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Establishing evidence for practice in medical nutrition therapy: a case study of the impact of a high amylose resistant starch diet on clinical indicators of the insulin resistant syndrome

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ESTABLISHING EVIDENCE FOR PRACTICE IN MEDICAL NUTRITION THERAPY: A CASE STUDY OF THE IMPACT OF A HIGH AMYLOSE RESISTANT STARCH DIET ON CLINICAL INDICATORS OF THE INSULIN RESISTANT SYNDROME

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CERTIFICATION

I, Vanessa Brenninger, declare that this thesis, submitted in fulfilment of the requirements for the award of Master of Science – Research, in the Department of Biomedical Sciences, University of Wollongong, is wholly my own work unless otherwise referenced or acknowledged. The document has not been submitted for qualifications at any other academic institution.

Vanessa Brenninger

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iii List of abbreviations

ANOVA: analysis of variance

ANZFA: Australia and New Zealand Food Authority

AUC: area under the curve

BMI: Body Mass Index

CA: Conversation Analysis

Ca: Calcium

CHO: Carbohydrate

Chol: Cholesterol

Clamp: Hyperinsulinaemic Euglycaemic Clamp

CSIRO: Commonwealth Scientific and Industrial Research Organisation

DAA: Dietitian's Association of Australia

DF: Dietary Fibre

DH: Diet History

DXA: Dual-energy x-ray absorptiometry

E: Energy

EE: Energy Expenditure

EI: Energy Intake

GI: Glycaemic Index

HARS: High Amylose Maize Starch

HDL: High Density Lipoprotein

Hood: Delta-trac metabolic monitor hood (indirect calorimetry)

Ht: Height

IR: insulin resistance

kJ: kilojoule

LDL: Low Density Lipoprotein

MRNA: Messenger ribonucleic acid

MUFA: Monounsaturated Fatty Acids

n-3 FA: Omega 3 Fatty Acids

n-6 FA: Omega 6 Fatty Acids

NHMRC: National Health and Medical Research Council

NIDDM: Non Insulin Dependant Diabetes Mellitus

NSP: non-starch polysaccharides (can be soluble and insoluble)

PAI-1: plasminogen activator inhibitor-1

Ptn: Protein

PUFA: Polyunsaturated Fatty Acids

RCT: randomised controlled trial

RIA: Radio-immuno Assay

RMR: Resting Metabolic Rate

RQ: Respiratory Quotient

RS: Resistant Starch

SCFA: Short Chain Fatty Acids

SFA: Saturated Fatty Acids

TG: triglyceride

WHO: World Health Organisation

Wt: Weight

iv Acknowledgements

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v Abstract

INTRODUCTION

In the context where current strategies employed by health professionals are not able to slow the increasing rates of obesity, diabetes mellitus and insulin resistance, collectively known as the insulin resistance syndrome (metabolic syndrome, syndrome X), evidence-based practice is central to implementing appropriate and targeted guidelines to the individual. The central hypothesis argued here is that for evidence based practice to have relevance there is value in collecting this evidence from both quantitative and qualitative research methodologies. The aim of this thesis is to explore a number of aspects of research that produce evidence for the management of diet related disease. It uses as a reference point, a randomised controlled trial investigating the feasibility and efficacy of the incorporation of high amylose maize resistant starch on clinical, and dietary outcomes in an overweight sample of the population. Current research aims to develop the optimal nutrient mix for the insulin resistance syndrome, however, the challenge and focus now should be to make the benefits achievable in the 'real world' (Storlien, Tapsell, Fraser, Leslie, Ball, Higgins, Helge and Owen 2001). To this end, a rigorous framework addressing dietetic and lifestyle issues was included in the randomised controlled trial.

The nutrient of choice for the intervention trial was resistant starch (RS); a form of carbohydrate that reaches the lower gastrointestinal tract undigested and is consequently fermented. Resistant starch is composed of two polysaccharide forms; amylose and amylopectin. The beneficial effects are particularly evident from the amylose form

compared to the more readily digested amylopectin. It demonstrates probiotic and dietary fibre-like characteristics hypothesised to be beneficial for people with the insulin resistance syndrome, hypercholesterolaemia and colon cancer due to its reduced availability as a source of energy, reduced energy density and its ability to lower colonic pH. Therefore RS has potential to be used in the dietary management for reducing risk factors for the insulin resistance syndrome.

METHODOLOGY

Three preliminary studies were performed to enable the accurate recording of significant lifestyle variables. The first employed sociolinguistics to conceptualise how and why inaccuracy in reporting of dietary intake occurs. Secondly, a lifestyle history questionnaire was developed to examine possible sources of baseline variation between subjects in the study. Finally, an intervention trial survey was designed to analyse subject's experiences post-intervention such as barriers to adherence.

Following these, a dietary intervention trial was conducted in overweight (BMI: 25-35kg/m^2) adult volunteers. Subjects with any of the following were excluded: diabetes mellitus (fasting blood glucose level ≥ 6.1mmol/L), known hypercholesterolaemia or hypertension, inflammatory bowel disease, coeliac disease, renal disease, current smokers, pregnancy and those reporting a significant weight change in the previous 6 months. Twenty-five volunteers were randomly assigned to receive advice on either a diet high in RS or to a control diet low in RS. Control groups were maintained at a level of 6 grams of various types of RS, based on the Australian average consumption, while the RS group received 25 grams of RS derived from commercially manufactured RS

containing an high amylose to amylopectin ratio.

Subjects recorded foods used to achieve differences in RS using a daily checklist form. Foods recorded on daily checklist forms were analysed by counting. Repeated diet history (DH) interviews were performed in weeks 0, 3, 6, 9 and 12. Dietary data were entered into a nutrient analysis software package, *FoodWorks* (v2.10.136, Xyris Software, Highgate Hill, Brisbane) for further statistical comparisons. To estimate the accuracy of reporting dietary intakes the ratio of reported energy intake to estimated basal metabolic rate (BMR) was calculated. This method provides an index for comparison with cut-off limits that assess the validity of the reported energy intakes.

Baseline metabolic and biochemical indicies were compared to those at 12 weeks after intervention. Insulin resistance was measured by hyperinsulinaemic euglycaemic clamp. Fasting respiratory quotient (RQ) and resting metabolic rate (RMR) was measured by indirect calorimetry. Fasting plasma glucose, insulin, triglycerides, total cholesterol, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol were measured by standard assays. Body mass index (BMI) was calculated by weight in kilograms divided by height in meters squared and body composition was assessed by dual-energy x-ray absorptiometry (DXA).

In the same subjects the acute response to RS diets and control diets were performed by a meal challenge (breakfast and lunch) at 12 weeks. The following variables were collected from participants while fasted and then postprandially on an hourly basis thereafter: RQ, RMR, plasma glucose, insulin, triglyceride excursions and satiety.

Statistical comparisons were made within groups initially and on completion and between groups over time using a statistical software package, *JMP* (Version 3.2, SAS institute Inc, Cary NC, 1989-1996).

In addition, as derived from the preliminary studies, subjects completed lifestyle history questionnaires initially in week 0 and an intervention trial survey at 12 weeks. Survey responses were reviewed using content analysis to identify themes and applying a ranking of significance based on frequency of their occurrence.

RESULTS

Of the twenty-five subjects randomly assigned with random numbers to a high or low amylose-rich RS diet, twenty-two completed the trial. Twenty of these were classified as insulin resistant. The two subjects who were not insulin resistant had been randomly assigned to the high RS diet group. The discontinuing participants caused groups to become mismatched for gender, BMI and HDL cholesterol. In addition this caused the RS and control groups to be significantly different for insulin sensitivity with a mean and standard deviation of 6.01 ± 0.79 versus 3.51 ± 0.42 mg/kg.min respectively at week 12 (p=0.006). There were no significant effects of 12 weeks intervention with control or RS diets on body composition (% change in body fat 6.3 versus 1.7 respectively, p>0.05) and metabolic variables (change in insulin sensitivity 2.8% versus –8.4% respectively, p>0.05) despite reported compliance to the dietary goals for intervention foods.

Assessment of the meal challenges displayed a smaller rise in glucose excursion in response to the RS pretreated group challenged with either low or high RS meals. The differences between fasting glucose response to a breakfast meal was significantly affected by the intervention diet (p=0.016). There was also a significant effect of test meal composition on insulin excursion reflecting an increased insulin response to low RS meals in both groups (p=0.04). The remaining variables measured during meal challenges were not significantly affected by meal composition or intervention diet.

The lifestyle history questionnaire identified several variables, such as weight cycling and level of physical activity in the intervention group that may produce variation in response and further may explain the equivocal results. The final survey confirmed previous reports that individualised treatment is more effective and that the provision of foods in an intervention trial enhances compliance to dietary regimens.

The preliminary study of diet history interviews emphasised the need for the interviewer to listen for verbal cues such as “probably” and “it depends”. These were most prominently identified in relation to energy dense foods and thereby assisted the interviewer in obtaining more accurate dietary descriptions. Visual displays of food quantities also needed to be available for more precise reporting of problematic meals to recount such as dinner. The diet history interview data collected during the intervention trial indicated a mean score for valid reporting for weeks 0, 3, 6 and 9, though greater under-reporting resulted in a decline in validity at week 12.

DISCUSSION

After 12 weeks the lack of significant differences between control and intervention groups in terms of changes in body composition, serum lipids, substrate utilisation and fasting plasma glucose/insulin levels suggested that, at least with this profile of subjects, there is no effect of habituation with 25g RS in the diet. This may reflect the impact of dosage (25g RS estimated for bowel health may not be enough for metabolic health), the small sample size of the study and/or attrition rates. An increase in insulin resistance of about 10% in the RS group was consistent with the data (mean change = -9.8%; 95% confidence limit: 29 + 9) however, approximately 40 subjects would have been required to detect an effect of this magnitude using the current protocol. A reduction in the insulin excursion when challenged with the high RS meals was reasonable considering what is known about RS metabolism, however this significant result was not reflected in the glucose values overall, nor did it translate to a metabolic benefit from chronic exposure. Overall, with the consumption of relatively moderate quantities of RS, and given that reported meal patterns and intakes of some nutrients varied over the duration of the trial, the metabolic effect could be explained by a variety of differentials.

Human metabolic and behavioural variability are significant factors to consider in trials establishing the evidence for the optimal nutrient mix for the metabolic syndrome. First, there is diversity among humans in their genetic predisposition to disease. Second there are numerous points within a clinical trial where error in measurements may occur.

In current practice clinicians are asked to support their approach to the management of diet related disease with evidence-based guidelines. To date the most recognised form of best evidence is in the RCT, which presents limitations in relation to assessing the effect of dietary intake on the management of chronic disease as demonstrated here. The results of the thesis reported here using a RCT as its basis and made relevant to the 'real world' through the collection of naturalistic practice based evidence, showed that the effects of high amylose RS on the insulin resistance syndrome were equivocal. The reasons for this may be explained in the way in which outcomes were measured and assessed.

Results from the preliminary work on the collection of dietary data supported the need for research that studies the way outcomes are measured and assessed. The verbal descriptors used by participants were shown to correlate with their difficulty in reporting accurate food intake. This thesis demonstrates that problematic reporting of caloric intake was typically associated with energy dense foods. As diet-disease relationships need accurate recording of dietary intake to demonstrate cause and effect, qualitative studies such as this are fundamental to improving accurate gathering of energy intake. The methods developed here for identifying accurate reporting and applied to this randomised controlled intervention trial can be used in further trials and applied to clinical practice.

Results gained in clinical trials of dietary manipulation need to be able to be reproduced in the real world to have significant outcomes on the incidence of type 2 diabetes and the metabolic syndrome. Hence, to establish the evidence for practice in medical

nutrition therapy[1] information from both objective scientific[2] research and naturalistic[3] observations have been collected and analysed. Holistic patient care is necessary if individuals are to adapt recommended dietary guidelines to their modern lifestyle. Despite limitations in the relatively short duration of the RCT presented here, it serves as a template to analyse the outcomes of dietary intervention in the long term. To prove RS as a therapeutic dietary agent in the control of risk factors for the insulin resistance syndrome, further investigations using combined methodologies are indicated.

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[1] Medical Nutrition Therapy refers to the application of nutrition knowledge and clinical data in the management of diet-related disease using an evidence based approach (Franz 2003)

[2] Scientific – The scientific (positivist) paradigm uses a reductionist stance, examining mostly laboratory-based interventions with a predetermined question of causality between stable, tangible variables (Guba and Lincoln 1981 and 1985).

[3] Naturalistic – With regards to the experimental environment in human feeding research, naturalistic research studies the free-living environment. Naturalistic implies a less precise, less accurate and less controlled evidence though greater in ecological relevance when compared to intervention or laboratory formed evidence. They are constructed in the natural environment where behaviour is less disrupted, there are no controlled manipulations and allow for a variable environment (Blundell and Stubbs 1997).

vi Structure of the thesis

Well-recognised confounders in human based research vastly dictate the challenge in establishing sound evidence-based practice. These aspects reflect the reality of human variability, the need for individualised therapies and the existence of lifestyle derived confounders such as diet and activity levels and the problems associated with gathering information on these factors. The challenges raised form the ambiance for this thesis, taking the theoretical position that establishing the evidence from a dietetic perspective must draw on the scientific and naturalist dichotomies in the research context. Current human research does not commonly combine these modalities of analysis. The RCT is positioned as high-level evidence, yet inadequately captures less tangible attributes of human variability that naturalistic research can identify. The reductionist approach enforced by a RCT does not detect or accommodate for non-quantifiable and often significant personal environmental barriers to individual adoption of recommended lifestyle modifications. However, non-RCT forms of research are often perceived to be insufficient in rigor and robustness to base clinical practice upon.

The RCT, the accepted design for establishing evidence based practice, is of limited value on its own. This is because the extent of human variability from both biological and social influences makes it difficult for studies of a size feasible in practice to produce definitive results where biological outcomes are tested. Evidence based practice would benefit from research that includes both qualitative and quantitative methodologies so that practitioners have a range of information on which to base their decisions.

This thesis hypothesises that researchers should provide naturalist evidence in a complimentary fashion when researching diet-disease relationships with more widely accepted scientific (positivist) high-level evidence such as the RCT for appropriate integration into clinical practice. This hypothesis is tested through a RCT complimented by observational naturalistic research. The diet-disease relationship chosen for this comparison and testing was carbohydrate manipulation in an overweight insulin resistant population.

vii Publications and presentations related to this thesis

◈ ***Full Manuscripts Published in Refereed Journals***

1. Barnard, JA, Tapsell, LC, Davies, PSW, **Brenninger, VL,** Storlien, LH (2000) Relationship of high energy expenditure and variation in dietary intake with reporting accuracy on 7 day food records and diet histories in a group of healthy adult volunteers. *European Journal of Clinical Nutrition*.

2. Tapsell, LC, **Brenninger, VL** and Barnard, JA (2000), Applying conversation analysis to support accurate reporting in the diet history interview. *Journal of the American Dietetic Association* 100, 818-24.

◈ ***Conference Proceedings and Presentations***

1. **Brenninger, VL** (2002) Carbohydrates and the metabolic syndrome. Oral presentation. *Queensland Dietitians Association of Australia, Yeppoon, August 2002.*

2. Ngai, HHY, **Brenninger, VL**, Tapsell, LC, Brown, IL (2001), The acute effect of resistant starch on postprandial satiety in an overweight population. Oral presentation and proceedings publication. *Nutrition Society of Australia, Canberra, December 2001*.

3. **Brenninger, V**, Tapsell, L, Barnard, J (2001), Assessing energy intake: qualitative and quantitative methods account for variations. Oral presentation and proceedings publication. *Public Health Association of Australia Annual Conference, Sydney, September 2001*.

4. **Brenninger, VL**, Tapsell, LC (2001), Considerations for dietary intervention trials in an overweight population. Poster presentation and proceedings publication. *4th International Conference on the Scientific Basis of Health Services, Sydney, September 2001*.

5. **Brenninger, VL**, Tapsell, LC, Jenkins, AB, Barnard, JA (2001), Food sources of starch: implications for an intervention study involving resistant starch. Poster presentation and proceedings publication. *DAA 20th National Conference, 'Nutrition and Dietetic Practice: Reflections and New Horizons', Adelaide, May, 2001*.

6. Ngai, H, Tapsell, L, **Brenninger, V**, (2000), Resistant Starch: the acute effect on postprandial substrate oxidation and satiety; implications for obesity. Poster presentation and proceedings publication. *Masters in Dietetics Research Day, University of Wollongong, November 2000.*

7. **Brenninger, VL**, Tapsell, LC, Barnard, JA. (1999), Assessing usual dietary intakes: straightforward vs problematic reporting. Oral presentation and proceedings publication. *2nd South-West Pacific Nutrition and Dietetic Conference*, Auckland, *September, 1999*.

8. Barnard, JA, Tapsell, LC, **Brenninger, VL**, Higgins, J, Jenkins, AB, Davies, PSW and Storlien, LH (1999), Accurate reporting of diet and physical activity: identifying "ideal" subjects for dietary intervention trials. Oral presentation and proceedings publication. *2nd South-West Pacific Nutrition and Dietetic Conference, Auckland, September, 1999.*

9. Tapsell, LC, Barnard, J, **Brenninger, V**, Higgins, J, Jenkins, AB, Davies, PSW and Storlien LH (1999), Dietary reporting in 'free-living' individuals: implications for intervention trials. Poster presentation. *Diet and the Metabolic Syndrome. The Swedish Nutrition Foundation 21st International Symposium, Ystad, August, 1999.*

◈ ***Awards***

1. Poster Presentation Award (2001) *Dietitians Association of Australia, 20th National Conference, Adelaide, SA*. (**Brenninger, VL**, Tapsell, LC, Jenkins, AB, Barnard, JA (2001), Food sources of starch: implications for an intervention study involving resistant starch.)
2. Poster Presentation Award (2001) *Student Research Day, University of Wollongong, Wollongong, NSW*. (**Brenninger, VL**, Tapsell, LC, Jenkins, AB, Barnard, JA (2001), Food sources of starch: implications for an intervention study involving resistant starch.)
3. Poster prize (2000), Major projects (MSc Nutr. Diet.) University of Wollongong. (Ngai, H, Tapsell L, **Brenninger, V**, (2000), Resistant Starch: the acute effect on postprandial substrate oxidation and satiety; implications for obesity.