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Consumption of red and processed meat and refined grains for 4 weeks decreases insulin sensitivity in insulin-resistant adults: A randomized crossover study☆,☆☆

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ABSTRACT

Background. Red and processed meat and refined grains are associated with an increased risk of type 2 diabetes. Interventions are limited. We hypothesized that a diet high in red and processed meat and refined grains (HMD) would decrease insulin sensitivity compared to a diet high in whole grains, nuts, dairy and legumes with no red meat (HWD).

Methods. Forty-nine subjects without diabetes [15 men and 34 women, age, 35.6 ± 15.7 years, body mass index (BMI), 27 ± 5.9 kg/m^2] underwent two 4-week weight-stable dietary interventions in a randomized crossover design. The insulin sensitivity index (ISI) was calculated from the last 30 min of a continuous low-dose insulin (25 mU/kg·h) and glucose (4 mg/kg·min) infusion test (LDIGIT $_{120–150min}$) at the end of each diet.

Results. The population fell into two very discrete groups: those with a very low insulin response in the LDIGIT $_{120–150min}$ on HMD (Group 1 < 56 pmol/L, n = 24), and those with relatively normal insulin responses (Group 2 > 56 pmol/L, n = 25). Group 2 had significantly higher insulin concentrations [(median and interquartile range) 153, 180 for HMD vs. 123, 149 pmol/L for HWD; $P = 0.019$] and glucose concentrations [(mean ± standard deviation) 7.4 ± 1.3 for HMD vs.6.7 ± 1.2 mmol/L for HWD; $P = 0.05$], resulting in a significantly decreased ISI [(median and interquartile range) 21.1, 34.2 for HMD vs. 31.6, 39.4 for HWD; $P = 0.014$] compared to HWD. Log ISI after HMD was significantly correlated with BMI ($r = −0.5$; $P = 0.009$), fat mass ($r = −0.55$; $P = 0.004$) and self-reported activity levels ($r = −0.45$; $P = 0.024$).

Abbreviations: AGE, advanced glycation end product; AUC, area under the curve; BMI, body mass index; DBP, diastolic blood pressure; DXA, dual energy X-ray absorptiometry; GI, glycemic index; GLP-1, glucagon like peptide-1; GL, glycemic load; Ginf, glucose infusion rate; Gss, steady-state blood glucose; HDL-C, high density lipoprotein cholesterol; HMD, a diet high in red and processed meat and refined grains; HOMA-IR, homeostasis model assessment of insulin resistance; hsCRP, high sensitivity C-reactive protein; HWD, a diet high in whole grains, nuts, dairy and legumes; iAUC, incremental area under the curve; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; ISI, insulin sensitivity index; ISS, steady-state serum insulin; LDIGIT, low-dose insulin and glucose infusion test; NGT, normal glucose tolerance; OGTT, oral glucose tolerance test; PYY, peptide tyrosine-tyrosine; SBP, systolic blood pressure; SCFAs, short chain fatty acids; T2DM, type 2 diabetes mellitus.

☆ This trial is registered with the Australian New Zealand Clinical Trials Registry www.anzctr.org.au/ (ACTRN12614000519651).

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Conclusions. A dietary pattern high in red and processed meat and refined grains decreased insulin sensitivity compared to a dietary pattern high in whole grains, nuts, dairy products and legumes only in relatively insulin-resistant adults.

1. Introduction

Insulin resistance is involved in the pathogenesis of type 2 diabetes mellitus (T2DM) [1,2]. Although certain dietary patterns are known to be associated with the development of T2DM independent of other lifestyle factors [3], exactly which components are able to influence the risk of T2DM is not clear. Meta-analyses of prospective studies have shown that processed meat consumption is associated with an increased risk of T2DM [4,5]. A limited number of intervention studies investigating the effect of lean red meat consumption on insulin sensitivity in the absence of weight loss have shown conflicting results [6–8]. There are no weight-stable intervention studies of a processed meat-rich diet. In a recent meta-analysis yoghurt and ice-cream were protective although the association between total dairy intake and T2DM was relatively weak with a small effect size [9,10], consistent with the contradictory results on insulin sensitivity of randomized controlled trials of dairy-rich diets [6,11]. Epidemiological studies have shown that whole-grain consumption is associated with a reduced risk of T2DM [12,13] but weight-stable interventions of a whole grain-rich diet have shown mixed results [14–17]. The Predimed study has shown a reduced incidence of T2DM with 30 g/d of mixed nuts (almonds, walnuts and hazelnuts) [18], but in another trial no differences were seen in HOMA-IR in participants who received walnuts and cashews compared to those who did not receive nuts [19]. Prospective studies have observed no association of T2DM with vegetable and fruit consumption, but an inverse association with consumption of green leafy vegetables has been found [20,21].

This study aimed to examine the effect of a diet high in red and processed meat and refined grains on insulin sensitivity compared to a diet high in dairy, whole grains, nuts and legumes containing no red meat, using sensitive measures of insulin sensitivity in weight stability. The primary hypothesis was that a diet high in red and processed meat and refined grains would induce greater insulin resistance compared to a diet high in dairy, whole grains, nuts and legumes, with a secondary hypothesis that a diet high in dairy, whole grains, nuts and legumes would improve lipid profiles compared to a diet high in red and processed meat and refined grains.

2. Methods

2.1. Ethical Approval and Registration

This study was approved by the University of South Australia Human Research Ethics committee and all study participants gave their written informed consent prior to participating. The trial was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12614000519651). AUD$ 240 was offered to the participants on completion of both diets. Recruitment began in June 2014 and ended in September 2015.

2.2. Study Participants

A total of 51 participants [body mass index (BMI) 18–45 kg/m^2], aged over 18 years, were recruited by public advertisement and a recruiting agency. An initial screening questionnaire was carried out via email or telephone. Exclusion criteria were diabetes, medication or supplements which could affect glucose metabolism, a history of metabolic illness including liver or kidney disease, pregnancy or breastfeeding, significant weight gain or weight loss over the last 3 months and food allergy or lactose intolerance. We planned to exclude people if weight gain or loss was 3 kg or more over the previous 3 months but no volunteers were excluded. Initially we aimed to recruit only overweight and obese participants but slow recruitment led us to widen the entry criteria to normal weight subjects knowing we might have to analyze the groups separately. We did not test HOMA-IR prior to randomization.

Responders who passed the screening criteria visited the Sansom Institute for Health Research Clinical Trial facility at the University of South Australia in the morning after an overnight fast. Written informed consent was obtained. Blood pressure was measured four times after sitting quietly for 10 min (Omron, Kyoto, Japan). Height was measured on a wall mounted stadiometer (Seca, Hamburg, Germany) and body weight was measured on electronic digital scales (Tanita, Tokyo, Japan) in light clothing and without shoes. Body composition was measured by whole-body dual-energy x-ray absorptiometry (DXA) (Luna Prodigy, Lunar Radiation, Wisconsin, USA). A 75 g oral glucose tolerance test (OGTT) was performed to exclude people with diabetes. A simple survey on activity levels was performed at baseline (sedentary or moderately active).

Details of study recruitment and participant flow are shown in Fig. 1.

2.3. Dietary Intervention

Eligible participants were randomly allocated to either a diet high in red and processed meat and refined grains (HMD) or a diet high in whole grains, nuts, legumes, dairy and devoid of red and processed meat (HWD) for 4 weeks, and then were crossed over to the alternative diet for 4 weeks. Randomization was performed via an online random number generator (www.randomization.com) by a researcher who was not involved in this study. Analyses were performed by an investigator blinded to the diet order. A minimum of a 2-week washout period (on average 3 weeks) between the two diets with a return to usual diet was planned.