Manipulation of dietary fatty acids and soluble fibre: controlled intervention trials investigating cardiovascular and type 2 diabetes risk

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CANDIDATE'S CONTRIBUTION TO THE WORK DESCRIBED IN THE THESIS

I carried out and was responsible for all human aspects of these trials at the University of Auckland, Human Nutrition Unit. Placement of indwelling venous canulae were performed in collaboration with a clinician from the School of Biological Sciences. All biochemical analyses were carried out at the University of Auckland, School of Biological Sciences under my direct supervision. Analysis of erythrocyte membrane fatty acids was carried out in collaboration with the Department of Chemistry. Hamatological indices were analysed by a commercial laboratory, Diagnostic Medlab Ltd. Direct analysis of diets was carried out by Milk and Health Research Centre, Massey University and Crop and Food Research Ltd, Palmerston North. Statistics were carried out in collaboration with a University statistician in the Department of Statistics.

ABSTRACT

Cardiovascular disease and type 2 diabetes mellitus are two of the leading causes of death in developed countries and the prevalence of these integrally linked disease states continues to grow. A number of modifiable risk factors contribute to the development of cardiovascular disease including raised blood cholesterol, hypertension and obesity, the latter also being an important modifiable risk for type 2 diabetes mellitus. Diet is also a critical factor underpinning the development and progression of these adult-onset diseases, however the complete role of diet in modifying risk has not yet been fully ascertained. This thesis describes a series of randomised, controlled cross-over intervention trials that have investigated the potentially beneficial effects of alterations in the macronutrient composition of the diet, specifically lipid and carbohydrate composition, in relation to both cardiovascular and type 2 diabetes risk.

Trial 1 investigated whether modifying the fatty acid profile of a bovine butter-fat, using simple feeding methods to substitute a moderate proportion of the saturated fatty acids with mono- and polyunsaturated fatty acids, could improve blood lipid profile and haemostatic clotting factors in 20 healthy men following a tightly controlled dietary regimen in which butter-fat was incorporated into a typical Western diet. Results showed that the inclusion of the modified butter-fat led to a clinically significant reduction in serum total ($P < 0.05$) and low-density lipoprotein cholesterol ($P < 0.01$) without a concomitant reduction in high-density lipoprotein cholesterol. The 7% decrease in serum low-density lipoprotein cholesterol, achieved with only a small alteration in the fatty acid composition of the total diet, would represent a significant reduction in cardiovascular risk if applied across a whole population.

The sub-study of Trial 1 investigated changes in erythrocyte membrane fatty acid composition during a period of controlled fat feeding in order to assess whether dietary change could alter membrane fatty acid composition over a 3 week period, and hence determine whether it may be a useful short-term biomarker of dietary compliance. The results showed some significant changes in erythrocyte membrane saturated, mono- and polyunsaturated fatty acids within 3 weeks following alterations in dietary fatty acid composition. All fatty acids changed in parallel with diet but in this group of 20 men only C18:0 and C18:1 had altered significantly ($P < 0.05$) by 3 weeks. The results of this trial suggest that the measurement of erythrocyte membrane fatty acid composition may be a valuable, independent, qualitative measure of dietary compliance in short-term intervention trials that currently rely on self-reported intake data, however they can provide no quantitative information.

Trial 2 assessed postprandial metabolic outcomes associated with cardiovascular risk, including triacylglycerol, triacylglycerol-rich lipoproteins, cholesterol-rich lipoproteins, haemostatic clotting factors, glucose, insulin and amylin, using the high saturate and high mono- and polyunsaturated fatty acid butter-fat as the fat challenge. The study, carried out in 18 healthy men, showed a significant increase in plasma triacylglycerol in the 3 hours immediately following ingestion of the high mono- and polyunsaturated fat feeding compared with the high saturated fat ($P < 0.05$). No other differential effects were observed. When both treatment groups were combined the total lipaemia induced by an acute fat bolus caused a delayed and prolonged increase in serum cholesterol and cholesterol-rich lipoproteins, confirming evidence from previous trials that fatty meals may cause cholesterol to be elevated for many hours postprandially and thereby confounding measures taken in the fasted state.

Trial 3 investigated the effects of adding a highly enriched barley-derived β-glucan (75% w/w) into a typical Western diet, in 18 'at risk' hypercholesterolaemic men following a highly controlled dietary protocol. The addition of 10g/day β-glucan to the diet failed to demonstrate significant improvements in lipid or glucose control, and hence no evidence of improvement in cardiovascular disease or type 2 diabetes mellitus risk. The inability to reduce serum cholesterol may have been a consequence of structural changes that occurred during the enrichment process converting the natural barley cereal into a high β-glucan product, as has been shown during similar enrichment processes of oat β-glucan.

These trials have demonstrated that under strictly controlled experimental conditions changes in the fatty acid composition of the diet can lead to improvement in cardiovascular disease risk, as measured by alterations in serum lipids, over a 3 week period. However, beneficial changes in postprandial markers of cardiovascular disease were not observed, nor were markers of type 2 diabetes risk in this group of individuals with normal lipid and glucose metabolism. The measurement of erythrocyte membrane fatty acid composition identified some potentially useful biomarkers of dietary compliance that may be useful in short-term trials. The dietary fibre manipulation described did not result in any significant improvements in cardiovascular disease or type 2 diabetes risk factors and raised important issues regarding the physiological activity of highly processed soluble fibre products, and highlighted the fact that not all β-glucan products have beneficial cholesterol-lowering properties.

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24h	24 hours
24h N	24 hour nitrogen balance
ADA	American Diabetes Association
AHA	American Heart Association
ALT	alanine transaminase
ANOVA	analysis of variance
apo A	apolipoprotein A
apo B	apolipoprotein B
AST	aspartate transaminase
AUC	area under the curve
BMR	basal metabolic rate
BMI	body mass index
C10:0	capric acid
C12:0	lauric acid
C14:0	myristic acid
C15:0	pentadecanoic acid
C16:0	palmitic acid
C16:1	palmitoleic acid
C17:0	heptadecanoic acid
C18:0	stearic acid
C18:1	oleic acid
C18:2	linoleic acid
C18:3	linolenic acid
C20:4	eicosatetraenoic acid
C20:5	eicosapentaenoic acid
C22:4	docotetraenoic acid
C22:6	docohexaenoic acid
CHO	carbohydrate
CVD	cardiovascular disease
DBP	diastolic blood pressure
DHA	docosahexaenoic acid
EDTA	ethylenediamine tetraacetate
e.g.	Latin *exempli gratia* meaning 'for example'
EI	energy intake
en%	percentage of total energy
EPA	eicosapentaenoic acid
et al	Latin *et alii* meaning 'and others'
FAMES	fatty acid methyl esters
FAO	Food and Agriculture Organisation
FFA	free fatty acid
FVIIc	factor VII coagulant activity
FVIIa	activated factor VII
g	gram
g	gravitational force
GGT	γ-glutamyltransferase
g/L	grams per litre
Hb	haemoglobin
Hb_{A1c}	glycated haemoglobin
HDL-C	high-density lipoprotein cholesterol
IGT	impaired glucose tolerance

kg	kilogram
kJ	kilojoule
LDL-C	low-density lipoprotein cholesterol
MEDLINE	National Library of Medicine, Bethesda, MD
mg	milligram
MJ	megajoule
mM	millimolar
mmol/L	millimole per litre
MUFA	monounsaturated fatty acid
mU/L	milliunits per litre
MW	molecular weight
N	nitrogen
nm	nanometer
NADH	nicotinamide dinucleotide
NCEP	National Cholesterol Education Program
NI	nitrogen intake
NSP	non-starch polysaccharide
°C	degrees celcius
OGTT	oral glucose tolerance test
PABA	*para*-amino benzoic acid
pers comm	personal communication
per se	meaning 'by or in itself' from Latin
pmol/L	picamole per litre
PUFA	polyunsaturated fatty acid
RBC	red blood cell
RDA	recommended daily allowance
RIA	radio-immunoassay
RS	resistant starch
SAS	statistical analysis software™
SBP	systolic blood pressure
SCFA	short-chain fatty acid
s.d.	standard deviation
s.e.m.	standard error of the mean
SFA	saturated fatty acid
SST	serum separation tube™
T2DM	type 2 diabetes mellitus
TC	total cholesterol
TG	triacylglycerol
T4	thyroxin
TRL	triacylglycerol-rich lipoprotein
TSH	thyroid stimulating hormone
UK	United Kingdom
U/L	units per litre
Umol/L	micromole per litre
USA	United States of America
USFDA	United States Food and Drug Administration
VLDL-C	very low-density lipoprotein cholesterol
VLDL-TG	very low-density lipoprotein triacylglycerol
WBC	white blood cell
WHO	World Health Organisation
WHR	waist:hip ratio