様式第４－２号（規準第１０条、第１３条関係）

論文内容の要旨

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Chapter 1. Simultaneous ingestion of fructose with fat exacerbates postprandial exogenous lipidemia in young healthy Japanese women

Aim: To investigate the acute effects of simultaneous ingestion of fructose and fat on postprandial lipoprotein metabolism in young healthy women.

Methods: Nine young healthy Japanese women with a normal weight (body mass index: 18.5≤–<25 kg/m^2), a normal ovarian cycle and an apolipoprotein E 3/3 phenotype were enrolled as participants and studied on four occasions. At each session, the subjects ingested one of four beverages containing either glucose or fructose (0.5 g/kg body weight each) with or without OFTT cream (1 g/kg, 0.35 g/kg as fat) in a randomized crossover design. Blood samples were collected at baseline and 0.5, 1, 2, 4 and 6 h after ingestion.

Results: The ingestion of fructose combined with fat led to significantly higher rise in the serum triglyceride (TG), remnant-like particle (RLP)-TG, remnant lipoprotein-cholesterol (RemL-C) and apolipoprotein B-48 (apoB48) concentrations with delayed peaks compared with that observed following ingestion of the other three types of beverages. The incremental area under the curve (⊿AUC)-TG and ⊿AUC-apoB48 were larger than those observed for the ingestion of fat only. The serum RLP-TG and apoB48 concentrations returned to the fasting levels (0 h) at the end of the test (6 hours) following the ingestion of fat only; however, these concentrations did not return to the fasting levels following the intake of fructose combined with fat.

Conclusion: These findings suggest a delay in the clearance of intestinal TG-rich lipoproteins, namely chylomicron and its remnant, following the ingestion of fructose combined with fat. The simultaneous ingestion of fructose and fat markedly enhances postprandial exogenous lipidemia in young healthy Japanese women.

Chapter 2. The ingestion of a fructose-containing beverage combined with fat cream exacerbates postprandial endogenous lipidemia in young healthy women

Aim: To investigate the acute effects of the ingestion of a fructose-containing beverage, particularly when combined with fat, on postprandial lipoprotein metabolism.

Methods: Twelve young healthy Japanese women with apolipoprotein E phenotype 3/3 were enrolled in the study. At each of four sessions, the subjects ingested one of four sugar beverages containing fructose and/or glucose (totally 0.5 g/kg body weight) combined with OFTT cream (1 g/kg, 0.35 g/kg as fat) in a randomized crossover design. The four sugar beverages were: 100% (w/w) fructose (F100), 90% fructose+10% glucose (F90G10), 55% fructose+45%
glucose (F55G45), and 100% glucose (G100). Venous blood samples were taken at baseline and at 0.5, 1, 2, 4 and 6 h after ingestion.

Results: The concentration at 4 h and the ⊿AUC of hepatic triglyceride-rich lipoprotein-triglyceride (hTRL-TG) in the F100 and F90G10 trials were significantly higher or larger, respectively, than those observed in the G100 trial. However, the

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concentration of apoB(100) did not change during the 6 h. The concentration of apoB48 peaked at 2 h in the G100 trial, but at 4 h in the other trials, and did not return to baseline at 6 h except the G100 trial. At 4 h, the concentration of apoB48 in the F100 and F90G10 trials tended to be higher than that in the G100 trial.
Conclusion: The ingestion of a high-fructose-containing beverage with fat cream delayed the clearance of chylomicron and its remnant derived from the intestine, and enhanced the secretion of triglyceride-rich lipoprotein particles from the liver, inducing postprandial lipidemia, even in young healthy women.

Chapter 3. Ingestion of a large volume of water disturbs fructose absorption in young healthy women
Aim: To examine the absorption of fructose by measuring the concentration of breath hydrogen (BH) after the intake of fructose-containing beverages.
Methods: Seventeen young healthy Japanese women were enrolled as participants and were studied on four occasions. At each session, subjects ingested one of four beverages after a 12-h overnight fast. The beverages were prepared as follows; 10%F (Control): 25 g of fructose with 250 mL of water, 5%F: 25 g of fructose with 500 mL of water, 10%F+0.5hW: control beverage (0 h) and 250 mL of water at 0.5 h, 10%F+1hW: control beverage (0 h) and 250 mL of water at 1 h. Abdominal symptoms were recorded by the visual analog scales (VAS).
Results: BH in the 10%F, 10%F+0.5hW and 10%F+1hW trials was significantly increased at 45 or 60 min, and peaked at 75 or 90 min, and returned to the baseline level at 120 or 135 min. BH in the 5%F trial was significantly increased at 45 min and peaked at 75 min, but did not return to the baseline level at 180 min. The ΔAUC-BH in the 5%F trial was significantly larger than that in the 10%F trial. Abdominal symptoms occurred in all trials, however, there were no significant differences in the strength of each symptom and the number.
Conclusion: Fructose malabsorption and gastrointestinal symptoms were caused in all trials. Of these, BH was significantly increased in the 5% trial, suggesting that, even at a low concentration, fructose absorption may be disturbed by the intake of a large volume of water.

Final Conclusion

Simultaneous ingestion of a high-fructose- (but not glucose-) containing beverage and fat cream caused both exogenous and endogenous lipidemia postprandially even in young healthy Japanese women. The ratio of fructose to glucose was a determinant of metabolic disturbance when sugar load was equicaloric. Fructose-containing beverages were also liable to induce malabsorption and gastrointestinal symptoms.

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様式第４－４号（規準第１０条、第１３条関係）

論文審査の要旨

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（審査及び調査の要旨）

近年、砂糖の代替品として、果糖の割合を高めた異性化糖が清涼飲料水に多用されている。海外では、異性化糖含有飲料の長期摂取における内臓脂肪の増加、空腹時 TG、LDL の上昇の報告がみられる。また、単回摂取でも果糖と脂肪の同時摂取後の TG 上昇は著しいことが確認されているが、これらの実験対象者は、肥満者や 2 型糖尿病患者の結果であることが多く、健常な日本人を対象とした研究報告はみられない。本研究では、健常若年女性を対象として、果糖含有飲料摂取後の血中糖・脂質変動を調べた。一方で、果糖含有飲料は一時的な腹痛や下痢等を伴うことがあるとの報告があるため、呼気中水素濃度の測定によって果糖の消化吸収を調べた。本研究は、果糖含有飲料が健常若年女性の糖・脂質代謝および消化吸収に及ぼす影響を明らかにすることを目的とした。

第 1 章では、果糖およびブドウ糖含有飲料摂取後の糖・脂質代謝を調べた。日常的には、果糖含有飲料と脂質を多く含む食品（ファストフード、洋菓子等）との同時摂取する機会が多いことから、試験食には果糖と脂肪の混合も加えた。負荷前、負荷後 0.5、1、2、4、6 時間に血中成分を測定し、脂肪単独摂取と比較して、果糖と脂肪の同時摂取後には TG、RLP-TG、apoB48 の著しい上昇とピーク時間の遅延がみられ、外因性リポタンパク代謝が遅延することを明らかにした。

第 2 章では、市販されている清涼飲料水に含まれる果糖とブドウ糖の割合をもとに、試験食を調整し、脂肪との同時摂取後の糖・脂質代謝を調べた。この章では、果糖含有飲料と脂肪の同時摂取後に、肝臓から分泌される VLDL 粒子に含まれる TG 量が増加する、即ち VLDL 粒子が大粒子化することを示し、飲料に含まれる果糖の割合が増加するほど内因性リポタンパク代謝が増悪することを明らかにした。

第 3 章では、果糖含有飲料摂取後の呼気中水素濃度の測定を行い、摂取後の腹部症状の程度と消化吸収を調べた。果糖 25 g/250 mL (10%)の飲料よりも 25 g/500 mL (5%)の方が呼気中水素濃度の上昇が高く、濃度が低くとも、同時に摂る水分量が多いと果糖の吸収不良をきたしやすいことを示した。また、個人差はあるが、果糖含有飲料摂取後は、腹痛、腹部膨満感、腹鳴、放屁、下痢症状を引き起こしやすいことが確認された。

以上、本研究では、果糖含有飲料と脂肪との同時摂取は、健常若年女性においても食後の外因性および内因性脂質代謝の遅延を引き起こすことを示した。また、果糖含有飲料の大量摂取は一時的な腹部症状を引き起こす恐れもあることを示した。

よって、本論文は博士（人間生活科学）の学位論文として価値あるものと認める。

（試験の結果の要旨）

なお、2014　年　2　月　21　日、論文及びそれに関連した分野にわたり試問した結果、博士（人間生活科学）の学位を授与される学力が十分あるものと認めた。

（注）
1　Ａ４判縦置き横書きとする。
2　学位授与の要件が大学院学則第１３条第２項による場合は、本様式中「（試験の結果の要旨）…」以後の文言は削除し、これに代わり様式第４号の５を添付する。