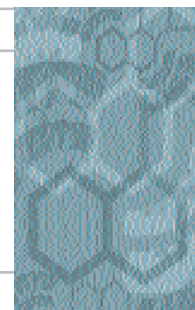


Clinical insights into the lifestyle and dietary management of insulin resistance syndrome



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Insulin resistance syndrome and its associated abnormalities are recognised as major public health issues. Abnormalities associated with the syndrome include, but are not limited to, cardiovascular disease, hypertension, diabetes and polycystic ovary syndrome. Identifying the insulin resistance syndrome in practice has been clinically challenging in recent years. The American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) have published a position statement on insulin resistance syndrome, indicating how to clearly identify the syndrome and recognise associated abnormalities. Obesity is a factor that contributes to an increased risk of developing the insulin resistance syndrome; however, insulin resistance does not cause obesity. Dietary and lifestyle factors that facilitate weight reduction will reduce an individual's risk for developing the insulin resistance syndrome. Furthermore, dietary factors can positively affect some of the abnormalities associated with the syndrome such as cardiovascular disease, diabetes and hypertension. This review further illustrates that the manipulation of macronutrient intake and macronutrient subtypes within an appropriate energy restriction may further be of benefit and directly impact on insulin sensitivity and hyperinsulinaemia associated with the insulin resistance syndrome.

Insulin resistance syndrome describes a condition characterised by decreased tissue sensitivity to the action of insulin, leading to a compensatory increase in insulin secretion. Insulin resistance is not a disease in and of itself, but rather a physiological abnormality that increases the risk of developing one or more abnormalities, including some degree of glucose intolerance, abnormal uric acid metabolism, dyslipidaemia, haemodynamic changes, abnormalities pertaining to prothrombotic factors, inflammatory markers and endothelial dysfunction. This metabolic dysfunction leads to a cluster of abnormalities with serious clinical consequences, including cardiovascular disease and type 2 diabetes, polycystic ovary syndrome (PCOS), non-alcoholic fatty liver disease (NAFLD) and other illnesses.¹

It is well recognised that diet and lifestyle factors play an important role in the management of 'diseases of lifestyle' that include type 2 diabetes, obesity, coronary heart disease and hypertension. Dietary intervention has further been recognised to be valuable for the management hyperuricaemia and more recently PCOS. There is substantial evidence to support the beneficial effects of dietary intervention in that the dietary manipulation of fat intake can affect serum lipid profiles, adjusting sodium intake may affect

hypertension, and by adjusting carbohydrate intake blood glucose regulation can be manipulated. It is clear that dietary and lifestyle intervention can positively affect some of the abnormalities associated with insulin resistance syndrome. However certain questions need to be raised, viz: (i) whether diet and lifestyle intervention can affect insulin resistance and associated hyperinsulinaemia directly, thereby further impacting on the abnormalities associated with the syndrome, and (ii) whether diet and lifestyle factors can reduce the incidence of the syndrome.

This review briefly discusses difficulties associated with identifying the syndrome and the role of nutrition and lifestyle intervention in prevention and management of the syndrome. It presents current findings which indicate that the manipulation of nutritional components may indeed affect insulin resistance syndrome positively.

Identifying the syndrome

Despite recognition of the importance of this syndrome, identifying individuals who have the syndrome is difficult, as there is no simple available clinical test to diagnose it.¹ In 1998, the World Health Organisation proposed criteria for definition of the syndrome,

indicating that the measurement of insulin resistance and obesity could be used by clinicians when identifying the syndrome.² Subsequently in 2001 the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATPIII) redefined criteria for diagnosing 'metabolic syndrome'.³ These criteria excluded the need to identify insulin resistance by laboratory means, yet still included obesity through the measurement of waist circumference as one of the criteria used to identify the syndrome.³ Given these criteria, it is reasonable to understand why clinicians recognised a need to test serum insulin levels for the assessment of insulin resistance using the HOMA (homeostasis model assessment) and quantitative insulin sensitivity check index (QUICKI) formulae.⁴ However it has recently been recognised that methods to quantify plasma insulin concentrations are not standardised, and it is difficult to compare values in different clinical laboratories. Further, plasma insulin concentrations have not been suggested as a means of identifying the insulin resistance syndrome.^{1,5}

Another faulty assumption resulted from these criteria, primarily because obesity was lumped with other abnormalities associated with insulin resistance syndrome such as dyslipidaemia and hypertension. Obesity has been incorrectly viewed as an abnormality precipitated by the syndrome rather than an abnormality contributing to the development of the syndrome.

Fortunately there is a way forward. A task force formed by the American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) has published a position statement on insulin resistance syndrome, which defines the syndrome more clearly and indicates absolutely that insulin testing is not necessary for the identification of the syndrome and that plasma glucose concentration 2 hours after a standard oral glucose challenge is a better indicator of insulin resistance.¹ Again this test and the identification of an abnormality should not be used alone to identify the syndrome but in conjunction with other criteria as set out by the AACE and ACE task force.¹

With regard to obesity, the task force indicates that the most powerful modulators of insulin action are differences in degree of obesity and physical activity, and there is evidence in both Pima Indians and Caucasians that approximately 50% of the variability in insulin-mediated glucose disposal can be attributed to variations in degree of obesity and physical fitness.¹ However they clearly state that obesity is not a consequence of insulin resistance or hyperinsulinaemia, but rather a physiological variable that decreases insulin-mediated glucose disposal. It must be recognised that not all insulin-resistant individuals are overweight or obese, nor are all obese or overweight individuals insulin-resistant.^{1,6} Obesity and overweight

should therefore be viewed as factors that increase the likelihood of insulin resistance syndrome, and not as an abnormality resulting from the syndrome. Nonetheless interventions aimed at treating obesity and overweight and increasing physical activity will improve insulin sensitivity.¹

Treatment of the insulin resistance syndrome

Treatment considerations must differentiate between efforts focused on improving insulin sensitivity itself and those aimed at the treatment of any of the specific manifestations of the insulin resistance syndrome.

Efforts to improve insulin sensitivity

Weight loss

Weight loss of 5 - 10% of body weight in overweight/obese individuals who are also insulin resistant, will significantly enhance insulin sensitivity, lower ambient plasma insulin concentrations, and improve the manifestations of the insulin resistance syndrome.^{1,6}

Numerous different diets have been recommended for weight loss. They all produce weight loss through the restriction of energy intake independent of the macronutrient distribution.⁷ Nonetheless, the fact that differences in macronutrient composition of diets identical in energy content have no discernible effect on body weight does not necessarily mean that impact on satiety will be similar.⁸ Suitable dietary intervention should be aimed at promoting satiety thereby enhancing dietary compliance. A nutritionally balanced energy-restricted eating plan is the most successful method of weight reduction. An energy deficit of 2 000 - 4 000 kJ daily usually causes fat stores to be mobilised to meet energy needs.⁹ Nonetheless many popular dietary regimens appear to ignore the importance of energy restriction.

Popular diets can be classified into three groups depending on the extreme macronutrient distribution (Table I).⁷

Diets with extreme macronutrient distribution are normally very restrictive and prescriptive and serve as a poor tool to educate individuals towards healthy eating habits and the management of weight loss as a lifestyle change.⁷ Traditionally low-fat/high-carbohydrate diets have been advocated for weight loss. On the other hand the most salient feature of insulin resistance is the body's inability to handle carbohydrate — to inhibit hepatic glucose production and to facilitate removal into tissues for use as energy. The question then arises whether it is in fact helpful to focus on high-carbohydrate diets which may have the effect of loading the system with carbohydrate when it is

Table I. Characterisation of diets as percentage of energy intake

Diet type	Carbohydrate (%)	Protein (%)	Fat (%)
High-fat, low-carbohydrate diet	< 20 (< 100 g)	25 - 30	55 - 65
Moderate-fat prudent diet	55 - 60	15 - 20	20 - 30
Low-fat and very-low fat and high-carbohydrate diet	> 65	10 - 20	10 - 19

already struggling to handle this macronutrient.¹⁰ Despite the fact that a low-fat and high-carbohydrate diet with concomitant energy restriction will promote weight loss, these diets are still not recommended for individuals with insulin resistance syndrome. This is primarily because once weight loss has been achieved the weight maintenance diet should not be high in carbohydrate for the individual with insulin resistance syndrome. Manifestations of the insulin resistance syndrome will be accentuated when the insulin-resistant person increases the amount of carbohydrate in the diet.¹ From the point of view of changing lifestyle it seems prudent to educate insulin-resistant individuals on the merits of a controlled and moderate carbohydrate intake (45% of total energy intake) from the onset of the dietary treatment intervention rather than changing the dietary recommendations once weight loss has occurred. A moderate carbohydrate intake is achieved through replacing saturated fat in the diet with unsaturated fat rather than carbohydrate.^{1,11,12} This dietary manipulation can further prevent the decrease in high-density lipoprotein (HDL) cholesterol and the increase in triglycerides that can occur in an insulin-resistant individual's response to high-carbohydrate and low-fat diets.^{1,8,12}

Beyond manipulation of the macronutrient content of the diet and a concomitant energy restriction, practitioners and supportive health care professionals need to recognise that successful weight loss regimens require intensive interventions that address the multiple variables affecting dietary behaviour and physical activity.¹⁰ The first step toward achieving successful dietary change and weight loss is to establish a collaborative alliance that will facilitate adherence and behaviour change.¹³ Then multiple intervention-related strategies can be used to further enhance adherence to treatment and elicit behaviour change. These strategies include self-monitoring, stimulus control, cognitive restructuring, stress management, social support, physical activity, and relapse prevention. Interventions that incorporate these strategies are effective in producing gradual and moderate weight loss in persons with obesity.¹³ Such interventions are time consuming and require consistent monitoring. Most practitioners and specialist physicians do not have the time or the inclination to engage in these intensive collaborative relationships.

This is where the dietitian as a behavioural counsellor and nutrition educator should intervene to facilitate the desired behaviour and lifestyle changes.

Physical activity

Any increase in physical activity will promote an increase in energy expenditure, which will help insulin-resistant individuals maintain or lose weight. It is also possible to enhance insulin sensitivity directly if an individual is able to exercise aerobically for 30 - 40 minutes four times per week.¹

Efforts to treat the manifestations of insulin resistance syndrome

A number of studies¹ have shown that the macronutrient composition of the diet impacts on the manifestations of the insulin resistance syndrome.^{1,8,10,11,14,15}

Fat

Research clearly shows that not all fats are equal metabolically. There are significant differences between fatty acids and their influence on energy balance and insulin sensitivity. Animal studies have shown differences between saturated and unsaturated fatty acids. These differences relate to the rate of storage and mobilisation of fat in and out of the fat cells respectively. Unsaturated fats tend to have a higher rate of fat oxidation when compared with saturated fats. It is well recognised that the skeletal cell membrane structure plays an important role towards insulin signalling. Unsaturated fat contributes to increased cell membrane fluidity, and adipocytes with oleic acid cell membranes show a higher stimulated glucose transport rate due to the change in oleic/linoleic acid ratio.^{16,17} The KWANU study confirms these findings in human subjects.¹⁵ Although insulin secretion is not affected, a shift of saturated to monounsaturated fat in the phospholipid structures of skeletal cell membranes under isoenergetic conditions contributes to increased insulin sensitivity.^{15,18}

At any given body mass index (BMI), insulin resistance increases the risk for the development of coronary heart disease and type 2 diabetes.¹⁹ With regard to

dyslipidaemia associated with the insulin resistance syndrome, many studies indicate that replacing saturated fat with monounsaturated fat in the diet without any other dietary modifications causes a reduction in LDL cholesterol without any adverse effect on HDL cholesterol levels and LDL size.²⁰

Other significant polyunsaturated fats (PUFAs) are omega-3 fatty acids, which do not affect insulin sensitivity directly. However the hypotriglyceridaemic effect of omega-3 fatty acids can contribute to improved insulin action.¹⁷ Published data consistently advocate the beneficial effects of omega-3 fatty acids in the form of fish and/or supplements, on blood lipids. In normal as well in hyperlipidaemic individuals omega-3 fatty acids significantly reduce triglycerides (TG) through inhibition of hepatic TG synthesis and secretion. omega-3 fatty acids cause no change in HDL and although some studies^{20,21} have noted an increase in LDL cholesterol in hypercholesterolaemic patients, this was of short duration.

A large number of studies support the use of fish oil supplementation in causing a small but significant reduction in blood pressure in hypertensive individuals. Apart from their effects on blood lipids and blood pressure, fish oils have additional anti-atherosclerotic effects such as decreased platelet aggregation and reduction of endothelial dysfunction via several anti-inflammatory actions.²²

Most studies^{11,12,14,15,20} support the beneficial effect of unsaturated fat on blood lipids when fat provides 30% or more of total energy intake, with monounsaturated fats providing 20% and saturated no more than 7% of total fat intake.

However, it seems that the beneficial effect of monounsaturated fats on insulin sensitivity is not seen when a fat intake higher than 37% of total energy intake is achieved, even if the saturated fat intake was less than 7%.^{11,14,15}

It must be remembered that dietary fat intake cannot promote obesity independent of energy intake. The energy density of the diet is far more important than the percentage of fat *per se*, and manipulation of macronutrient composition independent of energy balance does not change insulin action.^{7,10}

Carbohydrate

Carbohydrate is metabolised to glucose, which has a direct impact on the amount of insulin that must be secreted in order to maintain glucose homeostasis.⁸ While carbohydrate diets are not recommended for the management of insulin resistance syndrome, the resultant postprandial glucose levels following carbohydrate ingestion can be further manipulated in the diet by using the glycaemic index (GI) and determining the glucose load (GL).

The GI is a concept of ranking carbohydrate foods based on their effects on postprandial glycaemia. However the GI does not relate to the amount of carbohydrate usually consumed in a given portion of food. A more valuable tool used to determine the effect of carbohydrate selection on postprandial glycaemia is the glycaemic load. The glycaemic load is calculated by multiplying the amount of carbohydrate in a given portion of food with the GI number for that particular food.²³ This in turn provides a useful dietary tool indicating the amount of glucose that will enter the bloodstream postprandially.

Although ranking carbohydrate foods based on their glycaemic effect does not provide any information on their insulinogenic effect, research supports a linear correlation between the GI and the insulinaemic index (II) of most starchy foods. This correlation excludes fruit, milk and milk products.²⁴ Fructose produces much lower glucose and insulin responses than starch because it is slowly converted to glucose in the liver and only some of the glucose is released into the circulation.²³ Although most milk products have a low GI, the casein protein in these foods elicits a higher insulin response than other protein foods.¹⁰

Studies^{23,24} comparing the metabolic outcomes of diets using high-GI carbohydrate foods versus low-GI foods demonstrate that low GI carbohydrates are beneficial with regard to insulin sensitivity and weight loss, and the use of low-GI index carbohydrates is recommended within controlled proportions.

Further studies confirm a positive effect on TG levels when high-GI foods are replaced with low-GI foods. However, high-carbohydrate diets may be associated with a reduction in HDL levels regardless of the GI of the diet or changes in TG levels.^{24,25}

A moderate carbohydrate intake of 40 - 45% of total energy intake is recommended, and is achieved by replacing some of the carbohydrate in the diet with unsaturated fat.^{8,11,26}

Protein

When protein is consumed it increases the postprandial insulin response yet decreases the postprandial glucose response. Apart from the saturated fat content of protein foods, the type of protein itself can have an impact on insulin action.²⁷ Studies done with different amounts of protein in the diet found that 90% of the variance in postprandial insulin responses was explained by the glycaemic load of the meal.²⁸ At present the information from human studies is conflicting and too little information is available to make specific recommendations regarding the type of protein. However in order to reduce the saturated fat and trans-fatty acid content of the diet, recommendations should focus on giving preference to fatty fish and lean unprocessed protein-rich foods.^{9,21,22}

Protein should make up the balance of energy requirements and should provide between 15% and 20% of total energy intake.

Significance of lifestyle intervention

Lifestyle intervention is very difficult and is often viewed sceptically. Nonetheless, current studies done on lifestyle programmes that include physical activity, nutrition and psychological intervention confirm that they are of benefit when promoting weight loss. The Diabetes Prevention Program Research Group reported a 58% reduction in the incidence of developing diabetes with lifestyle intervention.²⁸

Melin *et al.*²⁹ tested a behaviour modification and nutritional counselling programme for the treatment of obesity in a randomised 2-year clinical trial. After 2 years, 65% of the subjects had reached weight stability with an average weight reduction of 8.5 kg, while 9.3% of subjects had gained weight and 26% had dropped out during the programme.²⁹

Clearly, nutrition and lifestyle intervention programmes have the potential to impact significantly on obesity and insulin resistance and their associated abnormalities.

Conclusion

The insulin resistance syndrome is increasingly appreciated as posing a major public health problem. Identifying individuals who have the syndrome is difficult. However the AACE and ACE task force position statement¹ provides practitioners and health care workers with clearer criteria for identification of the syndrome.

Intervention is primarily aimed at lifestyle change and affects dietary practice, physical activity and behaviour modification. Results are most likely to be realised when individuals are supported by a health care professional who can provide them with ongoing support, education and counselling toward the attainment of dietary and lifestyle objectives. Dietary recommendations should promote weight loss if the individual is overweight or obese yet should simultaneously aim to treat the manifestations of insulin resistance syndrome. At present nutritional recommendations point toward a moderate carbohydrate intake coupled with an increase in unsaturated fat and reduction in saturated fat, with the balance of energy being provided by lean protein foods

and fish. Regardless of the macronutrient split, emphasis must be placed on an appropriate energy intake, which will need to be restricted in order to promote weight loss if the individual is overweight or obese. Lifestyle intervention programmes show promising results. However the success of intervention appears to be related to multiple variables requiring considerable time and effort on the part of the practitioner and/or health care worker or dietitian.

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