DIETARY MANAGEMENT OF

POLYCYSTIC OVARY SYNDROME

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DECLARATION

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.

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DESCRIPTION OF THESIS

Chapters 2–6 were submitted for publication prior to the completion of this thesis. Chapters 2 and 4 have been accepted and published, Chapters 3 has been accepted and is in press and Chapter 5 is currently under review. For this reason, this thesis was prepared in a similar style to a Thesis by Publication. The bulk of the study methodology is included within the relevant chapters conforming to the style of the relevant journal to which the chapters were submitted. Additional methodological information is provided in Appendix 2. Where new information pertinent to the topic of the chapter has been published after the relevant paper, it is discussed in the final conclusion as opposed to the Chapter/Paper discussion being amended. Paper co-authors are acknowledged in the Acknowledgement Section and Appendix 3 contains the published papers.
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ABSTRACT

Background

Polycystic ovary syndrome (PCOS) is a common endocrine condition in women associated with obesity, reproductive and metabolic abnormalities. It improves with weight loss, however currently no specific dietary recommendations exist and there may be abnormalities in appetite regulation in PCOS that contribute to difficulty in weight management.

Aims

To assess the effect of 1) short and long-term weight loss and weight maintenance strategies on weight loss, reproductive and metabolic parameters in overweight women with PCOS and to 2) assess the relative effect of weight loss on cardiovascular risk factors and 3) post-prandial appetite, appetite hormones (ghrelin, CCK, PYY) and food intake in overweight women with and without PCOS.

Results

Overweight women with PCOS followed an 8-week weight loss (2 meal replacements/day, 4904.4±127 kJ, n=32) followed by a 6 month carbohydrate (<120 g/day) or fat restricted (<50 g/day) weight maintenance regime (n=23). Reductions in weight (5.6±2.4 kg) and improvements in body composition, insulin, reproductive hormones and menstrual cyclicity occurred and were sustained equivalently for both diet groups. We then assessed the effect of weight loss (4.2±0.7 kg over 8 weeks as described above) in overweight women with (n=15) and without (n=17) PCOS on cardiovascular risk factors. All subjects had similar improvements in body composition, triglycerides, reproductive hormones and fasting and post-prandial insulin. C-reactive protein decreased with weight loss for non-PCOS women (-1.2±0.5 mg/L, P=0.025) but not for PCOS women.
We finally assessed appetite regulation in PCOS. Women with (n=20) and without (n=12) PCOS followed a standard protein (55% carbohydrate, 15% protein) or high protein diet (40% carbohydrate, 30% protein) for 16 weeks (~6000 kJ/day). Non-PCOS subjects were more satiated (P=0.001) and less hungry (P=0.007) after the test meals and had a 70% higher fasting baseline ghrelin (P=0.011), a greater increase in fasting ghrelin (57.5 versus 34.0%, P=0.033), a greater post-prandial ghrelin decrease at week 16 (113.5±46.3 versus 49.3±12.2 pg/mL, P=0.05) and a greater maximal decrease in post-prandial ghrelin (-144.1±58.4 versus -28.9±14.2 pg/mL, P=0.02) following weight loss than subjects with PCOS. Lastly, women with (n=14) and without (n=14) PCOS undertook an 8-week weight loss regime (4.2±0.7 kg as described above). At week 0 and 8, women with PCOS again displayed lower ghrelin levels (P=0.01 and P=0.097 respectively) and a lesser post-prandial ghrelin decrease (P=0.048 and P=0.069 respectively) but similar post-prandial appetite, buffet consumption and fasting or post-prandial peptide YY and cholecystokinin compared to women without PCOS.

**Conclusion**

Meal replacements and moderate macronutrient restriction are effective strategies for the dietary management of PCOS. Equivalent weight losses improved cardiovascular risk factors similarly for overweight women with and without PCOS with the exception of CRP which did not decrease with weight loss for overweight women with PCOS. PCOS status is associated with altered fasting and post-prandial ghrelin levels but is not consistently associated with other impairments in post-prandial gut peptides or food intake. Further investigation is required to assess if appetite regulation is impaired in PCOS and the optimal strategies and amount of weight loss for improvement of reproductive and metabolic parameters in PCOS.
PUBLICATIONS ARISING FROM THIS THESIS


**Conference proceedings**


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Published Abstract:

PRESENTATIONS ARISING FROM THIS THESIS

Oral presentations

2006:
Androgen Excess Society International Meeting, Athens, Greece
‘Obesity and Polycystic Ovary Syndrome’. Moran LJ and Norman RJ.

International Congress of Obesity, Sydney, Australia

2005:
Dietetics Association of Australia State Conference, Adelaide, Australia
‘Diet and Polycystic Ovary Syndrome’, Moran LJ.

Poster presentations

2006:
International Congress of Obesity, Sydney, Australia

2005:
North American Society for the Study of Obesity International Conference,
Vancouver, Canada
Australasian Society for the Study of Obesity National Conference, Adelaide, South Australia
Nutrition Society of Australia National Conference, Melbourne, Victoria

**2004:**

Nutrition Society of Australia National Conference, Brisbane, Queensland
Australasian Society for the Study of Obesity, Brisbane, Queensland


**2003:**

Endocrine Society of Australia National Conference, Melbourne, Victoria
Australian Medical Research Council National Conference, Adelaide, South Australia
Nutrition Society of Australia National Conference, Hobart, Tasmania
Dietetics Association of Australia State Conference, Adelaide, South Australia

ABBREVIATIONS

α-MSH: α-melanocyte stimulating hormone
ADP: Adenosine diphosphate
AgRP: Agouti-related peptide
AI: Adequate intake
AMH: Anti-mullerian hormone
Apo A-IV: Apolipoprotein A-IV
ATP: Adenosine triphosphate
AUC: Area under the curve
BIA: Bioelectrical impedance analysis
BMI: Body mass index
BNRP: Bombesin/bombesin related peptides
CART: Cocaine and amphetamine regulated transcript
CC: Carbohydrate counting
CCK: Cholecystokinin
CHO: Carbohydrate
CIGMA: Continuous infusion of glucose with model assessment
CRF: Corticotropin-releasing factor
CRP: C-reactive protein
CV: Coefficient of variation
CVD: Cardiovascular disease
DBP: Diastolic blood pressure
DEXA: Dual X-ray absorptiometry
DHEA: Dehydroepiandrosterone
DHEAS: Dehydroepiandrosteronesulfate
5α-DHT: 5α- Dihydrotestosterone
DHT: Dihydrotestosterone
ER: Energy restriction
FAI: Free androgen index
FC: Fat counting
FFA: Free fatty acid
FSH: Follicle-stimulating hormone
FSIVGTT: Frequently sampled intravenous glucose tolerance test
hCG: Human chorionic gonadotrophin
GH: Growth hormone
GHRH: Growth hormone releasing hormone
GHS-R: Growth hormone secretagogue receptor
GI: Glycaemic index
GL: Glycaemic load
GLP-1: Glucagon-like peptide 1
Glucose-6-P: Glucose-6 phosphate
GLUT4: Glucose transporter 4
GnRH: Gonadotrophin releasing hormone
HA: Hyperandrogenism
HDL-C: High density lipoprotein cholesterol
HOMA: Homeostasis model assessment
HP: High protein
3βHSD: 3β-hydroxysteroid dehydrogenase
17βHSD: 17β-hydroxysteroid dehydrogenase
20αHSD: 20α-hydroxysteroid dehydrogenase
HSD: Hydroxysteroid dehydrogenase
IGF: Insulin-like growth factor
IGFBP: Insulin-like growth factor binding proteins
IGT: Impaired glucose tolerance
IL: Interleukin
IR: Insulin resistance
IRS: Insulin receptor substrate
IST: Insulin sensitivity test
ITT: Insulin tolerance test
IVF: In vitro fertilization
LDL-C: Low-density lipoprotein cholesterol
LH: Luteinising hormone
LP: Low protein
MAPK: Mitogen activated protein kinase
MCH: Melanin-concentrating hormone
MTT: Meal tolerance test
MUFA: Monounsaturated fatty acid
NIH: National Institute of Health
NPY: Neuropeptide Y
OGTT: Oral glucose tolerance test
OXM: Oxyntomodulin
P450AR: Cytochrome P450 aromatase
P450cscc: Cytochrome P450 side chain cleavage
P450c11AS: Cytochrome P450 11 aldosterone synthetase
P450c11B: Cytochrome P450 11-hydroxylase
P450c17α: Cytochrome P450 17α hydroxylase
P450c17,20: Cytochrome P450 17,20 lyase
P450c21: Cytochrome P450 21-hydroxylase
PAI-1: Plasminogen-activator inhibitor activity
PCO: Polycystic Ovary Syndrome
PCOS: Polycystic Ovary Syndrome
PI3-K: Phosphatidylinositol 3-kinase
POMC: Pro-opiomelanocortin
PP: Pancreatic polypeptide
PPAR: Peroxisome proliferator activator receptor
PUFA: Polyunsaturated fatty acid
PVN: Paraventricular nucleus
PYY: Peptide YY
QUICKI: Quantitative insulin sensitivity check index
RDI: Recommended dietary intake
REE: Resting energy expenditure
RR: Relative risk
RQ: Respiratory quotient
SFA: Saturated fatty acid
SHBG: Sex-hormone binding globulin
SP: Standard protein
StAR: Steroidogenic acute regulatory protein.
T2DM: Type II diabetes mellitus
TFM: Total fat mass
TFFM: Total fat free mass
TNF-α: Tumour necrosis factor α
TSH: Thyroid stimulating hormone
VAS: Visual analogue scores
VLCD: Very low calorie diets
VLDL: Very low density lipoprotein
VO_{2max} : Maximal oxygen consumption
WHR: Waist-hip ratio
WM: Weight maintenance