Can dietary intervention produce long-term reduction in insulin resistance?

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Insulin sensitivity is potentially enhanced by a range of diet-related changes including reduction of visceral adiposity, a reduction in saturated fatty acids, and possibly a redistribution of the proportions of various unsaturated fatty acids. While there is evidence to suggest that lifestyle changes can reduce the risk of progression of impaired glucose tolerance to type 2 diabetes, there are no clinical trials which have conclusively demonstrated that any measure can reduce insulin resistance in the long term to an extent that can prevent the development of type 2 diabetes and other clinical complications. Evidence concerning the possibilities for reducing visceral adiposity and altering the nature of dietary fat are therefore considered. Attempts to achieve prolonged and substantial weight reduction in adults have not been encouraging, and it may be that preventing further weight gain is the most realistic target in this age group. In childhood the attempts have been more successful. The development of new approaches to achieving behavioural change and an environment which facilitates physical activity and appropriate food choices will be essential for more successful individual and population attempts to facilitate reduction in insulin resistance by weight loss. Changes in the nature of dietary fat appear to be more easily achieved. This is already a component of dietary advice aimed at cardiovascular risk reduction, and should be reinforced now with a view to also achieving a reduction in insulin resistance.

Insulin resistance: Visceral adiposity: Dietary fat: Lifestyle-related factors

Introduction

There is no doubt that lifestyle-related factors are important determinants of insulin resistance, and that insulin sensitivity in experimental animals and humans can be enhanced by dietary modifications. Visceral adiposity appears to be the most important potentially modifiable determinant of insulin resistance (Torjesen *et al*. 1997; Goodpaster *et al*. 1999) and short-term studies have shown a significant correlation between improved insulin sensitivity and percentage decrease in visceral adipose tissue (Goodpaster *et al*. 1999). The fatty acid composition of various tissues which may be potentially modifiable by diet change also influences insulin sensitivity. In particular a high percentage of saturated fatty acids (especially palmitic acid), reduced levels of α-linolenic acid, a low ratio of *n*-3 to *n*-6 fatty acids, and a high proportion of dihomo γ-linolenic acid have been shown to be positively correlated with insulin resistance (Borkman *et al*. 1993; Vessby *et al*. 1994; Storlien *et al*. 1996; Rocchini *et al*. 1997). There is evidence from experimental studies in humans that replacing saturated with monounsaturated fatty acids can enhance insulin sensitivity (Vessby 1999). However there are several unanswered questions:

(1) can the improvement in insulin sensitivity which has been demonstrated in short-term studies be sustained over longer periods?
(2) what is the extent of the dietary change required to achieve an appreciable improvement in insulin sensitivity?
(3) is the extent of the improvement in insulin sensitivity which can be achieved by dietary modification sufficient to appreciably reduce the risk of type 2 diabetes and other clinical consequences of insulin resistance?

While several studies have demonstrated the potential for lifestyle modification to reduce the risk of progression from impaired glucose tolerance to diabetes and to reduce several of the cardiovascular risk factors associated with insulin resistance (Eriksson & Lindgärde, 1991; Pan *et al*. 1997; Eriksson *et al*. 1999), there are no published long-term studies which can definitively answer the three questions listed. This paper examines the extent to which it has been possible to influence the diet-related determinants of insulin resistance.

Weight reduction

Several excellent reviews and meta-analyses have reported on the innumerable studies which have attempted to achieve weight loss in overweight and obese individuals, or compared different approaches to achieving this end (Glenny *et al*. 1997; Miller *et al*. 1997). On average it appears that a 15-week diet or diet-and-exercise programme can achieve

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an approximately 11 kg weight loss, with a 6·6 ± 0·5 and 8·6 ± 0·8 kg maintained loss after 1 year. Few studies appear to have been continued for longer than a year, and those that have seem to show generally disappointing results. For example, Wing and colleagues examined the effects of intensive diet and exercise programmes over 2 years in 154 non-diabetic participants who were 30–100 % over ideal body weight and had one or both parents with diabetes (Wing *et al*. 1998). They were randomized to diet (reduced calories and fat intake), exercise (goal, 1500 kcal/week of moderate activity), combination (diet plus exercise) or control groups. During the first 6 months the weight loss and changes in cardiovascular risk factors were impressive in the diet and combination treatment groups, but after 6 months there was a gradual deterioration so that by 2 years there was virtually no difference between any of the intervention groups and the control group. However, buried in these outwardly disappointing results are some interesting and encouraging findings. Firstly, amongst those who succeeded in losing 4·5 kg or more, regardless of treatment group, the risk of developing type 2 diabetes was reduced by about 30 % compared with those who lost no weight. Secondly, it is important to appreciate the means by which the intervention programme was delivered. During the first 6 months subjects attended relevant weekly meetings conducted by a behaviour therapist, registered dietitian and exercise therapist, depending upon the nature of the group. Individualized advice was also given. During the second 6 months biweekly meetings were held, and during the second year two 6-week refresher courses were offered. Thus it would seem that frequency of contact may be an essential component of successful individualized weight-reducing strategies. However it may well be that preventing further weight gain might be a more realistic strategy than attempting to achieve weight loss when dealing with adults. An interesting approach which succeeded in achieving this (although the initial goal was to achieve weight loss) was undertaken in Auckland, New Zealand amongst a group of Pacific Island people who are prone to both obesity and type 2 diabetes (Simmons *et al*. 1998). A church-based diet and exercise programme was introduced in one group of churches, another group acting as control. The intervention programme was associated with a measurable improvement in knowledge, behaviour and weight maintenance, whereas the control group continued to gain weight over the follow-up period.

A major barrier to maintaining long-term weight loss is likely to result from the motivation behind most individuals who enter weight-reducing programmes. The majority appear to do so for cosmetic rather than 'health' reasons, and few appear to achieve their desired target. The resulting disappointment may lead to an appreciable reduction in long-term compliance. These various observations have led many to the conclusion that the more cost-effective strategies to reduce obesity might be those which are population-based rather than those aimed at individuals. A number of such programmes have been introduced, though no detailed long-term evaluations are yet available.

Information regarding the prevention of obesity in childhood and adolescence is limited, but the results offer a little more cause for optimism. Flodmark *et al*. (1993) compared family therapy with conventional treatment (dietary counselling by a dietitian and visits to a pediatrician) and a no-treatment group in children aged 10–11 years with a BMI greater than 23 kg/m^2. After 1 year, amongst those in the family therapy group (conventional treatment plus six family therapy sessions during the year), 5 % had developed 'severe obesity' (BMI > 30 kg/m^2) compared with 29 % in the control group. No significant differences emerged between conventional treatment and control groups. In Singapore, growth monitoring in children aged 3–6 years followed by either individual or group counselling (depending upon the degree of overweight) resulted in appreciable reductions in rates of overweight and obesity (Ray *et al*. 1994). In a community of Pima Indians with immensely high rates of type 2 diabetes (Cook & Hurley, 1998), a school-based programme which included biochemical and anthropometric assessments, classroom instruction about diabetes, increased daily physical activity at school, and a structured school breakfast and lunch programme appeared to help slow weight gain and may reduce the epidemic proportions of diabetes in the community. The most impressive study in schools is that of Gortmaker *et al*. (1999) who carried out a randomized controlled field trial of five intervention and five control schools. The 'Planet Health' programme involved inclusion of health sessions within existing curricula using classroom teachers in four major subjects and physical education. Sessions focused on reducing television viewing, decreasing consumption of high-fat foods, increasing fruits and vegetables, and increasing moderate and vigorous physical activity. The prevalence of obesity among girls in the intervention schools was appreciably lower after 2 years than in the control schools (odds ratio 0·47, 0·24–0·93), with no difference amongst the boys. There was also greater remission of obesity amongst intervention girls versus control girls (odds ratio 2·16, 1·07–4·35). Reduction in television viewing was the most important predictor of the beneficial effect.

There have been several attempts to determine whether any particular macronutrient composition is preferable to another in achieving weight reduction. There is no disagreement regarding the need to reduce saturated fatty acids to 10 % or less of total energy. Most western populations obtain an appreciably greater proportion of total energy from saturated fat, and reduction of dietary saturated fatty acids has the potential to enhance insulin sensitivity. However there has been considerable debate as to the most appropriate proportions of energy which should be derived from fibre-rich carbohydrate and unsaturated fatty acids with a *cis* configuration. In any weight-reducing dietary regimen there is a need to reduce total energy intake. Protagonists of the high-carbohydrate–high-fibre approach argue that carbohydrate-rich foods derived from vegetables, fruit and appropriately processed cereals are often high in dietary fibre, may have a low glycaemic index and tend to enhance satiety, thus reducing intake of many energy-dense foods. There is epidemiological evidence which justifies the use of diets providing 55–70 % total energy from carbohydrate (FAO/WHO, 1998). Those advocating a 'fat-modified diet', i.e. a diet in which total fat intake is about 35 % total energy, argue that high carbohydrate intakes may raise triglyceride levels and reduce high-density lipoprotein, and that an optimum lipoprotein profile results from relatively

high intakes of *cis* monounsaturated fatty acids and modest intakes of *n*-3 and *n*-6 polyunsaturated fatty acids (Connor & Connor, 1997; Katan *et al*. 1997). However there is no evidence from either epidemiological studies or long-term clinical trials that sustained intake of appropriate high-carbohydrate diets (i.e. those rich in vegetables, fruits and appropriately processed cereals) are associated with hypertriglyceridaemia or low HDL levels. While there are no clinical trials demonstrating conclusively the benefit of one type of diet versus another, expert opinion weighs in favour of the suggestion that appropriate carbohydrate-containing foods could predominate on a weight-reducing dietary regimen (FAO/WHO, 1998).

Modification of dietary fat

Several studies have shown that modifying the nature of dietary fat in a manner which alters the proportions of various fatty acids in blood and in tissues can be sustained in the long term. The Lyons Heart Study has demonstrated that over a 5-year period it is possible to significantly reduce the percentage of stearic acid (data for palmitic acid not reported) and increase the percentage of oleic, α-linolenic and eicasapentaenoic acids, as well as the ratio of *n*-3 to *n*-6 polyunsaturated fatty acids (de Lorgeril *et al*. 1994). In our long-term prospective study of low-carbohdyrate (LC) and modified-fat (MF) dietary advice carried out in Oxford patients with type 2 diabetes, the proportion of palmitic acid was lower and of linoleic acid higher in MF than LC 10 years after dietary advice was first offered (N.J. Lewis-Barned, R.D. Carter, T.D.R. Hockaday, R. Howarth and J.I. Mann, unpublished results). Neither of these studies was designed to examine the effect on insulin resistance of changing the nature of dietary fatty acids, but they do indicate the potential to achieve long-term changes in the nature of dietary fat with appreciably less effort than appears to be required to achieve weight reduction. Changes in dietary and tissue fatty acid composition which might be expected to reduce insulin resistance are relatively easily achieved by using the appropriate oils, margarines, oily fish, grains, seeds and nuts, and consuming fewer high-fat dairy products, convenience and confectionary foods which are high in saturated and *trans* unsaturated fatty acids. The extent to which these changes in tissue composition can influence insulin resistance remains to be established.

Approaches for achieving dietary change

While the ability to modify the nature of dietary fat is encouraging, the difficulty involved in achieving reduction in adiposity, the major determinant of insulin resistance, is of concern. It suggests that unless alternative strategies to the conventional approaches can be developed it may not be possible to make major inroads into reducing the clinical consequences of insulin resistance in the present generation. Much current interest centres around models of achieving behavioural change which were primarily developed for purposes other than achieving dietary change. The two major models which have been suggested for this purpose are the Transtheoretical Model (Stages of Change Model) (Horwath 1999) and the Social Cognitive Theory (Baranowski *et al*. 1997). The former approach identifies an ordered set of 'stages of readiness to change' into which people can be classified, and identifies the different types of interventions most effective in facilitating movement from one stage to the next (Table 1). For example, there is little point in giving advice on how to make dietary changes to those who have not yet made a clear decision to change (precontemplation – no intention of changing; or contemplation – considering change in the next 6 months). For people in these stages, the most effective interventions are those which produce a shift in the relative perceptions of the benefits and barriers of dietary change. However, for those fully committed to change (preparation stage – intending to change in the next month), interventions are appropriate that build skills and confidence in how to make changes. Tailoring advice to individuals might be regarded as common sense, but there are very few controlled studies in which these approaches have been formally tested as a means of achieving dietary change. Most of the research carried out thus far relates to attempts to reduce cigarette smoking. However Campbell *et al*. (1994) demonstrated in a randomized clinical trial that reduction in fat was nearly three times greater when this approach was formally compared with a non-tailored approach to providing dietary advice. Social Cognitive Theory is more complex, and emphasizes the influence of environment on behavioural change as well as empowerment of the individual. The central idea is that environmental, personal and behavioural factors are continually interacting and influence each other ('reciprocal determinism'). This theory stresses the importance of anticipating positive reinforcements in shaping behaviour (e.g. anticipate weight loss if less fried food is eaten); the role of observational learning (i.e. incorporating role models into the learning experience); the development of a belief in one's ability to make a specific dietary change ('self-efficacy'); and the ability to set goals and to cope with stressful situations that may trigger relapse to less healthy eating habits. These and other approaches are not mutually exclusive, and have the potential to profoundly influence the extent to which lasting dietary change can be achieved. Further clinical trials are required.

Table 1. Description of the Transtheoretical (Stages of Change) Model

Precontemplation	No intention to change in next 6 months
Contemplation	Thinking about changing in next 6 months
Preparation	Intends to change within next month, some movement towards action
Action	Changing overt behaviour for $<$6 months
Maintenance	$\geqslant$6 months' overt behaviour change

Conclusions

There are at present no studies which demonstrate conclusively that dietary intervention can produce long-term reduction in insulin resistance. Reduction of visceral adiposity in overweight and obese individuals appears to provide the best means of increasing insulin sensitivity, but studies attempting to achieve long-term weight reduction have been disappointing. It may well be that preventing weight increase

is the most which can be achieved in the majority of overweight and obese individuals identified for the first time in adulthood. An environment which facilitates physical activity, and enables appropriate food choices and the development of new approaches to achieve behavioural change at the individual level, will be essential if the epidemic proportions of obesity and its consequences are to be reversed in future generations. Long-term changes in the nature of dietary fat (especially reducing saturated fatty acids and increasing the *n*-3 : *n*-6 polyunsaturated fatty acid ratio) appears to be easier to achieve than weight loss and would also be expected to enhance insulin sensitivity. Such advice is a pivotal component of most nutrition recommendations because of the potential to reduce coronary heart disease. It may now also be justified in terms of increasing insulin sensitivity and reducing the clinical consequences of resistance to the action of insulin.

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