Role of long chain omega-3 polyunsaturated fatty acids on weight management

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B Ed  MES

Thesis submitted in fulfilment of the requirement to obtain the degree of Doctor of Philosophy in Human Physiology

School of Biomedical Sciences and Pharmacy
University of Newcastle, Australia

November 2012
Statement of originality

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. I give my consent to this copy of my thesis, when deposited in the University Library, being made available for loan and photocopying subject to the provision of the Copyright Act 1968.

........................................
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I hereby certify that this thesis is in the form of a series of published papers of which I am a joint author. I have included as part of my thesis a written statement from each co-author, endorsed by the Faculty Assistant Dean (Research Training), attesting to my contribution to the joint publications.

............................

Irene Munro
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Research publications central to this thesis

1. **Chapter 3**
   
   **Statement of contribution:** Major contribution to: the conception and design of the study; the recruitment of participants, collection and recording of data; drafting of the manuscript; revision of the manuscript.

2. **Chapter 4**
   
   **Statement of contribution:** Recruited participants; conducted the intervention and collected the clinical data; sample analysis; entered, analysed and interpreted the data; wrote the manuscript.

3. **Chapter 5**
   
   **Statement of contribution:** Recruited participants; conducted the intervention and collected the clinical data; sample analysis; entered, analysed and interpreted the data; wrote the manuscript.

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Oral presentations with published abstracts


Poster presentation with published abstracts


Additional publications relevant to this thesis


Additional oral presentations with published abstracts relevant to this thesis


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List of abbreviations

AF  adipose fraction
AGHE  Australian Guide to Healthy Eating
ALA  alpha linolenic acid
AMPK  activated protein kinase
ANOVA  analysis of variance
apoE  apolipoprotein E
BIA  bioelectrical impedance assessment
BL  baseline
BMI  body mass index
CCL2  chemokine ligand 2
CCR2  chemokine receptor 2
CETP  cholesteryl ester transfer protein
CHD  coronary heart disease
CHO  carbohydrate
cm  centimetre
CoA  coenzyme A
COX  cyclooxygenase
CPT-1  carnitine palmitoyl transferase-1
CRP  C-reactive protein
CV  coefficient of variation
CVD  cardiovascular disease
d  day
DEXA  dual-energy X-ray absorptiometry
DLGA  dihomo-gamma-linoleic acid
DNA  deoxyribonucleic acid
EDTA  ethylene-diamine-tetra-acetic acid
ELISA  enzyme linked immunosorbent assay
FA  fatty acid
FFM  fat free mass
FM  fat mass
FO  fish oil
g  gram
GC  gas chromatography
GI  glycaemic index
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<td>HEWLD</td>
<td>healthy eating weight loss diet</td>
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<td>high sensitivity</td>
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<td>peroxisome proliferator-activated receptor</td>
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<td>PUFA</td>
<td>polyunsaturated fatty acids</td>
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<td>RQ</td>
<td>respiratory quotient</td>
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SEM standard error of mean
sd standard deviation
SAT subcutaneous adipose tissue
SFA saturated fatty acids
SPSS Statistical Package for the Social Sciences
SR scavenger receptor
SREBP sterol regulatory element-binding protein
SVF stroma vascular fraction
TBW total body water
TC total cholesterol
TG triglyceride
TLR4 toll like receptor 4
TNF-α tumour necrosis factor-alpha
TX thromboxanes
T2D type 2 diabetes
VAT visceral adipose tissue
VLED very low energy diet
VLC very long chain
VLDL very low density lipoprotein
WC waist circumference
µg microgram
^{14}C (radioisotope) carbon-14
Synopsis of thesis

Despite an ever-growing body of research on obesity, investigating causes and possible solutions to address the problem, the prevalence of obesity continues to escalate. A major cause of obesity is attributed to poor eating behaviours driven by food advertising, lack of nutrition knowledge, lack of physical activity, lack of time and lack of will power to control food intake, and there is a plethora of research with a focus on changing dietary behaviour for weight management.

In part, this research also addressed dietary change, employing a reduced energy intake for weight loss supported with nutrition education and counselling to enable maintenance of the weight lost. However, consideration was also given to the internal interactions and changes that occur in the body when energy intake exceeds energy output resulting in weight gain and obesity, and whether these mechanisms could be manipulated to reduce weight gain through the inclusion of long chain omega-3 polyunsaturated fatty acids (LCω-3PUFA) in the diet.

Prospective studies in humans have reported that high levels of LCω-3PUFA were associated with low levels of obesity in males while higher intakes of LCω-3PUFA were associated with higher rates of obesity in females. The data on LCω-3PUFA concentrations in males and females had been sourced from dietary records with questionable reliability. Thus the first aim of this research was to investigate whether there was a relationship between plasma LCω-3PUFA and weight status in humans. The first research chapter (Chapter 3) reports on the relationship observed between plasma LCω-3PUFA composition and weight status in free living adults. Obese individuals, both males and females, had significantly lower levels of LCω-3PUFA compared to healthy-weight individuals.

Thus the aim of the first clinical trial (Chapter 4) was to investigate whether LCω-3PUFA supplementation, combined with a healthful diet with portion control and energy restriction would facilitate weight loss, improve blood lipids and inflammatory mediators. This was a double-blinded randomised controlled trial with two parallel groups. Both groups were instructed to follow the same diet for 12 weeks, one group consumed fish oil capsules and the other group consumed placebo capsules (monounsaturated oil). Despite a two-fold increase of EPA and
DHA in the treatment group, there were no significant differences in outcome measures between the two groups. Both the placebo and the fish oil supplemented groups lost similar amounts of weight, fat mass and fat free mass. Overall dietary compliance was poor representing a possible confounding factor on the outcomes.

The aim of the next clinical trial (Chapter 5) was to investigate whether LCω-3PUFA supplementation would facilitate weight loss, but this time in combination with a very-low-energy-diet (VLED), using meal replacements (MRs), to improve dietary compliance. The protocol for this trial was the same as the previous one apart from the change to the diet and with a shortened intervention of 4 weeks. Also, because of the anticipated rapid weight loss, a 10 week weight maintenance phase with continued supplementation was included. Although there was a greater than two-fold increase of EPA and DHA in the treatment group, there were no significant differences in outcome measures between the two groups after 4 weeks of weight loss. However, after a further 10 weeks of supplementation during weight maintenance, there was a significant reduction in anthropometric measurements, apart from fat free mass, in the treatment group but not the placebo group. The differences between the two groups were not significant.

The final clinical trial (Chapter 6) investigated potential benefits of loading the body cells/membranes with LCω-3PUFA prior to following a weight loss program. The protocol for the trial was similar to the previous two, but commenced with 4 weeks of prior-supplementation with fish oil or placebo in the treatment and placebo groups, respectively, while consuming their usual diet. This was followed by 4 weeks of dietary intervention where both groups again consumed a VLED with MRs plus continued supplementation. The same measurements were taken as for the previous trials. After 4 weeks of prior-supplementation there were no significant differences in outcome measures for either group. However, at 8 weeks a significant 3-way interaction between time, group and gender was observed for percentage reduction in weight and BMI, suggesting a significant effect of LCω-3PUFA for the fish oil group. There was also a significant reduction in percentage weight loss for females in the fish oil group. These results suggest that prior-supplementation with LCω-3PUFA, followed by supplementation with LCω-3PUFA and a VLED regimen may assist weight loss.