 448 &- [7.95 \times \text{age (y)}] \\ &+ \{\text{PA} \times [11.4 \times \text{weight (kg)} + 619 \times \text{height (m)}]\} \quad (1)\end{aligned}$$

where PA is the physical activity coefficient: PA = 1.16 (low activity).

To overcome problems with calculations and comparisons, lactating women received the same intake as nonlactating women, and no further intake was provided to account for milk production (ie, the extra $\approx$400 kcal recommended for exclusive breastfeeding).

Women (and their infants if the women were lactating) were admitted to the GCRC before 1600 on day 1 of the study to allow time for administrative paperwork to be completed and a pregnancy test and physical examination to be conducted. At 1700, an antecubital intravenous catheter was placed in one arm under ELA-MAX cream (Astra Pharmaceuticals, Wayne, PA) analgesia for blood sampling. At 1800, a basal blood (and milk in lactating women) sample was collected. The women then received a standardized mixed meal providing 15% protein, 50% carbohydrate, and 35% fat followed by a snack at 2000. Thereafter, except for water, the subjects fasted until 0600 the following morning (day 2). Starting at 0600 on day 2, both nonlactating and lactating women consumed the drink containing either glucose or galactose every 3 h until 2000 on day 3. Throughout the study, the breastfeeding women were asked to feed their infants at $\approx$3-h intervals and to breastfeed from both breasts at each feeding time. Infants were weighed before and after each breastfeeding to determine the volume of milk consumed (21, 22). With the completion of each feeding, the women were asked to empty their breasts of residual milk using a standard electric breast pump (Embrace; Playtex, Dover, DE). A small milk sample from each breast was collected during the middle of each feeding and was saved for lactose, fat, and protein analysis. The volume of milk produced was the sum of the milk consumed, pumped, and collected for analysis (22).

During the first 3 d of the stay, a small blood sample was drawn for the measurement of plasma glucose concentrations at 6-h intervals. On the evening of study day 3, a second intravenous tube was placed in the contralateral arm under ELA-MAX cream analgesia for infusions. From 2000, each subject fasted except for ad libitum water until 0900 the following morning. On study day 4, between 0400 and 0900, a simultaneous primed-constant rate intravenous infusion of [6,6-$^2H_2$]glucose (22 μmol $\cdot$ kg^{-1} and 0.36 μmol $\cdot$ kg^{-1} $\cdot$ min^{-1}) and [2-^{13}C]glycerol (5.5 μmol $\cdot$ kg^{-1} and 0.09 μmol $\cdot$ kg^{-1} $\cdot$ min^{-1}) was administered to measure the rate of appearance (Ra) of glucose and glycerol (an index of total lipolysis). From 0630 to 0900, a primed-constant rate intravenous infusion of [U-^{13}C]palmitate bound to human albumin (0.90 μmol $\cdot$ kg^{-1} and 0.015 μmol $\cdot$ kg^{-1} $\cdot$ min^{-1}) was administered to measure the Ra of palmitate [index of free fatty acid (FFA) turnover]. Blood samples (5 mL each) were obtained at baseline (0300), 0700, and every 15 min from 0800 to 0900 (representing the overnight fasting condition).

Between 0900 and 1500, the women were offered small drinks (25 mL every 15 min) that had the same composition and provided the same amount of calories as consumed over the previous 2 d (either glucose or galactose). In addition, the women received isotope infusions identical to those received between 0400 and 0900, except that the rate of [6,6-$^2H_2$]glucose was increased to 0.70 μmol $\cdot$ kg^{-1} $\cdot$ min^{-1}. Blood samples were drawn hourly from 1000 to 1300 and every 15 min from 1400 to 1500 (representing the feeding condition).

Carbon dioxide production and oxygen consumption were measured hourly from 0700 to 0900 and from 1300 to 1500 by using indirect calorimetry for the calculation of substrate oxidations. Urine was collected during the last 24 h of the study (one collection representing the first 12 h followed by two 6-h collections during the last 12 h).

On completion of the study, the women were discharged from the GCRC. They were readmitted to the GCRC after 1–2 wk for the second study. The second study was performed by using a design identical to the first except that the drink had a different carbohydrate source (glucose or galactose). Nonlactating women were studied by using an identical protocol, except that, obviously, no breast-milk samples were obtained.

The large commitment of time in the GCRC and limitations with GCRC bed availability, particularly on weekends because of reduction in National Institutes of Health funding for the GCRC, made it very difficult to recruit subjects per the above protocol. Therefore, after completion by 5 lactating and 4 nonlactating women, we shortened the duration of the initial dietary period to one full day of diet (drink) with the infusion study occurring the following morning. Thus, the study was shortened from 4 d and 3 nights to 2 d and 1 night. For this shortened protocol, subjects were admitted to the GCRC at 0700 on day1 and received drinks every 3 h between 0900 and 2000, which corresponded to 24 h of intake in the long protocol. The infusions were performed on the following day in an identical fashion to that described above for the long protocol. The results from the first 9 subjects studied on the long protocol were indistinguishable from those of the 5 subjects (3 nonlactating and 2 lactating women) studied on the shortened protocol (comparison data not shown but available on request).

Materials

[6, 6-$^2H_2$]Glucose (99 atom% ^2H), [2-^{13}C]glycerol (99 atom% ^{13}C), [$^2H_5$]glycerol (99 atom% ^2H), [1, 2-$^{13}C_2$]palmitic acid (99 atom% ^{13}C), and [U-^{13}C]palmitate (99 atom% ^{13}C) (potassium salt) were purchased as sterile and pyrogen free from Cambridge Isotope Laboratories (Andover, MA). The isotopes were again determined to be sterile and pyrogen free in the investigation pharmacy of Texas Children's Hospital. [6, 6-$^2H_2$] Glucose and [2-^{13}C]glycerol were dissolved in isotonic saline, and the solutions were filtered through a 0.2-μm filter (Millipore Corp, Bedford, MA) into sterile syringes. The [U-^{13}C]palmitate tracer was dissolved in heated sterile isotonic saline (60°C) and passed through a 0.2-μm filter into warm (50°C) human serum albumin solution (25%) (Baxter Health Corporation, Westlake Village, CA). The sterile solutions were prepared <48 h before the study and were maintained at 4°C until just before their use, as previously described (23).

Analytic methods

Substrate and hormone concentrations

Plasma glucose and lactate concentrations were measured by using enzyme-specific methods (YSI Glucose Analyzer; YSI, Yellow Springs, OH), plasma insulin and C-peptide concentrations by electrochemiluminescence with a Roche Elecsys 1010 analyzer (Roche Diagnostics Corporation, Indianapolis, IN), plasma lipids with standard laboratory techniques, and plasma FFAs and β-hydroxybutyrate by microfluorometric enzyme analyses as previously described (24). Plasma glycerol and palmitate concentrations were measured by reverse isotope dilution and gas chromatography–mass spectrometry (GC-MS) by using the internal standards [$^2H_5$]glycerol (23) and [1, 2-$^{13}C_2$]palmitic acid (25), respectively.

Milk lactose concentrations were measured by using an enzyme-specific method (YSI Glucose Analyzer; YSI), protein concentrations with a bicinchoninic acid protein assay kit (Novagen, Madison, WI) (26, 27), and fat concentrations with a colorimetric method as previously described (28). Production, composition, and the caloric content of the breast milk were calculated as previously described (26).

Isotopic enrichments

The penta-acetate derivative of glucose was prepared, and the isotopic enrichments of [6,6-$^2H_2$]glucose were measured by GC-MS as described previously (23, 29). The tripropionate derivative of glycerol was prepared, and the isotopic enrichments of [2-^{13}C]glycerol and [$^2H_5$]glycerol were measured by GC-MS (HP 5890/HP5970; Hewlett-Packard Co, Palo Alto, CA) and an HP-1701 column (30 m × 0.25 mm × 0.25 μm) (Agilent Technologies, Wilmington, DE). The electron impact ionization mode was used with selected ion monitoring of *m/z* 173–176 for glycerol. Palmitate (in the FFA pool) was converted to the palmitate pentafluorobenzyl bromide derivative. Enrichments of [U-^{13}C]palmitate and the internal standard [1, 2-$^{13}C_2$]palmitate were measured by GC-MS by using a quadrupole instrument (HP 5890/HP5970; Hewlett-Packard Co) and an SP2380 column (60 m × 0.25 mm × 0.25 μm) (Supelco Inc, Bellefonte, PA) according to the established method (30). Negative chemical ionization mode was used with methane as the reagent gas and selected ion monitoring of *m/z* 255–257 and 271. Lactose obtained from milk samples during the tracer infusions were hydrolyzed to glucose and galactose enzymatically, and enrichment of the resultant sugars was analyzed as previously described (17, 31). All measurements were made in the Stable Isotope Core Laboratory of the Children's Nutrition Research Center.

Indirect calorimetry

Indirect calorimetry was performed by using a MedGraphic Model Indirect Calorimeter (MedGraphics Inc, Minneapolis, MN). Substrate oxidation rates of protein, glucose, and lipid and resting energy expenditure were calculated by using the gaseous exchange equations previously described (32). The substrate oxidation rates were calculated as follows:

$$\text{Lipid oxidation} = 1.67(\dot{V}CO_2 - \dot{V}O_2) - 1.92N \quad (2)$$

$$\text{Glucose oxidation} = 4.55\dot{V}CO_2 - 3.21\dot{V}O_2 - 2.87N \quad (3)$$

$$\text{Protein oxidation} = N/6.25 \quad (4)$$

where $\dot{V}CO_2$ and $\dot{V}O_2$ are the gaseous exchanges (L/min) obtained from the calorimeter, and N is total nitrogen urinary excretion (g/min).

Calculations

Kinetic measurements

The Ra values of glucose, glycerol (total lipolysis), and palmitate (indicator of total FFA Ra) into the systemic circulation were calculated under near steady state conditions by using the following standard isotope dilution equation:

$$\text{Ra} = [(E_i/E_p) - 1] \times I \quad (5)$$

where E_i and E_p are the infusate and plasma enrichments, respectively, of the tracers [6,6-$^2H_2$]glucose, [2-^{13}C]glycerol, and [U-^{13}C]palmitate, and I is the rate of infusion of the tracers. Ra FFA was calculated according to the following equation:

$$\text{Ra FFA} = \text{Ra palmitate/plasma (palmitate/FFA) ratio} \quad (6)$$

The fraction of glucose and galactose (product pool) in milk lactose that was derived from plasma glucose (precursor pool) and the fraction derived from de novo synthesis were calculated as previously described (17, 23).

Insulin sensitivity

Insulin sensitivity in the fasting condition was calculated by using the average baseline insulin and glucose values with the homeostasis model of assessment (HOMA) of insulin resistance and the quantitative insulin-sensitivity check index (33).

Statistical analysis

Values obtained during each near steady state period of tracer infusion (0800–0900 and 1400–1500, representing overnight fasting and the feeding state, respectively) were averaged for each subject and are presented as means ± SEs. Generalized Estimating Equations (GEEs) (SPSS 17.0) were used to assess the effects of the type of carbohydrate (glucose compared with galactose) and the interactions due to group × type of carbohydrate. Post hoc procedures (least significant difference) provided by GEE were used to perform the comparisons within groups and when all women were combined with regard to glucose and galactose after the overnight fasting and feeding conditions. The effect of the different sugars on milk volume and composition was compared by using Student's paired t test. Software program SPSS (version 17; SPSS Inc, Chicago, IL) was used for all statistical analyses. Significance was defined as $P < 0.05$.

RESULTS

After the overnight fast

Few differences in the metabolic variables measured after the overnight fast were observed between the glucose and galactose diets. When the data for all women were combined, plasma concentrations of C-peptide, cholesterol, LDL, and HDL were lower ($P < 0.05$) and concentrations of triglycerides were higher ($P < 0.01$) during the galactose diet than during the glucose diet (**Table 1**). In the lactating women, only C-peptide and glucose Ra were slightly but significantly ($P < 0.05$) lower during the galactose diet than during the glucose diet.

TABLE 1
Substrate and hormone concentrations, kinetic measures, energy expenditure (EE), and substrate oxidation after the overnight fast[1]

	All women (n = 14)		Nonlactating women (n = 7)		Lactating women (n = 7)	
	Glucose	Galactose	Glucose	Galactose	Glucose	Galactose
Glucose (mmol/L)	5.10 ± 0.08	5.09 ± 0.8	5.23 ± 0.12	5.10 ± 0.07	4.97 ± 0.09	5.09 ± 0.15
Insulin (μU/mL)	12.3 ± 2.2	9.5 ± 1.2	17.5 ± 4.3	13.0 ± 2.2	7.0 ± 1.1	6.0 ± 0.9
C-peptide (ng/mL)	3.0 ± 0.4	2.4 ± 0.3**	3.5 ± 0.7	2.8 ± 0.5	2.5 ± 0.3	2.0 ± 0.2*
Galactose (μmol/L)	21 ± 2	20 ± 2	14 ± 3	13 ± 3	28 ± 3	27 ± 3
Lactate (mmol/L)	0.95 ± 0.1	0.86 ± 0.1	1.06 ± 0.1	1.04 ± 0.09	0.83 ± 0.1	0.67 ± 0.0
β-Hydroxybutyrate (mmol/L)	115 ± 13	116 ± 11	67 ± 15	49 ± 14	163 ± 22	184 ± 16
FFA (μmol/L)	637 ± 52	610 ± 43	529 ± 47	504 ± 57	745 ± 92	717 ± 67
Cholesterol (mg/dL)	169 ± 10	161 ± 8**	174 ± 16	165 ± 13*	164 ± 11	158 ± 10
LDL (mg/dL)	103 ± 8	96 ± 6*	109 ± 13	100 ± 11*	97 ± 9	93 ± 7
HDL (mg/dL)	44 ± 3	40 ± 3**	39 ± 3	33 ± 2*	49 ± 4	46 ± 4
Triglycerides (mg/dL)	106 ± 14	132 ± 13**	124 ± 15	167 ± 15**	87 ± 18	96 ± 23
Glycerol (μmol/L)	76 ± 5	71 ± 5	59 ± 5	55 ± 3	92 ± 8	87 ± 9
Palmitate (μmol/L)	152 ± 10	138 ± 7	120 ± 11	108 ± 7	184 ± 17	168 ± 18
Palmitate/FFA	0.24 ± 0.01	0.23 ± 0.01	0.23 ± 0.02	0.23 ± 0.02	0.26 ± 0.02	0.24 ± 0.02
HOMA	2.86 ± 0.70	2.15 ± 0.36	4.21 ± 1.21	2.95 ± 0.56	1.52 ± 0.24	1.35 ± 0.20
QUICKI	0.34 ± 0.01	0.35 ± 0.01	0.35 ± 0.01	0.35 ± 0.01	0.36 ± 0.01	0.37 ± 0.01
Glucose Ra (μmol^{-1} · kg^{-1} · min^{-1})[2]	8.15 ± 0.22	7.91 ± 0.23	7.10 ± 0.31	7.09 ± 0.31	9.19 ± 0.30	8.73 ± 0.33*
Glycerol Ra (μmol^{-1} · kg^{-1} · min^{-1})[2]	2.55 ± 0.13	2.46 ± 0.15	2.13 ± 0.18	2.07 ± 0.17	2.98 ± 0.19	2.84 ± 0.25
Palmitate Ra (μmol^{-1} · kg^{-1} · min^{-1})[2]	1.47 ± 0.10	1.38 ± 0.10	1.26 ± 0.10	1.22 ± 0.11	1.68 ± 0.16	1.55 ± 0.17
FFA Ra (μmol^{-1} · kg^{-1} · min^{-1})[2]	6.21 ± 0.54	6.06 ± 0.49	5.67 ± 0.61	5.56 ± 0.54	6.57 ± 0.89	6.56 ± 0.81
RQ	0.82 ± 0.01	0.82 ± 0.01	0.83 ± 0.01	84 ± 0.01	0.81 ± 0.01	0.80 ± 0.01
EE (kcal/d)	1501 ± 26	1479 ± 31	1485 ± 41	1475 ± 56	1518 ± 32	1483 ± 29
Fat oxidation (g/d)	84 ± 4	80 ± 6	82 ± 6	72 ± 9	86 ± 5	88 ± 6
CHO oxidation (g/d)	147 ± 11	144 ± 10	155 ± 17	169 ± 17	140 ± 15	119 ± 12
Protein oxidation (g/d)	37 ± 5	42 ± 7	32 ± 5	37 ± 4	42 ± 9	46 ± 12

[1] All values are means ± SEMs. RQ, respiratory quotient; FFA, free fatty acid; Ra, rate of appearance; CHO, carbohydrate; HOMA, homeostasis model of assessment; QUICKI, quantitative insulin-sensitivity check index. Post hoc procedures provided by Generalized Estimating Equations were used to perform the comparisons of glucose and galactose within groups and in all women combined. *,**Significant difference between the glucose and galactose diets: *$P < 0.05$, **$P < 0.01$.

[2] Based on total body weight.

TABLE 2
Plasma substrate concentrations during glucose and galactose feeding[1]

	All women (n = 14)		Nonlactating women (n = 7)		Lactating women (n = 7)	
	Glucose	Galactose	Glucose	Galactose	Glucose	Galactose
Glucose (mmol/L)	5.84 ± 0.09	5.20 ± 0.08**	6.02 ± 0.12	5.19 ± 0.07**	5.66 ± 0.14	5.21 ± 0.14**
Insulin (μU/mL)	34.8 ± 6.6	15.5 ± 2.2**	53.8 ± 12.7	20.8 ± 4.0**	15.8 ± 3.8	10.1 ± 1.8**
C-peptide (ng/mL)	6.6 ± 0.9	3.2 ± 0.3**	8.3 ± 1.6	3.5 ± 0.6**	4.9 ± 0.6	2.8 ± 0.2**
Galactose (μmol/L)	19 ± 2	125 ± 10**	14 ± 4	155 ± 15**	24 ± 2	95 ± 13**
Lactate (mmol/L)	0.93 ± 0.1	1.26 ± 0.1**	1.03 ± 0.1	1.44 ± 0.1**	0.84 ± 0.1	1.07 ± 0.1**
β-OH-Butyrate (μmol/L)	33 ± 6	41 ± 10	26 ± 8	17 ± 6	40 ± 8	64 ± 18
FFA (μmol/L)	211 ± 22	436 ± 36**	102 ± 11	288 ± 31**	320 ± 43	584 ± 65**
Cholesterol (mg/dL)	168 ± 10	167 ± 9	172 ± 14	173 ± 16	163 ± 14	160 ± 9
LDL (mg/dL)	105 ± 8	96 ± 6**	109 ± 11	97 ± 10*	102 ± 12	94 ± 7
HDL (mg/dL)	43 ± 2	41 ± 2	37 ± 1	36 ± 3	48 ± 3	46 ± 4
Triglycerides (mg/dL)	97 ± 13	154 ± 20**	126 ± 20	209 ± 37**	69 ± 16	99 ± 17**
Glycerol (μmol/L)	49 ± 2	66 ± 4**	33 ± 2	47 ± 4**	65 ± 5	86 ± 7**
Palmitate (μmol/L)	55 ± 5	102 ± 9**	30 ± 4	71 ± 7**	80 ± 10	134 ± 17*
Palmitate/FFA	0.28 ± 0.01	0.24 ± 0.01	0.29 ± 0.01	0.25 ± 0.01	0.26 ± 0.03	0.23 ± 0.02

[1] All values are means ± SEMs. FFA, free fatty acid. Post hoc procedures provided by Generalized Estimating Equations were used to perform the comparisons within groups and all women combined with regard to glucose and galactose. *,**Significant difference between the glucose and galactose diets: *$P < 0.05$, **$P < 0.01$.

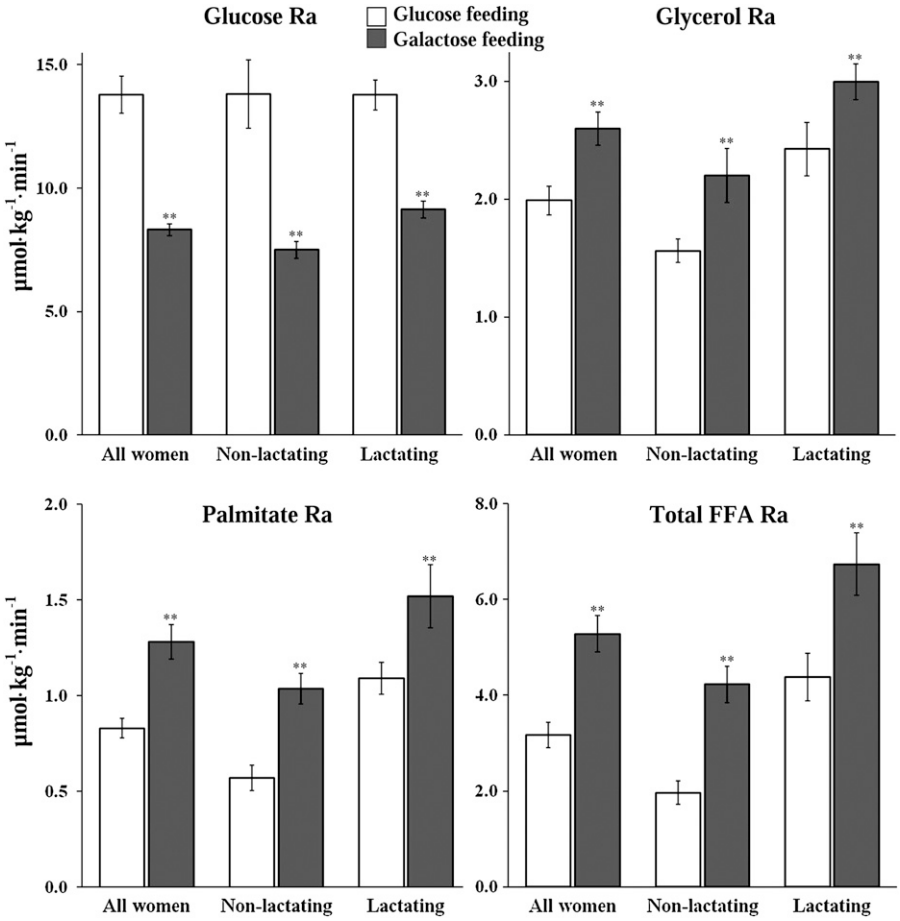

FIGURE 1. Mean (±SEM) rates of appearance (Ra) of glucose, glycerol, palmitate, and total free fatty acids (FFAs) during the feeding of glucose (□) and galactose (■) in all women combined (n = 14), in nonlactating women (n = 7), and in lactating women (n = 7). The calculations are based on total body weight (kg). Post hoc procedures provided by Generalized Estimating Equations were used to perform the comparisons of glucose and galactose within groups and in all women combined. **Significant difference between the glucose and galactose diets, $P < 0.01$.

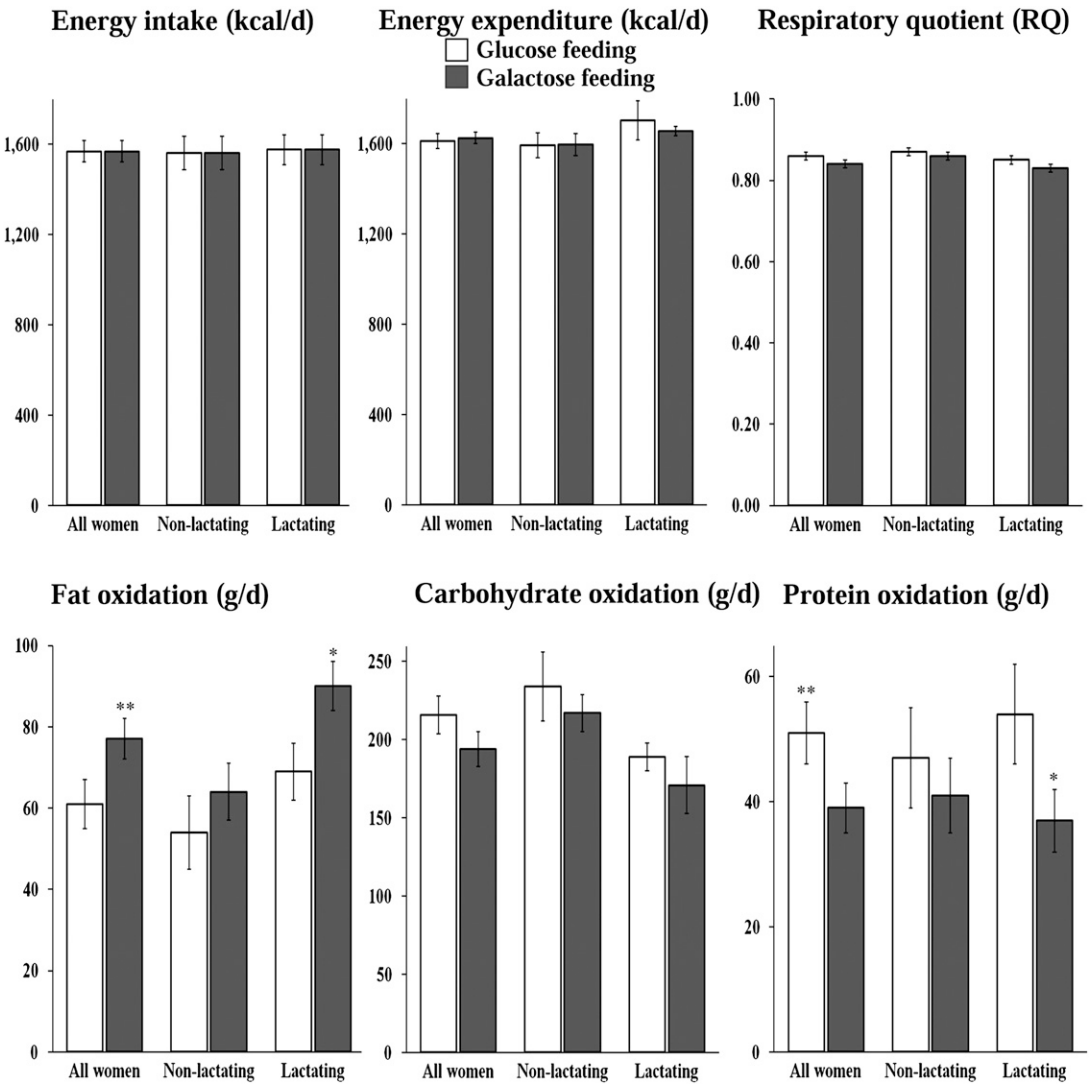

FIGURE 2. Mean (±SEM) energy intake and expenditure, respiratory quotients, and substrate oxidation during the feeding of glucose (□) and galactose (■) in all women combined ($n = 14$), in nonlactating women ($n = 7$), and in lactating women ($n = 7$). Post hoc procedures provided by Generalized Estimating Equations were used to perform the comparisons of glucose and galactose within groups and in all women combined. *·**Significant difference between the glucose and galactose diets: $*P < 0.05$, $**P < 0.01$.

During feeding

Substrate and hormone concentrations

Within both groups and when all women were combined, plasma concentrations of glucose, insulin, and C-peptide were lower ($P < 0.01$) and those of galactose, lactate, triglycerides, FFA, glycerol, and palmitate were higher ($P < 0.01$) (**Table 2**) during the galactose diet than during the glucose diet.

Glucose and lipid kinetics

Within both groups and when all women were combined, glucose Ra was lower ($P < 0.01$) and Ra values of glycerol, palmitate, and total FFA were higher during the galactose diet than during the glucose diet ($P < 0.01$) (**Figure 1**).

Energy expenditure and substrate oxidation

No differences in the RQ, energy expenditure, or carbohydrate oxidation rates were observed between the glucose and galactose diets within either group or when all women were combined. However, when all women were combined, fat oxidation was higher ($P = 0.01$) and protein oxidation was lower ($P < 0.01$) during the galactose diet than during the glucose diet (**Figure 2**).

Milk production and composition

Milk production and composition were similar between the glucose and galactose diets (**Table 3**). Regardless of the fasting or feeding condition, the percentage of milk lactose derived from plasma glucose was lower ($P < 0.05$) and the percentage derived from mammary hexoneogenesis was higher ($P < 0.05$) during the galactose diet than during the glucose diet (**Table 4**).

DISCUSSION

The present study indicates that consumption of a liquid meal of galactose as the sole carbohydrate source increases the rate of endogenous lipolysis when compared with glucose in both obese

TABLE 3
Milk production and composition[1]

	Glucose	Galactose
Volume (mL/d)	656 ± 77	702 ± 61
Caloric content (kcal/d)	409 ± 89	425 ± 88
Lactose		
(g/dL)	6.1 ± 0.1	6.1 ± 0.1
(g/d)	39 ± 4	41 ± 4
Fat		
(g/dL)	4.0 ± 0.4	3.8 ± 0.4
(g/d)	26.4 ± 4.0	26.3 ± 3.0
Protein		
(g/dL)	2.0 ± 0.1	1.9 ± 0.1
(g/d)	12.7 ± 1.2	13.1 ± 1.4

[1] All values are means ± SEMs; $n = 7$. The effect of the different sugars on milk volume and composition was compared by using Student's paired t test. No significant differences were found.

lactating and nonlactating women. As we anticipated, galactose ingestion resulted in lower plasma concentrations of glucose and insulin than did glucose ingestion (17–19). Despite the fact that the plasma glucose concentration was only 12% lower, glucose Ra decreased by 66%. This was associated with a >50% reduction in the plasma insulin concentration, which is most likely responsible for the higher Ra of glycerol (23%), palmitate (35%), and total FFA (40%). This is in keeping with the higher plasma concentrations of palmitate, glycerol, and FFA during the galactose diet than during the glucose diet. Thus, these findings collectively prove our hypothesis and are consistent with the well-known antilipolytic effect of insulin (34–36).

We did not detect any significant differences in energy expenditure or carbohydrate oxidation between the glucose and galactose diets. However, we did observe that fat oxidation was higher (30%) and protein oxidation was lower (45%) during the galactose diet than during the glucose diet in the lactating women. In 5 of 7 nonlactating women, fat oxidation was higher with galactose feeding than with glucose feeding. However, the difference between feedings (18%) was not significant ($P = 0.15$). This may have been the result of a type 2 error because, when the data from all 14 women studied were pooled (no interaction between group × carbohydrate type), the higher fat oxidation (28%) and lower protein oxidation (30%) were highly significant ($P < 0.01$). Several studies have compared the effects of low- with those of high-glycemic-index diets on substrate utilization during subsequent exercise in women (37) and men (38). No differences were reported in substrate oxidations or energy expenditure during the postprandial period (during resting); however, fat oxidation was significantly higher during exercise after the low-glycemic-index diets (37, 38).

Generally, the effects of the 2 sugars after the overnight fast were similar, suggesting a lack of carryover effect from day to day. The plasma concentrations of cholesterol, LDL, and HDL were slightly lower but those of triglycerides were higher during the galactose diet than during the glucose diet. Plasma C-peptide concentrations but not insulin were elevated on the glucose diet. This may reflect the higher insulin secretion in response to the glucose feeding and the slower rate of disappearance of C-peptide when compared with insulin (39).

In this short-term study, lactation performance was not affected by the type of carbohydrate in the maternal feeding because milk volume and composition were similar between the 2 diets. We (26) and others (40) have reported that dietary macronutrient composition affects milk composition, because a high-fat diet increases milk fat concentration compared with a low-fat diet. Conversely, the source of milk sugars (plasma glucose or mammary hexoneogenesis) was not affected by the macronutrient composition after an overnight fast or during feeding (26). However, in the present study, we observed that the source of milk sugars was affected by the type of dietary carbohydrate; lactose derived from plasma glucose was lower and, thus, mammary hexoneogenesis was higher during the galactose diet. This activation of mammary hexoneogenesis suggests a compensatory mechanism to provide substrate for lactose synthesis. Additionally, under the present experimental condition, it is possible that plasma galactose during galactose feeding could contribute directly to milk galactose (17).

In summary, we showed the proof of principle that oral consumption of galactose promotes endogenous fat mobilization and oxidation during meal absorption in obese women while not adversely affecting milk production. On the basis of these data, long-term studies are warranted to determine whether galactose consumption in conjunction with moderate caloric restriction will facilitate body fat loss in obese lactating and nonlactating women. These studies should not be contemplated in obese pregnant women until such a program is shown to be safe for both the pregnant mother and the fetus.

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TABLE 4
Source of milk lactose during the fasting and fed states[1]

	Fasting		Fed	
	Glucose	Galactose	Glucose	Galactose
Milk glucose from plasma glucose (%)	81 ± 2	70 ± 3*	100 ± 2	94 ± 2
Milk glucose from hexoneogenesis (%)	19 ± 2	30 ± 3*	0 ± 2	6 ± 2
Milk galactose from plasma glucose (%)	71 ± 2	62 ± 3	95 ± 2	83 ± 2**
Milk galactose from hexoneogenesis (%)	29 ± 2	38 ± 3	5 ± 2	17 ± 2**
Milk lactose from plasma glucose (%)	76 ± 2	66 ± 2*	98 ± 2	89 ± 2*
Milk lactose from hexoneogenesis (%)	24 ± 2	34 ± 2*	2 ± 2	11 ± 2*

[1] All values are means ± SEMs; $n = 7$. The effect of the different sugars on the source of milk sugars during the fasting and fed states was compared by using Student's paired t test. *,**Significant difference between the glucose and galactose diets: $*P < 0.05$, $**P < 0.01$.

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