Forebyggelse af metabolisk syndrom vha. mejeriprodukter

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Mejeriforskningens Dag
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Metabolic Syndrome (MeS) (IDF-definition)

20 – 25 % of adults in Western countries have MeS

• Apple form (central obesity)

+ (two of the following 4 factors):
• Increased fasting Triglyceride
• Reduced HDL Cholesterol
• Increased blood pressure
• Increased fasting glucose

MeS increases the risk of CVD X 2 and T2D X 5
Agenda: Can we combat features of the metabolic syndrome?

- Dairy products and weight
- Dairy products and triglycerides
- Dairy products and blood pressure
- Dairy products, blood glucose and risk of type 2 diabetes
Agenda

• Dairy products and weight
• Dairy products and triglycerides
• Dairy products and blood pressure
• Dairy products, blood glucose and risk of type 2 diabetes
Weight change between dairy and control groups

<table>
<thead>
<tr>
<th>Study (year)</th>
<th>Mean difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>With energy restriction</strong></td>
<td></td>
</tr>
<tr>
<td>Zemel et al. (2004)</td>
<td>-4.47 (-10.45, 1.51)</td>
</tr>
<tr>
<td>Thompson et al. (2005)</td>
<td>-1.80 (-5.45, 1.85)</td>
</tr>
<tr>
<td>Zemel et al. (2005)</td>
<td>-5.07 (-8.61, -1.54)</td>
</tr>
<tr>
<td>Zemel et al. (2005)</td>
<td>-1.64 (-3.17, -0.11)</td>
</tr>
<tr>
<td>Harvey-Berino et al. (2005)</td>
<td>-1.20 (-4.88, 2.48)</td>
</tr>
<tr>
<td>Zemel et al. (2009)</td>
<td>-1.46 (-3.19, 0.27)</td>
</tr>
<tr>
<td>Faghhi et al. (2010)</td>
<td>-1.56 (-2.61, -0.51)</td>
</tr>
<tr>
<td>Van Loan et al. (2011)</td>
<td>-0.30 (-1.70, 1.10)</td>
</tr>
<tr>
<td>Smilowitz et al. (2011)</td>
<td>-1.70 (-8.01, 4.61)</td>
</tr>
<tr>
<td>Josse et al. (2011)</td>
<td>0.20 (-1.73, 2.13)</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td>-1.29 (-1.98, -0.60)</td>
</tr>
<tr>
<td><strong>Without energy restriction</strong></td>
<td></td>
</tr>
<tr>
<td>Barr et al., Females (2000)</td>
<td>1.40 (-2.31, 5.11)</td>
</tr>
<tr>
<td>Barr et al., Males (2000)</td>
<td>4.00 (-0.99, 8.99)</td>
</tr>
<tr>
<td>Zemel et al. (maintenance) (2005)</td>
<td>0.20 (-1.33, 1.73)</td>
</tr>
<tr>
<td>Gunther et al. (2005)</td>
<td>0.70 (-0.74, 2.14)</td>
</tr>
<tr>
<td>Weenersberg et al. (2009)</td>
<td>0.00 (-0.94, 0.94)</td>
</tr>
<tr>
<td>Palacios et al. (2009)</td>
<td>0.90 (-5.02, 6.82)</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td><strong>0.33 (-0.35, 1.00)</strong></td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td><strong>-0.61 (-1.29, 0.07)</strong></td>
</tr>
</tbody>
</table>

Conclusion

Increased dairy consumption without energy restriction may not lead to a change in weight or body composition.

Inclusion of dairy products in energy-restricted weight loss diets affects body weight, body fat mass, lean body mass and waist circumference compared with that in usual weight loss diets.
Weight loss in short-term (< 1 year) and long-term studies

Conclusion

Dairy products may have modest benefits in facilitating weight loss in short-term or energy-restricted RCTs.

In 2016 this meta-analysis showed a positive effect of total dairy intake on obesity.

In adults a 25% RR of obesity

The dose-response analysis between total dairy products consumption and risk of obesity.

Explanations for the weight reducing effect

• Increased calcium intake (reduced lipogenesis; reduced fat absorption)

• Whey protein (beneficial effects on muscle sparing and lipid metabolism)

• Conjugated linolenic acid (regulate adipogenesis)

• Other milk fats?
Long-term study

ORIGINAL ARTICLE
The effects of proteins and medium-chain fatty acids from milk on body composition, insulin sensitivity and blood pressure in abdominally obese adults

M Bohl¹, A Bjørnshave¹², MK Larsen³, S Gregersen¹ and K Hermansen¹
Design of DairyHealth

- 12-week, randomized, double-blinded, diet intervention study.
- Inclusion: abdominal obese participants, weight stable > 3 month, min. 18 years old.
  - 63 subjects randomized into four diets.
  - 60 g protein supplement
  - 63 g milk fat supplement

Dietary supplementation (12-week intervention)

- 60 g protein (powder + shaker)
- 63 g milk fat/day (2 rolls, 1 cake, 25 g butter)
  - 6.9 g/day of MCFA in low-MCFA butter
  - 8.5 g/day of MCFA in high-MCFA butter
  - A relative increase of 24% in high- compared with low-MCFA
- Daily energy intake from test products: 6,200 kJ (baseline mean daily energy intake ~ 8,200 kJ)
Body composition

- Evaluated by Dual-Energy X-ray Absorptiometry (DEXA) scans

Results

Lean body mass increased with 981 g (P = 0.010) after high-compared with low-MCFA

Results

Body fat percentage increased by 0.70 percentage points (P = 0.024) after low compared with high-MCFA.

Changes after the 12-week dietary intervention of body composition

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Whey + low MC-SFA (n = 12)</th>
<th>Whey + high MC-SFA (n = 13)</th>
<th>Casein + low MC-SFA (n = 13)</th>
<th>Casein + high MC-SFA (n = 13)</th>
<th>Two-factor ANOVA, P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total body mass (g), change</strong></td>
<td>1030 (128, 1932)</td>
<td>1846 (469, 3222)</td>
<td>1295 (400, 2190)</td>
<td>1500 (603, 2397)</td>
<td>0.923</td>
</tr>
<tr>
<td><strong>Lean body mass (g), change</strong></td>
<td>-26 (-930, 879)</td>
<td>981 (4, 1958)</td>
<td>-18 (-653, 617)</td>
<td>938 (28, 1593)</td>
<td>0.961</td>
</tr>
<tr>
<td><strong>Lean body percentage (% of total body mass), change</strong></td>
<td>-0.7 (-1.4, -0.1)</td>
<td>-0.2 (-0.8, 0.3)</td>
<td>-1.0 (-1.8, -0.2)</td>
<td>0.1 (-0.6, 0.8)</td>
<td>0.919</td>
</tr>
<tr>
<td><strong>Body fat mass (g), change</strong></td>
<td>1060 (523, 1596)</td>
<td>885 (184, 1586)</td>
<td>1318 (444, 2192)</td>
<td>635 (-163, 1433)</td>
<td>0.997</td>
</tr>
<tr>
<td><strong>Body fat percentage (percentage points), change</strong></td>
<td>0.8 (0.1, 1.4)</td>
<td>0.3 (-0.2, 0.9)</td>
<td>1.0 (0.3, 1.8)</td>
<td>0.1 (-0.5, 0.7)</td>
<td>0.991</td>
</tr>
</tbody>
</table>

Values are the means; 95% CIs unless otherwise indicated. MC-SFA: medium-chain saturated fatty acid.

Conclusion

• Enhanced intake of MC-SFA increased the lean body mass and caused a significantly lower total body-fat percentage compared with lower intake of MC-SFA.

• Consequently, the composition of dairy fat should also be considered when evaluating the impact of dairy products on body composition.
Agenda

• Dairy products and weight
• Dairy products and triglycerides
  • Dairy products and blood pressure
  • Dairy products, blood glucose and risk of type 2 diabetes
Association of TG with CVD

N = 27,000 women's health study; follow up 11.4 years

Figure 2. Association of Triglyceride Levels With Individual Cardiovascular End Points, According to Fasting Status

Hazard ratio (HR) and 95% confidence interval (CI) for highest vs lowest tertiles of triglyceride level (see Table 3 for values), adjusted for age, blood pressure, smoking, hormone use, levels of total and high-density lipoprotein cholesterol, diabetes mellitus, body mass index, and high-sensitivity C-reactive protein level.
Black circles = Myocardial infarction (MI) (n=17)
Open circles = Matched control subjects without prior MI (n=15)

Test meal: 1027 kcal (86 g fat, 51 g CHO, 8 g protein and vitamin A)
Conclusion

Type 2 diabetic males with prior MI had higher postprandial triglyceride-rich lipoprotein responses than those without MI, indicating that high responses may be a marker for a high-risk population.
Acute differential effects of dietary protein quality on postprandial lipemia in obese non-diabetic subjects

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\textbf{A R T I C L E \ I N F O}

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Triglyceride
Atherosclerosis
Dietary protein
Cross-over

\textbf{A B S T R A C T}

Non-fasting triglyceridemia is much closer associated to cardiovascular risk compared to fasting triglyceridemia. We hypothesized that there would be acute differential effects of four common dietary proteins (cod protein, whey protein, gluten, and casein) on postprandial lipemia in obese non-diabetic subjects. To test the hypothesis we conducted a randomized, acute clinical intervention study with crossover design. We supplemented a fat rich mixed meal with one of four dietary proteins i.e. cod protein, whey protein, gluten or casein. Eleven obese non-diabetic subjects (age: 40.68 years, body mass index: 30.3-42.0 kg/m\textsuperscript{2}) participated and blood samples were drawn in the 8-h postprandial period. Supplementation of a fat rich mixed meal with whey protein caused lower postprandial lipemia (P = 0.048) compared to supplementation with cod protein and gluten. This was primarily due to lower triglyceride concentration in the chylomicron rich fraction (P = 0.0293). Thus, we have demonstrated acute differential effects on postprandial metabolism of four dietary proteins supplemented to a fat rich meal in obese non-diabetic subjects. Supplementation with whey protein caused lower postprandial lipemia compared to supplementation with cod and gluten. As postprandial lipemia is closely correlated to cardiovascular disease, long-term dietary supplementation with whey protein may prove beneficial in preventing cardiovascular disease in obese non-diabetic subjects.
Results

**Triglycerides (plasma)**

- **Whey vs other P < 0.05**

**Retinyl palmitate**

- **Whey vs other P < 0.05**

N = 11; obese non-diabetic subjects

In conclusion, we accept the hypothesis of acute differential effects of dietary proteins on postprandial lipemia in obese non-diabetic subjects. A fat rich meal supplemented with whey protein caused lower postprandial lipemia compared to cod and gluten due to lower triglyceride concentrations in the chylomicron rich supernatant.
Lifestyle intervention

- Dairy proteins as dietary intervention on lipid metabolism:

<table>
<thead>
<tr>
<th>Milk protein (g)</th>
<th>Study design (duration)</th>
<th>Effect</th>
<th>Comparison group</th>
<th>Subjects (n)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>WPI or casein + fat-rich meal (45 g)</td>
<td>Acute</td>
<td>↓ TG response</td>
<td>Cod- and gluten protein</td>
<td>Obese non-diabetic (11)</td>
<td>[39]</td>
</tr>
<tr>
<td>WPI + fat-rich meal (45 g)</td>
<td>Acute</td>
<td>↓ TG response</td>
<td>Casein, cod- and gluten protein</td>
<td>T2D (12)</td>
<td>[49]</td>
</tr>
<tr>
<td>WPI (45 g)</td>
<td>Acute</td>
<td>↓ TG response</td>
<td>Casein, glucose</td>
<td>Postmenopausal women (20)</td>
<td>[53]</td>
</tr>
<tr>
<td>WPI or casein + fat-rich meal (45 g)</td>
<td>Acute</td>
<td>↓ TG concentration in chylomicron-rich fraction</td>
<td>Cod- and gluten protein</td>
<td>Obese non-diabetic (11)</td>
<td>[39]</td>
</tr>
<tr>
<td>Casein combined with carbohydrates and a fat-rich meal (45 g)</td>
<td>Acute</td>
<td>↓ TG concentration in chylomicron-rich fraction</td>
<td>Control meal, control meal + carbohydrates, control meal + casein</td>
<td>T2D (11)</td>
<td>[64]</td>
</tr>
<tr>
<td>WPI + fat-rich meal (45 g)</td>
<td>Acute</td>
<td>→ TG response</td>
<td>WP specific fractions</td>
<td>Obese non-diabetic (11)</td>
<td>[47]</td>
</tr>
<tr>
<td>WPI + fat-rich meal (45 g)</td>
<td>Acute</td>
<td>→ TG response</td>
<td>WP specific fractions</td>
<td>T2D (12)</td>
<td>[46]</td>
</tr>
<tr>
<td>WPI or casein + fat-rich meal (45 g)</td>
<td>Acute</td>
<td>↓ FFA</td>
<td>Cod- and gluten protein</td>
<td>Obese non-diabetic (11)</td>
<td>[39]</td>
</tr>
<tr>
<td>WPI + fat-rich meal (45 g)</td>
<td>Acute</td>
<td>↓ FFA</td>
<td>Casein, cod- and gluten protein</td>
<td>T2D (12)</td>
<td>[49]</td>
</tr>
<tr>
<td>WPI (2x27 g/d)</td>
<td>Chronic (12 weeks)</td>
<td>↓ Fasting TG, ↓ total cholesterol, ↓ LDL cholesterol</td>
<td>Glucose</td>
<td>Overweight and obese (70)</td>
<td>[31]</td>
</tr>
<tr>
<td>Casein (35 g/d)</td>
<td>Chronic (6 weeks)</td>
<td>↓ Total cholesterol</td>
<td>Baseline</td>
<td>Hypercholesterolemia (43)</td>
<td>[65]</td>
</tr>
<tr>
<td>WP (2x25 g/d)</td>
<td>Chronic (12 weeks)</td>
<td>→ Fasting lipids</td>
<td>Casein</td>
<td>Moderate obese (48)</td>
<td>[48]</td>
</tr>
</tbody>
</table>

Whey protein and TG – a meta-analysis

a. RCT of whey protein or derivates; b. Treatment > 4 weeks; c. A control or a comparison group

Zhang JW et al Eur J Clin Nutr 2016;70:879-885
CONCLUSION

Our findings demonstrated the modestly favorable effects of whey protein supplementation on circulating TG levels. No effects of whey protein on TC, LDL-C and HDL-C levels were found. Considering the limited studies and possible heterogeneity of trials, additional well-designed RCTs are needed to further clarify the effect of supplemental whey protein on TC and lipoprotein cholesterol.
Agenda

- Dairy products and weight
- Dairy products and triglycerides
- Dairy products and blood pressure
- Dairy products, blood glucose and risk of type 2 diabetes
Dose-response relationship (pr increment of 200g/d) between total dairy intake and hypertension (meta-analysis)

Soedamah-Muthu SS et al Hypertension. 2012 Nov;60(5):1131-7
Conclusion

- Total dairy, low-fat dairy and milk may contribute to the prevention of hypertension.

- Intervention studies are needed to confirm this!

Whey protein lowers blood pressure and improves endothelial function and lipid biomarkers in adults with prehypertension and mild hypertension: results from the chronic Whey2Go randomized controlled trial\textsuperscript{1,2}

Ágnes A Fekete\textsuperscript{3,4}, Carlotta Giromini\textsuperscript{3}, Yianna Chatzidiakou\textsuperscript{3}, D Ian Givens\textsuperscript{4}, and Julie A Lovegrove\textsuperscript{3,6}

**Design:** The trial was a double-blinded, randomized, 3-way–crossover, controlled intervention study. Forty-two participants were randomly assigned to consume $2 \times 28$ g whey protein/d, $2 \times 28$ g Ca caseinate/d, or $2 \times 27$ g maltodextrin (control)/d for 8 wk separated by a 4-wk washout. The effects of these interventions were examined with the use of a linear mixed-model ANOVA.
Whey protein, blood pressure and endothelial function

This novel study revealed that the consumption of whey protein (56 g/d) for 8 wk resulted in clinically relevant reductions in 24-h SBP (−2.9 ± 1.1 mm Hg) and DBP (−2.0 ± 0.7 mm Hg) compared with the effect of the control in adults with pre-hypertension and mild hypertension.

In conclusion, this novel RCT has several important observations. Compared with the control, whey protein significantly lowered 24-h SBP and DBP, central and peripheral SBP, and mean arterial pressure. Furthermore, compared with the control, both whey protein and calcium caseinate improved endothelial function, reduce adhesion molecules and vascular biomarkers of risk, and improved blood lipids. The magnitude of changes in the CVD risk markers observed is modest but may have important implications for public health.

FMP: Flow Mediated Dilation (Gold standard for endothelial dysfunction)
Agenda

- Dairy products and weight
- Dairy products and triglycerides
- Dairy products and blood pressure
- Dairy products, blood glucose and risk of type 2 diabetes
Dairy products and risk of type 2 diabetes

High fat dairy products

A

High-fat dairy products and type 2 diabetes, dose-response, per 200 g/d

Study
Soedamah-Muthu, 2013 (20)
von Ruesten, 2013 (24)
Louie, 2012 (23)
Struijk, 2012 (22)
Malik, 2011 (13)
Liu, 2006 (10)
von Dam, 2006 (15)
Choi, 2005 (7)
Montonen, 2005 (8)
Overall

Relative Risk
(95% CI)
1.36 (0.94, 1.98)
1.00 (0.85, 1.17)
0.89 (0.64, 1.24)
1.04 (0.71, 1.51)
0.81 (0.66, 0.98)
1.00 (0.94, 1.05)
1.01 (0.89, 1.15)
0.99 (0.90, 1.08)
0.92 (0.80, 1.06)
0.98 (0.94, 1.03)

0.1
0.25
0.5
0.75
1.0
1.5
2.0
3.0
Relative Risk

Low fat dairy products

C

Low-fat dairy products and type 2 diabetes, dose-response, per 200 g/d

Study
Soedamah-Muthu, 2013 (20)
von Ruesten, 2013 (24)
Louie, 2012 (23)
Struijk, 2012 (22)
Malik, 2011 (13)
Margolis, 2011 (19)
Liu, 2006 (10)
von Dam, 2006 (15)
Choi, 2005 (7)
Overall

Relative Risk
(95% CI)
0.98 (0.86, 1.12)
1.04 (0.92, 1.19)
0.91 (0.71, 1.17)
0.93 (0.81, 1.08)
0.75 (0.58, 0.97)
0.81 (0.69, 0.93)
0.94 (0.89, 1.01)
0.87 (0.77, 0.98)
0.87 (0.79, 0.93)
0.91 (0.86, 0.96)

0.1
0.25
0.5
0.75
1.0
1.5
2.0
3.0
Relative Risk

Youghurt intake and diabetes risk

**FIGURE 4** Spaghetti plot for the nonlinear association ($P$-nonlinearity: $<0.001$) between yogurt intake and diabetes risk (RR: 0.86 at 80 g/d compared with 0 g/d; 95% CI: 0.83, 0.90; $P < 0.001$), including 11 studies (12 study populations; $n = 438,140$ individuals).

Summary: can we combat features of the metabolic syndrome?

• Dairy products and weight
  - at least in energy restricted or short term trials

• Dairy products and triglycerides
  - in particular with whey protein

• Dairy products and blood pressure
  - at least low fat dairy, milk and possibly whey protein

• Dairy products, blood glucose and risk of type 2 diabetes
  – in fat reduced dairy products and youghurt
Conclusion

To know better how to combat metabolic syndrome we need more intervention studies e.g. on the impact of:

- Specific dairy products as such and as part of a Healthy diet both with and without energy restriction (diurnal blood pressure, insulin sensitivity, low grade inflammation).
- Different dairy fat types (e.g. medium chain saturated fatty acids) on the body composition (lean body mass, fat mass) measured with different methods (DEXA scan, MR scan).