Incorporating Dairy Foods into Low and High Fat Diets Increases the Postprandial Cholecystokinin Response in Men and Women

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ABSTRACT The postprandial period is a dynamic state of hormone and lipoprotein metabolism that can be influenced by dietary composition. The objective of this study was to determine whether the source of dietary fat [dairy (D) vs. nondairy (ND)] would modify the lipemic, insulin and cholecystokinin (CCK) response to high or low fat meals. Men and women (n = 24) consumed 4 test meals with a similar polyunsaturated:saturated (P:S; 0.12:1) fat ratio. The diets were high (38% energy) or low (20% energy) in fat, with or without fat from dairy sources. CCK responses were greater after consumption of meals containing D than ND, and for high compared with low fat meals. Women had higher CCK responses than men and were more sensitive to the differences in dietary treatments. Consumption of low fat meals resulted in greater insulin responses than high fat meals. However, after consumption of the low fat meals, the insulin response of D was about half of the ND response; no differences in insulin response were detected after the high fat meals. Triacylglyceride response was influenced primarily by the fat content of the diet. Consumption of dairy containing fat was associated with an enhanced CCK response, which may have implications for the regulation of food intake. Blunting glucose and insulin response in low fat meals containing fat from dairy products may be useful for glycemic control.


KEY WORDS: • dairy • triacylglycerides • insulin • cholecystokinin • food intake • dietary fat

The postprandial period is a dynamic state of hormone release, stimulated by consumption of a meal and the presence of food components, as well as lipoprotein metabolism related to lipid absorption. Dietary factors such as the amount of fat, fatty acid composition and dietary fiber are well recognized as affecting the hormonal and lipoprotein response to a meal (1–4). Less is understood regarding the effect of the physical state of fat within a food on these responses. We hypothesized that constituents of milk, including the presence of the fat globule membrane, would alter the way in which dairy fat is handled in the postprandial period (5,6). Such an effect should be evident in the pattern of hormone and lipoprotein response to meals prepared with fat from dairy products. To examine this question, we determined the postprandial lipid, glucose, insulin and cholecystokinin (CCK) response to meals with similar fat content and fatty acid composition, but prepared with or without dairy products. In addition to comparing the source of fat in the meal (dairy; D, nondairy; ND), two levels of dietary fat were investigated [20% of energy (en%) and 38 en% as fat]. Because CCK is associated with meal-induced satiety (1), we also examined the subjects’ subjective assessment of satiety after the various meals.
nonfat milk and coconut milk. All subjects consumed the meals readily.

**Study design and procedures.** In preparation for each of their 4 study visits, subjects kept detailed 24-h scale-weighted food records 2 d before, the day before and the day after each test session. On the day of each study session, subjects arrived at the laboratory between 0700 and 0800 h after an overnight fast (10 h). An intravenous catheter was placed in the nondominant arm of each subject to allow for multiple blood sampling. After the initial fasting blood draw, subjects rested for a few minutes, acquainted themselves with their dining area and completed their first set of visual analog scales (VAS). VAS are subjective measures of appetite and satiety relative to the test meal conditions. Specifically, participants rated their hunger, fullness, desire to eat and how much they thought they could eat on 100-mm lines scales. Questions such as “How hungry do you feel right now?” or “How strong is your desire to eat right now?” preceded a 100-mm line anchored by opposing phrases “not at all hungry” and “extremely hungry” or “very weak” and “very strong.” Other anchors consisted of the phrases “not at all full” and “extremely full” or “a large amount” and “nothing at all” or “very pleasant” and “not at all pleasant” to access fullness, prospective consumption and meal like/dislike. After completing the first VAS, subjects were given one of the four test meals to consume in 20 min. Blood samples were collected and VAS booklets were completed after meal ingestion at 20, 40, 60, 90, 120 (2 h), 180 (3 h), 240 (4 h), 300 (5 h) and 360 min (6 h). At the end of the test session, catheters were removed and subjects were given a selection of foods (preweighed) from a tray before leaving the study site. Subjects were required to record the food consumed from the tray along with foods eaten outside the laboratory for the next 36 h. After the final test meal study day, subjects were interviewed about their study experience and their knowledge of the purpose of the study and their study experience and their knowledge of the purpose of the study and their study experience and their knowledge of the purpose of the study.

Blood samples (~10 mL) were collected in EDTA-coated vacutainer tubes, immediately cooled in ice, and plasma was obtained by centrifugation at 2000 × g for 15 min at 23°C. Two 2-mL aliquots of plasma were extracted using octadecylsilica cartridges (Sep-Pak) and eluents frozen at −20°C for determination of CCK concentrations by RIA. Another portion (2 mL) of plasma was stored in microcentrifuge tubes and frozen at −20°C for subsequent analysis of glucose, insulin and triacylglyceride (TAG) concentrations. Plasma glucose and TAG were analyzed in the University of California, Davis Clinical Nutrition Research Unit, analytical core laboratory, NIH#DK35747, according to approved protocols (4). The plasma concentrations of apolipoprotein (apo) B48 and B100 in the TAG-rich fraction were determined by SDSL-PAGE as previously described (4). Apo B48 and B100 responses in the triacylglyceride-rich fraction were investigated only in the 38% fat test meals.

Plasma CCK was measured by RIA using a highly specific and selective antibody, Ab-92128 (gift from Dr. Jens Rehfeld, Rigshospitalet, Copenhagen, Denmark) (1,7). Plasma insulin was measured by RIA according to the basic method described by Yalow and Berson modified by using 0.05 mol/L phosphate buffer containing 4 g/L human serum albumin and the precipitation method described by Desbuquois and Aurbach, using polyethylene glycol to separate free and antibody-bound insulin (8,9).

**Statistical analysis.** To examine the satiety response to the four test meals, data from the VAS, the scale-weighted food records and the plasma insulin, glucose, TAG and CCK concentrations were analyzed by repeated-measures (RM)-ANOVA using the General Linear Models or MIXED procedures of SAS (SAS Institute, Cary, NC) with test meal, time and gender as main factors and subject as the blocking variable. Data analyzed from the VAS were first converted to increments above baseline to account for relative baseline variability among subjects. Substrate metabolites (glucose and insulin) and CCK were log transformed where appropriate based on univariate analysis for normal distribution. Significant differences among treatment means (adjusted for multiple comparisons) were analyzed by pairwise t test and Tukey’s honestly significant test for appropriate comparisons. The relationship between the subjective satiety response (VAS) and the biological satiety response (CCK) was tested using linear regression analysis. Values are means ± SEM; differences were considered significant at P < 0.05.

**RESULTS**

A total of 14 men and 10 women were recruited for the study. Mean ages of men and women were 31 ± 10 and 39 ± 6 y, respectively. Mean BMI (kg/m²) for the men and women were 25.5 ± 1.5 and 23.9 ± 2.0, respectively. All subjects maintained their body weight throughout the study. Food records collected provided information about the background diets of the men and women participating in the study. Nutrient and statistical analysis of the food records indicated that energy intake differed between men and women but not within gender. The daily energy intake for the women was 3030 ± 765 kcal and for the men 10,283 ± 670 kcal. Macronutrient composition did not differ between the groups with the average en% from fat, carbohydrate and protein being 30 ± 1, 55 ± 2 and 15 ± 1%, respectively. Patterns of food intake were consistent during the study period. The energy intake in the 36-h period subsequent to the test meal (calculated weight × test meal energy intake) was consistent between men and women meals. Combined energy intake (test meal + subsequent meals/snacks) showed that women compensated for the energy provided by the test meals so that study day intake was similar to their average daily intake. In contrast, men tended to have a slightly higher total energy intake on study days (~2300 kcal).

Statistical analysis of the CCK response for all subjects indicated strong test meal and time effects (both P < 0.0001) (data combined for all subjects are not shown). Based on the least-squares means (LSM), consumption of the dairy-containing meals produced higher concentrations of CCK during the experimental period than the ND meals, and consumption of the higher fat versions within each category of D or ND stimulated more CCK release than the lower fat meals. In addition to the test meal effects, a sex-by-meal interaction was observed (P < 0.02). Using the LSM values as an estimate of the response, women had higher plasma CCK levels than men (9.0 ± 1.0 and 5.9 ± 0.8 pmol/L, P < 0.03). In addition, women appeared to be more sensitive, as measured by CCK, to the dietary fat changes of the meals than the men. In women, meals containing dairy fat were more potent stimulators of CCK than meals that contained no dairy fat, a difference that was not detected in men (Fig. 1, Table 1).

Insulin and glucose concentrations increased significantly after the meal (Fig. 2, Table 1). The effect of diet treatment on insulin response was significant and there was no difference in response between men and women. Consumption of the 38 en% fat diets resulted in lower insulin concentrations than the 20 en% fat meals. When the fat content of the meal was 38%, there was no difference between the D- and ND-containing meals. However, at the lower fat level, the insulin concentrations were significantly lower after the D-containing meal than after the ND meal. Using LSM as an estimate of the response (Table 1), the use of dairy products in the low fat meal resulted in an insulin response that was about half the response of the ND meal. Consistent with the insulin response to the various meals, glucose concentrations were lower after the 38 en% fat meals than the 20 en% fat meals (P = 0.06 for the ND meals and P = 0.07 for the D meals); glucose was significantly lower after the D compared with the ND meals but only after the 20 en% fat meals. The D and ND meal glucose responses did not differ between the two 38 en% fat meals.

Triacylglyceride (TAG) concentrations increased after the meal; however, the differences in TAG concentrations were not significant among the dietary treatments (data not shown). The increase in TAG concentration was calculated by subtracting TAG concentration at time zero from each postmeal TAG concentration. In this analysis, the effect of
test meal was significant, and specific comparisons indicated that in comparing the two dairy-containing meals the 38 en% fat diet was significantly higher than the 20% fat meal; between the ND meals, however, this difference tended to be significant ($P < 0.12$) (Fig. 3, Table 1). Apo B100 concentrations in the TAG-rich fraction were significantly higher in men than women (131.8 and 93.5 nmol/L, respectively, SEM 23) and did not differ either by time or by test meal treatment (data not shown). The concentration of apo B48 in women was lower than in men ($P < 0.05$) and tended to increase over time ($P = 0.08$) and to be lower in the D meals than the ND meals ($P = 0.09$) (Table 2).

Visual analog scales (VAS) were used to evaluate the subjective satiety response to the test meals. The overall responses to the meals differed (meal effect $P < 0.0003$, $n = 24$). Individual VAS analysis (i.e., hunger, desire to eat, fullness, prospective consumption) indicated that hunger was suppressed more strongly by ND meals than by D meals over the 6-h experimental period (ND38/D38: 34.1 and 1.4, $P < 0.01$; ND20/D20: 38.4 and 1.5, $P < 0.05$) (Table 2). Scores for desire to eat and fullness showed differences within D and ND categories for the low fat meals, but not the high fat meals. For both desire to eat and

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**TABLE 1**

Plasma cholecystokinin (CCK), insulin, glucose and triacylglyceride concentrations in men and women who consumed test meals that varied in fat content (20% or 38% energy from fat) and dairy (D) or nondairy (ND) as the fat source

<table>
<thead>
<tr>
<th></th>
<th>D38</th>
<th>ND38</th>
<th>D20</th>
<th>ND20</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCK, pmol/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>11.8</td>
<td>8.1</td>
<td>9.1</td>
<td>7.2</td>
</tr>
<tr>
<td>Men</td>
<td>6.7</td>
<td>6.1</td>
<td>6.1</td>
<td>4.7</td>
</tr>
<tr>
<td>Insulin, pmol/L</td>
<td>55.5</td>
<td>42.9</td>
<td>124.6</td>
<td>214.2</td>
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<tr>
<td>Glucose, mmol/L</td>
<td>90.1</td>
<td>87.6</td>
<td>86.5</td>
<td>91.3</td>
</tr>
<tr>
<td>TAG, mmol/L</td>
<td>0.47</td>
<td>0.37</td>
<td>0.22</td>
<td>0.26</td>
</tr>
</tbody>
</table>

$^1$ Values are the least-squares means estimate from ANOVA $\pm$ SEM, $n = 14$ men and 10 women. Within a row, values not sharing a letter differ, $P < 0.05$. 

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**FIGURE 2** Insulin (upper panel) and glucose (lower panel) responses of men and women to meals that vary in type (D = dairy, ND = nondairy) and amount of fat (38 indicates 38% of energy and 20 indicates 20% of energy from fat). Values are means $\pm$ SEM, $n = 24$. Values for the four groups not sharing a common letter differ, $P < 0.05$; the corresponding values for the least-squares means are in Table 2.
fullness, the ND20 meal provided a stronger suppression of
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**DISCUSSION**

Dairy products provide 20–25% of the saturated fatty acids (SFA) consumed by Americans, at least one third of the riboflavin and about two thirds of the calcium. Although SFA are associated with increased risk of cardiovascular disease, consumption of dairy products has been associated with reductions in cardiovascular risk factors in humans as well as animal models (10–13). In addition, Newby et al. (14) reported that a diet pattern high in reduced-fat dairy products was associated with smaller gains in BMI and waist circumference. Recent studies indicated that increasing calcium intake by consumption of dairy products may protect against weight gain, although some questions remain about the strength of these associations (15–17). We hypothesized that provision of dietary fat from dairy products might result in different postprandial responses to these meals compared with meals from nondairy sources with similar fatty acid composition. This effect might be due to the presence of factors such as the fat globular membrane that could alter the utilization of the lipid in these foods. The present study was designed to test the effect of both the amount of fat in the diet as well as the source of fat (dairy vs. nondairy) on postprandial responses in men and women.

The insulin and glucose results suggest that in the context of a low fat meal, dairy products can reduce glycemic and insulinemic responses. This effect of dairy products, i.e., the reduced glycemic and insulinemic responses to a meal, were not observed when the fat content of the meal was higher, as in the D and ND test meals containing 38% fat. Undoubtedly, the differences noted in the responses between the high and low fat meals are due to the lower carbohydrate content of the high fat meals. The degree of fat saturation did not alter glycemic or insulinemic response to mashed potatoes in men (18). However, with a similar fatty acid pattern at 20 en% from fat, a significant difference due to source of fat in glucose and insulin response was observed, suggesting a potential benefit of using low fat dairy products in diets designed to lower risk for diabetes.

The data indicate that dairy fat is a more potent stimulator of CCK than a blend of nondairy fats with a similar P:S ratio. This effect was particularly evident in women, who had higher CCK concentrations than men in response to each of the meals. Moreover, the CCK response to meals by women tended to be more discriminating than that of the men except for the D20 meal, CCK concentrations did not differ among meals in men, whereas this was not the case for women. This finding is consistent with our previous studies showing a distinct sex difference in the CCK response to meals that vary in fat type and or content (1). Implications of this result are of interest when considering CCK function(s) and relative interactions with other hormones in response to eating. CCK mediates processes of digestion and absorption and is probably best known for its stimulatory action on the exocrine pancreas for digestive enzyme secretion and the gall bladder to release bile acids. In addition, however, CCK has been shown to slow gastric emptying, inhibit food intake and can have a role in controlling the glycemic response to a meal. Holt et al. (19) suggested that glycemic and insulin responses to carbohydrate foods are inversely proportional to CCK response. CCK is likely to modulate insulin and glucose response by delaying gastric emptying and increasing the sensitivity of tissues to insulin (20–22). Findings from the present study support this idea, but only in the context of the low fat, high carbohydrate meal relative to fat type, D vs. ND.

CCK release produces satiety; however, the exact mecha-

**TABLE 2**

<table>
<thead>
<tr>
<th>Time, h</th>
<th>Women*</th>
<th>Men</th>
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<tbody>
<tr>
<td>0</td>
<td>1.34</td>
<td>6.89</td>
</tr>
<tr>
<td>2</td>
<td>2.35</td>
<td>12.62</td>
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<td>11.10</td>
</tr>
<tr>
<td>6</td>
<td>4.02</td>
<td>9.60</td>
</tr>
<tr>
<td>SEM</td>
<td>0.87</td>
<td>1.93</td>
</tr>
</tbody>
</table>

*Values are the least-squares means estimate from ANOVA, n = 14 men and 10 women. Different from men, P < 0.05.
nism by which CCK contributes to satiety remains controversial (23–25). Previous work in our laboratory, in both animals and humans, indicated a strong relationship between CCK release and satiety. In animal studies, this relationship was demonstrated using meal pattern analysis coupled with various nutrient infusions, use of CCK antagonists as well as a direct measure of plasma CCK concentrations (26,27). In humans, we utilized VAS, food intake and measured plasma CCK concentrations over time relative to different meal challenges. In previous studies, we showed that in unrestrained eaters, the CCK response to meals is correlated with VAS (1). Moreover, in previous studies, we showed that in unrestrained eaters, the complexity of the meal design or the laboratory setting may have influenced subjects in subtle ways. Other studies in our laboratory (1), including unpublished data, have indicated that CCK and VAS are typically correlated. The consistent differences in CCK response suggest that dairy products have the potential to enhance the satiety of meals. It would be worth investigating whether enhanced CCK response contributes to the reported effects of dairy products on body weight.

Modifying the source of saturated fat in the diet did not change the TAG response to the meal, although a higher fat diet did result in a significantly larger incremental increase in TAG after such a meal. These results are consistent with other reports on fat load and plasma TAG (1,28). A diet high in monounsaturated fatty acids on postprandial lipemia and incretin responses in healthy subjects. Am. J. Clin. Nutr. 67: 31–38.


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LITERATURE CITED