Dietary treatment of the metabolic syndrome – the optimal diet

Gabriele Riccardi* and A. A. Rivellese

Department of Clinical and Experimental Medicine, Federico II University Medical School, Naples, Italy

The treatment of the metabolic syndrome aims to improve insulin sensitivity and correct/prevent the associated metabolic and cardiovascular abnormalities. Since many individuals with the metabolic syndrome are overweight, dietary treatment should be primarily focused on weight reduction. This approach can improve insulin sensitivity and exert beneficial effects on all the other abnormalities clustering in the syndrome. Insulin sensitivity can also be influenced by diet composition. In this respect, the specific effects of the quality of dietary fat are of great interest, given the considerable evidence in experimental animals that saturated fat in the diet may lead to insulin resistance. In man, there is indirect evidence that a higher saturated fat intake is associated with impaired insulin action. Human studies have also attempted to evaluate the relationship between total fat intake and insulin sensitivity. They are consistent in showing that fat intake is correlated with both plasma insulin values (positively) and insulin sensitivity (negatively). However, these correlations are largely mediated by body weight. Conversely, intervention studies are consistent in showing that when total fat intake is moderately increased (from 20 to 40 %), no major effect is observed on insulin sensitivity. We have recently undertaken a large, multicentre intervention study in 162 healthy individuals given either a high-saturated-fat or a high-monounsaturated-fat diet for 3 months. It shows that a high-monounsaturated-fat diet significantly improves insulin sensitivity compared to a high-saturated-fat diet. However, this beneficial effect of monounsaturated fat disappears when total fat intake exceeds 38 % of total energy. Independently of its effects on insulin sensitivity, diet composition can influence the factors clustering in the metabolic syndrome. Dietary carbohydrate increases blood glucose levels, particularly in the postprandial period, and consequently also insulin levels and plasma triglycerides. The detrimental effects of a high-carbohydrate diet on plasma glucose/insulin, triglyceride/HDL or fibrinolysis occur only when carbohydrate foods with a high glycaemic index are consumed, while they are abolished if the diet is based largely on fibre-rich, low-glycaemic-index foods. In conclusion, weight reduction is a powerful measure for the treatment of metabolic syndrome. Moreover, the diet for the treatment of the metabolic syndrome should be limited in the intake of saturated fat, while high fibre/low-glycaemic-index foods should be used without specific limitations. Moderate amounts of monounsaturated fat could be permitted as they do not induce detrimental metabolic effects.

Metabolic symdrome: Insulin sensitivity: Monounsaturated fat: Diet

The metabolic syndrome is a clustering of metabolic abnormalities and cardiovascular risk factors that occur in individuals with impaired insulin sensitivity. These individuals present two or more of the following conditions: high plasma insulin, high blood pressure, high plasma triglyceride, low HDL, diabetes or impaired blood glucose regulation. The treatment of the metabolic syndrome has to be targeted (i) to improve insulin sensitivity, and (ii) to correct/prevent the associated metabolic and cardiovascular abnormalities.

Usually any therapeutic manoeuvre that improves insulin sensitivity will also have beneficial effects on all the metabolic and cardiovascular abnormalities that are linked with insulin resistance. In contrast, some dietary factors that have no influence on insulin sensitivity are able to modify (in either direction) one or more features of the metabolic syndrome. Therefore a diet to treat individuals with this condition will have some general characteristics, but will have specific properties to take into account the abnormalities present in that individual patient (i.e. hypertension, diabetes, dyslipidaemia).

Most of the individuals affected by the metabolic syndrome are overweight, therefore dietary treatment should be primarily focused on weight reduction. This measure is able, *per se*, to improve insulin sensitivity and thus exert beneficial effects on all the other abnormalities clustering in the syndrome. Since abdominal obesity is an even stronger predisposing factor for the metabolic syndrome, specific nutritional influences on body fat distribution are important, although not yet exhaustively defined.

It is not necessary to achieve the ideal body weight to

* **Corresponding author:** G. Riccardi, fax +39 08174 62117, email nmcd@unina.it

Table 1. Effects of diet composition on insulin sensitivity

Author	Fat content	Participants	Duration (d)	Method	Outcome
Chen, 1988	55 versus 0 %	Healthy	4	FSIGT*	↓
Borkman et al. 1991	37 versus 22 %	Healthy	21	Clamp	=
Parillo et al. 1992	40 versus 20 %	Type 2 DM	14	Clamp	↑
Garg et al. 1992	50 versus 25 %	Type 2 DM	21	Clamp	=
Hughes et al. 1995	30 versus 20 %	IGT	84	Clamp	=

*FSIGT = frequent sampling intravenous glucose tolerance test (minimal model).

improve the metabolic profile – in most instances a 5–10 % weight reduction is sufficient to induce a clinically relevant effect (Weinstock *et al.* 1998). In fact, in many studies the improvement of insulin sensitivity due to weight reduction is between 30 and 60 %, which is more than that obtained with insulin-sensitizing drugs. The beneficial effects of weight reduction are usually preserved as long as weight is not regained. In this respect, intervention programmes have proven successful up to 2 years, but these studies are still in progress and longer follow-ups are needed.

Diet composition and insulin sensitivity

Insulin sensitivity can be influenced not only by total energy intake, but also by diet composition. In this respect, the specific effects of the quality of dietary fat are of great interest, as there is considerable evidence in experimental animals that saturated fat in the diet may lead to insulin resistance. In man there is indirect evidence for the same effect: a higher saturated fat intake is associated with impaired insulin action. However, intervention studies on changes in dietary fat quality and insulin sensitivity in humans have so far been inconclusive, perhaps because of the short duration of the study period and the inadequate sample size (Storlien *et al.* 1996).

Human studies have also attempted to evaluate the relationship between total fat intake and insulin sensitivity. Many epidemiological studies, both cross-sectional and prospective, are now available showing that fat intake is correlated with both plasma insulin values (positively) and insulin sensitivity (negatively). These correlations are largely mediated by body weight, which might explain why in these studies saturated and unsaturated fats (which have identical energy content) show similar relationships with insulin sensitivity. If the effect of total fat intake on body weight is properly accounted for, the relationship between dietary fat and insulin sensitivity becomes less consistent (Storlien *et al.* 1996).

A more appropriate study design to evaluate the effect of total fat intake on insulin sensitivity, independently of all possible confounders, is the intervention trial. Unfortunately few such studies are available in the literature. However these studies are consistent in showing that when total fat intake is increased from 20 to 40 %, no major effect is observed on insulin sensitivity (Table 1) (Borkman *et al.* 1991; Garg *et al.* 1992; Parillo *et al.* 1992; Hughes *et al.* 1995). Only more pronounced, non-physiological changes – as in the Chen Study where fat intake varied from 0 to 55 % – might be able to modify insulin sensitivity (Chen *et al.* 1988). In the study performed by our group, a reduction of

fat intake (monounsaturated fat) counterbalanced by an increased consumption of starchy foods slightly worsened insulin sensitivity. This was probably a consequence of glucotoxicity; our study participants had diabetes, and the increase in the carbohydrate load deteriorated their glycaemic control thus impairing their insulin sensitivity (Parillo *et al.* 1992).

In order to clarify the complex issue of the effects of dietary fat on insulin sensitivity, we have recently undertaken a large, multi-centre intervention study. The details of the results are still unpublished, but the main outcome has been presented at an international diabetes meeting. In short, this study, undertaken in 162 healthy individuals given either a high-saturated-fat or a high-monounsaturated-fat diet for 3 months, shows that a high monounsaturated fat diet significantly improves insulin sensitivity compared to a high-saturated-fat diet. However this beneficial effect of monounsaturated fat disappears in individuals whose total fat intake exceeds 38 % of total energy (Vessby *et al.* 1999).

There are few dietary components other than dietary fat that have been shown to influence insulin sensitivity (Table 2), and for most of these the available evidence is inconclusive. In summary, there are some indications that alcohol might be beneficial if consumed in limited amounts, whereas it might be detrimental when the intake exceeds 30 g/d (Facchini *et al.* 1994; Kiechl *et al.* 1996). Also, it has been suggested that a very high salt intake might impair insulin sensitivity (Donovan *et al.* 1993).

The effects of high-fibre and/or low-glycaemic-index (GI) foods on insulin sensitivity are particularly controversial. While there is strong evidence supporting their beneficial effects on blood glucose levels, data on their influence on insulin sensitivity are much less clear. In particular, so far no properly designed intervention study with a sufficient sample size has been undertaken to evaluate this issue. Therefore while it can be reasonably hypothesized that dietary fibre and/or low-GI foods might exert a beneficial effect on insulin sensitivity, this cannot be

Table 2. Influence of diet composition on insulin sensitivity

Diet	Insulin sensitivity
Total fat	↓ (threshold?)
Saturated fat	↓↓
Fibre and/or low GI	↑?
Alcohol	↑
NaCl	↓

taken for granted (Riccardi & Rivellese, 1991; Frost *et al.* 1996).

As to the effect of vitamins on insulin sensitivity, there is no firm evidence of any major role of antioxidant vitamin C and E (Sanchez-Lugo *et al.* 1997).

Effects of diet composition on metabolic abnormalities and cardiovascular risk factors clustering in the metabolic syndrome

Independently of its effects on insulin sensitivity, diet composition can influence each of the factors clustering in the metabolic syndrome. Among the various dietary components, the one that has been most extensively studied is dietary carbohydrate. Since dietary carbohydrate represents a major precursor of plasma glucose, it is obvious that increasing the amount of carbohydrate in the diet will elevate blood glucose levels, particularly in the postprandial period. Plasma glucose concentration represents an important triggering factor for insulin release, therefore a high-carbohydrate diet will also lead to increased insulin levels. The effects of a high-carbohydrate diet will be more pronounced on glucose or insulin levels according to the insulin secretory capacity of the endocrine pancreas (Parillo *et al.* 1996; Reaven, 1997).

Glucose and lipid metabolism are strongly related, and any derangement of carbohydrate metabolism induced by a high-carbohydrate diet will also increase plasma triglycerides and, possibly, decrease plasma HDL concentrations; this has been clearly shown by a meta-analysis of all studies comparing a high-monounsaturated-fat diet with a high-carbohydrate diet (Fig. 1; Garg 1998). Fibrinolysis is also worsened by a high-carbohydrate diet; this type of diet is associated with an increase of PAI1 in blood (Lopez-Segura *et al.* 1996).

In short, many features of the metabolic syndrome are worsened by dietary carbohydrate. However, these untoward effects are largely due to an abrupt perturbation, induced by carbohydrate-rich foods, of a metabolic steady state present in the fasting condition. The current hypothesis

is that the greater and the more rapid this perturbation, the more pronounced the effects. Therefore all detrimental effects of a high-carbohydrate diet could be minimized if carbohydrate digestion and absorption were slowed down. This has raised much interest in the properties of food that retard food digestion, and has led to a new classification of carbohydrate foods based on their physiological effects *in vivo*. The GI is the parameter most extensively utilized for this classification. It represents the plasma glucose response to a food, expressed as a percentage of the glucose response to a reference food. Although this index has been criticized for its quantitative approximation, it nevertheless differentiates among the carbohydrate-rich foods the 'fast' and the 'lente' ones, which clinical studies have shown as having diverging effects on most of the metabolic abnormalities and cardiovascular risk factors clustering in the metabolic syndrome (Asp *et al.* 1993; Jenkins & Jenkins, 1995).

In particular it is now clear that the detrimental effects of a high-carbohydrate diet on plasma glucose/insulin, triglyceride/HDL or fibrinolysis occur only when carbohydrate foods with a high GI are consumed, while they are abolished if the diet is based largely on fibre-rich, low-GI foods (Table 3) (Riccardi & Rivellese, 1991; Rivellese *et al.* 1994; Salméron *et al.* 1997; Frost *et al.* 1999).

The advantage of GI is that it allows us to predict the physiological effects of a food better than any other chemical or physical parameter. In this respect, although the fibre content of a food certainly contributes to delaying carbohydrate digestion, it is not the only food factor to have such an effect. Therefore, while foods with a high fibre content are often also characterized by a low GI, there still are some discrepancies between fibre content and GI, as in the case of pasta or parboiled rice which are not particularly fibre rich but have a low GI.

In addition to carbohydrate, other food constituents known to influence the metabolic abnormalities and cardiovascular risk factors clustering in the metabolic syndrome are listed in Table 3. In particular, an excessive alcohol intake
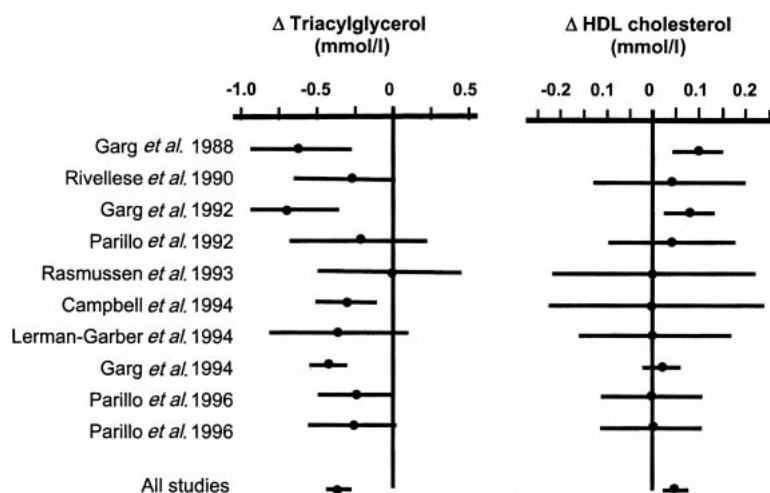

Fig. 1. Mean difference (95 % CI) in plasma triglyceride and HDL cholesterol concentrations between a high-monounsaturated-fat diet and a high-carbohydrate diet (modified from Garg, 1998).

Table 3. Effects of dietary components on the cardiovascular risk factors clustering with the metabolic syndrome

Risk factors	Dietary components with	
	Beneficial effects	Detrimental effects
Plasma glucose/insulin	Dietary fibre and/or low GI	High GI
Plasma triglyceride/HDL	Dietary fibre and/or low GI ω-3 fatty acids	High GI Alcohol
Blood pressure	Potassium salts ω-3 fatty acids (?)	Sodium chloride Alcohol Saturated fat

(more than 30 g/d) can increase both plasma triglyceride and blood pressure levels (Kiechl *et al.* 1996); in addition a high intake of sodium chloride can also elevate blood pressure. In contrast, the ω-3 fatty acids present in fatty fish and some leafy vegetables can reduce plasma triglycerides, whereas their beneficial effects on blood pressure are more controversial. Finally, the potassium salts present in vegetables, legumes and fruit can also contribute to reducing blood pressure, while saturated fat can increase it (Hornstra *et al.* 1998).

Individuals with the metabolic syndrome are excessively prone to cardiovascular diseases; therefore in defining the 'optimal diet' for these people, the need to reduce plasma cholesterol levels as much as possible and, in particular, low density lipoproteins (LDL), cannot be neglected. In this respect the reduction of saturated fat, which is beneficial for improving insulin sensitivity, is further reinforced as it contributes to lowering LDL. In addition, cholesterol intake has also to be reduced as it influences LDL concentrations and, more generally, cardiovascular risk (Hornstra *et al.* 1998).

Optimal composition of diet for the metabolic syndrome

On the basis of what is outlined above, it is not difficult to design a diet for the metabolic syndrome. It should have two basic requirements:

(1) reduced saturated fat;
(2) increased vegetables, legumes, fruit and low-GI starchy foods.

Two additional important features of this diet are a low salt content and a limited alchool intake.

The diet should also take into account both food habits and treatment goals; this would allow more flexibility and thus improve dietary compliance and efficacy (ADA Position Statement, 1996). However, in deciding the proportion of other nutrients it might be appropriate to follow some general guidelines based on available evidence and clinical experience. Protein intake should be similar to that of the rest of the population (allowing some fluctuations) with particular emphasis on vegetable proteins and fish (DNSG–EASD, 1995; Linn *et al.* 1996). About 45 % of the energy intake will be distributed between unsaturated fat and high-GI carbohydrate. Since an excessive intake of either one of these nutrients has detrimental metabolic effects, it might be better to indicate upper limits for consumption, although allowing some flexibility. These limits could be set at 25 %

energy for high-GI starchy foods and 20 % for monounsaturated fat (plus polyunsaturated fat, which is generally recommended not to exceed 10 % energy). As a consequence, total fat intake could range between 30 and 40 % and total carbohydrate intake between 45 and 55 % (Fig. 2).

Variations within the allowed ranges for carbohydrate and fat may be permitted not only to match (as far as possible) the composition of the habitual diet, but also to consider the specific treatment goals for such individuals. This means increasing either carbohydrate or fat intake in relation to whether the principal goal is weight reduction (in the case of overweight) or limiting the glycaemic load of the diet (in the presence of hyperglycaemia or hypertriglyceridaemia). In the presence of overweight, reducing the fat content might not be sufficient and the total energy intake should also be reduced by decreasing the consumption of all energy-dense foods (including soft drinks and sweets).

Conclusions

In conclusion, while it is firmly established that weight reduction is a powerful measure for the treatment of the metabolic syndrome, long-term and sufficiently powerful
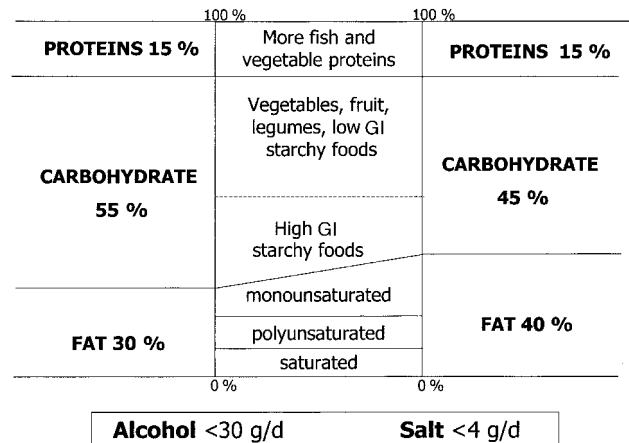

Fig. 2. 'Optimal diet' for the metabolic syndrome. Provided that saturated fat is reduced and most of the carbohydrate-rich foods have a high fibre content or a low GI, some flexibility might be allowed in the amount of fat and carbohydrate, e.g. exchanging about 10 % energy between monounsaturated fat and carbohydrate-rich foods with high GI.

(sufficient sample size) intervention studies are still needed to establish how changes in the diet composition can influence insulin sensitivity in humans. At present, on the basis of the best available evidence, the diet for treatment of the metabolic syndrome should be limited in the intake of saturated fat, for its known unfavourable effects on insulin sensitivity and blood pressure, as well as on plasma lipids. Carbohydrate-rich foods with a high GI should also be restricted for their unfavourable effects on the metabolic abnormalities and cardiovascular risk factors clustering in the metabolic syndrome. High fibre/low-GI foods should, instead, be preferentially used without specific limitations. Moderate amounts of monounsaturated fat could be permitted since they do not induce detrimental metabolic effects. If the diet has these characteristics (in addition to a low-salt and moderate alcohol consumption), it may not be necessary to drastically reduce the total amount of fat, as advocated in the past in order to provide cardiovascular disease protection. It is now clear that, with certain limits, it is the quality rather than the total amount of fat that really matters. Moreover, too much emphasis on the need to reduce total fat intake could lead people to increase their carbohydrate consumption. The fact that high-GI foods are often more palatable than low-GI/high-fibre foods could result in an inappropriately high glycaemic load that, in turn, will induce clinically significant untoward effects in people with established metabolic abnormalities. Setting an upper limit for fat consumption around 40 % is both realistic and biologically sound; so far, no clear clinical disadvantage has been demonstrated for diets deriving up to 40 % of energy as fat, provided that the saturated type is kept low. Moreover, since between one-third and one-half of the populations of most western countries derive more than 40 % of energy from fat, the goal of not exceeding this limit is more feasible than any drastic fat reduction which could discourage both patients and physicians from trying to achieve it (Hepp, 1995; Macdiarmid et al. 1996; Heini & Weinsier, 1997).

Properly designed intervention studies with an adequate sample size should be undertaken in order to evaluate the clinical benefits of an appropriate nutritional approach to treating the metabolic syndrome, possibly as compared with the multi-pharmacological approach presently adopted by most physicians. Unfortunately, for various reasons nutritional studies are not easily funded by either the food industry or institutional bodies. In the absence of clear scientific evidence, individuals with metabolic syndrome will continue to be treated with multiple drug prescriptions that mitigate the symptoms, but are inadequate to treat the disease.

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