Effect of Variations in Amount and Kind of Dietary Fat and Carbohydrate in the Dietary Management of Type 2 Diabetes

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INTRODUCTION

Treatment of patients with Type 2 diabetes must focus on the prevention of the long-term vascular complications of this syndrome. The results (1) of the United Kingdom Prospective Diabetes Study (UKPDS) have clearly shown that improved glycaemic control will decrease the development of microvascular disease in patients with Type 2 diabetes. Therefore, consideration of the role of energetic macronutrients of dietary fat and carbohydrate (CHO) in the management of patients with Type 2 diabetes must evaluate the impact of any recommendations in light of their effect on glycaemic control.

The results of the UKPDS were less encouraging concerning the ability of improved glycaemic control to reduce macrovascular disease (1). Indeed, neither lowering plasma glucose concentration (1), nor blood pressure (2), decreased myocardial infarction to the same degree as reported for the microangiopathic endpoints. The reason for this disparity between microvascular and macrovascular disease incidence in the UKPDS is not fully understood, but is at least partly due to the importance of abnormal lipoprotein metabolism in the genesis of coronary heart disease (CHD) in
patients with Type 2 diabetes. Consequently, recommendations concerning the CHO content of diabetic diets must take into account how they might affect dyslipidaemia in patients with Type 2 diabetes.

Although Type 2 diabetes is defined by hyperglycaemia, an increase in ambient glucose concentration is not the only metabolic abnormality in patients with Type 2 diabetes. In addition to diabetic dyslipidaemia, there is a cluster of abnormalities related to insulin resistance and circulating plasma insulin concentrations in patients with Type 2 diabetes (3–5). Since these changes may contribute to the increased prevalence of CHD, they must also be taken into account when dietary guidelines are proposed.

Finally, it is important to distinguish between the fat and CHO content of weight loss versus weight maintenance diets. The metabolic impact of variations in macronutrient content will vary enormously in these two situations, and this important difference cannot be ignored.

In this chapter an attempt will be made to discuss how variations in relative amount and kind of CHO could affect both microvascular and macrovascular outcome in patients with Type 2 diabetes, taking into account the considerations discussed above, and results of clinical studies of patients with Type 2 diabetes.

**CALORIE-RESTRICTED DIETS**

There is little doubt that weight loss in response to calorie-restricted diets will improve both glycaemic control and dyslipidaemia in patients with Type 2 diabetes (6–11). However, there are two questions concerning this issue that deserve some attention. In the first place, do variations in the relative proportion of macronutrients have any effect on the ability of patients with Type 2 diabetes to lose weight? Three relevant papers bearing on this issue have been published in the last few years, comparing weight loss in response to calorie-restricted diets, varying only in terms of relative proportions of CHO and fat. The results showed that weight loss was identical when dietary CHO varied from 10% to 70% of daily calories, with proportionate changes in fat content (9–11). Since the longest of these studies only lasted for 12 weeks (8), it could be argued that differences in rate of weight loss might have emerged if the patients had been followed for longer. On the other hand, there is no evidence that relatively large variations in the relative amounts of dietary CHO and fat present in energy-restricted diets have a discernible effect on the ability of patients with Type 2 diabetes to lose weight.

Variations in relative amounts of dietary CHO and fat did not prevent the improvement in glycaemic control associated with weight loss, but in two of the studies (9,10) the fall in plasma glucose concentration was significantly greater on a higher monounsaturated fat (MUF)–lower CHO diet. Plasma triglyceride
(TG) and high-density lipoprotein (HDL) cholesterol concentrations fell with weight loss, irrespective of macronutrient content, but the decrement in TG concentration was greater, and the fall in HDL cholesterol attenuated, in response to calorie-restricted diets relatively high in MUFA and low in CHO. Low-density lipoprotein (LDL) cholesterol concentration decreased when either MUFA or CHO replaced saturated fat (SF) in the diet, but the improvement in LDL cholesterol concentration did not take place if dietary intake of SF was not decreased. Finally, improvement in all of these variables in response to a diet relatively high in MUFA and lower in CHO persisted several weeks after a period of weight maintenance with the test diets.

In summary, weight loss in overweight patients with Type 2 diabetes is of substantial clinical benefit, and is almost certainly the most powerful lifestyle modification to improve clinical outcome in this population. Although variations in relative proportion of dietary fat and CHO in energy-restricted diets do not seem to affect the amount of weight loss, the metabolic benefit associated with weight loss was somewhat greater when the diet was relatively higher in MUFA and lower in CHO.

**METABOLIC EFFECTS OF VARIATIONS IN THE RELATIVE AMOUNTS OF DIETARY CARBOHYDRATE AND FAT CONTENT IN ISOCALORIC DIETS**

As emphasised in the introduction, dietary recommendations for patients with Type 2 diabetes must take into account the impact of variations in macronutrient content on both microvascular and macrovascular disease. In this section attention will be focused on the effect of changes in the relative amount of CHO and fat in weight maintenance diets, evaluating the impact of such variations on the metabolic abnormalities characteristic of patients with Type 2 diabetes.

**INSULIN RESISTANCE**

The ability of insulin to stimulate muscle glucose disposal is decreased in the vast majority of patients with Type 2 diabetes (12,13). Although weight loss will enhance insulin-mediated glucose disposal in patients with Type 2 diabetes (6), there appears to be no evidence in patients with Type 2 diabetes that the frequently recommended relatively low fat–high CHO diets have any beneficial effect on insulin-mediated glucose disposal (14–16). Indeed, there is evidence from one study (16) that insulin resistance is accentuated in response to low fat–high CHO diets as compared to diets higher in MUFA and lower in CHO.
PLASMA GLUCOSE AND INSULIN CONCENTRATIONS

Several studies have been published describing the effect of reciprocal increases in CHO and decreases in fat intake on plasma glucose and insulin concentration in patients with Type 2 diabetes (15,17–20). Furthermore, the results have been remarkably similar, given the differences in the experimental protocols, and quite consistent with what would have been predicted in view of the pathophysiology of this syndrome. If CHO intake is increased in patients with Type 2 diabetes, plasma glucose concentrations will tend to rise, stimulating the pancreas to secrete more insulin. If patients with Type 2 diabetes retain significant B-cell reserve, more insulin will be secreted in this situation, attenuating any rise in plasma glucose concentrations at the expense of higher plasma insulin concentrations. Conversely, the less able the patient is to secrete additional amounts of insulin in response to an increase in CHO intake, the greater will be the rise in plasma glucose concentration, with minimal increases in ambient insulin concentration. Obviously, these are two extreme examples of an almost infinite series of possible combinations of the changes in plasma glucose and insulin concentrations that will result from increasing the relative proportion of CHO in the diet. In fact, most published data show that both plasma glucose and insulin concentrations increase in response to diets relatively low in fat and high in CHO. Perhaps the best example of this general conclusion is the publication of Parillo and colleagues (21) showing that postprandial plasma glucose concentrations did not increase significantly when diet-treated patients with Type 2 diabetes consumed relatively more CHO, presumably due to the fact that the low fat–high CHO diets were associated with higher postprandial insulin concentrations. The situation was reversed in sulphonylurea-treated patients, with higher postprandial glucose and unchanged insulin concentrations, in response to increases in dietary CHO intake.

Based upon the above, there seems to be substantial evidence that postprandial glucose and/or insulin concentrations will increase when dietary fat content is decreased and CHO intake increased. The best one can hope for is that low fat–high CHO diets may not lead to decreased glycaemic control. However, even this can only be accomplished at the expense of increases in plasma insulin concentrations. The role of endogenous hyperinsulinaemia as a risk factor for CHD in patients with Type 2 diabetes is still unclear, but it may not be prudent to ignore the possibility that this, or abnormalities associated with it, may contribute to the accelerated atherogenesis that characterises these patients (22,23).

DYSLIPIDAEMIA

Diabetic dyslipidaemia is characterised by high plasma TG and low HDL cholesterol concentrations (22). Although less commonly measured, LDL
particle diameter tends to be decreased in patients with Type 2 diabetes (23), and the postprandial accumulation of TG-rich lipoproteins accentuated (24). The close association of the latter two abnormalities with hypertriglyceridaemia makes it less necessary to directly measure LDL particle diameter or postprandial lipaemia; if the plasma TG concentration of a patient with Type 2 diabetes exceeds 2 mM, it is almost certain that the individual will have smaller and denser LDL particles and day-long increases in remnant lipoprotein (RLP) concentration.

The fact that LDL cholesterol concentrations are not higher in patients with Type 2 diabetes than in non-diabetic individuals (22) does not preclude the need to consider how dietary recommendation would affect LDL cholesterol concentrations. Indeed, there is evidence that lowering of LDL cholesterol concentrations by pharmacological means will decrease risk of CHD (25,26).

Based on the above considerations, it seems clear that dietary recommendations for patients with Type 2 diabetes, above and beyond weight loss, must take into account the effects of a given intervention on both LDL cholesterol metabolism, and the atherogenic lipoprotein phenotype of hypertriglyceridaemia, low HDL cholesterol concentration, smaller and denser LDL particles, and an exaggerated degree of postprandial lipaemia. The goal is to maximally decrease CHD risk factors attributed to both forms of abnormal lipoprotein metabolism.

**LDL Cholesterol**

There is abundant evidence in non-diabetic individuals that replacing SF with either unsaturated fat or CHO will lower LDL cholesterol concentrations to a similar degree (27,28), and this appears to be the case in patients with Type 2 diabetes (15,17–20). Given the evidence that pharmacological lowering of LDL cholesterol decreases CHD risk in patients with Type 2 diabetes (25,26), the intake of SF should be limited to less than 10% of total calories in these individuals.

**TG-rich Lipoproteins**

The decision to replace SF with either unsaturated fat or CHO will have an enormous impact on the circulating concentration of TG-rich lipoproteins. There is substantial evidence in patients with Type 2 diabetes that diets low in SF and high in CHO will increase fasting plasma TG concentration as compared to substitution of SF with MUFA/PUFA (15,17–20). Evidence has recently been published that fasting RLP concentrations are also increased in patients with Type 2 diabetes (29), and the postprandial accumulation of RLPs of both endogenous (hepatic) and exogenous (intestine) origin are increased in patients with Type 2 diabetes (30). This latter observation is not simply a
function of the increase in fasting TG-pool size characteristic of patients with Type 2 diabetes, but appears to also involve a decrease in the removal rate from plasma of TG-rich lipoproteins following a mixed meal.

**HDL Cholesterol**

Although a low HDL cholesterol concentration in patients with Type 2 diabetes is usually associated with a high plasma TG concentration, the difficulty in raising HDL cholesterol concentration with dietary manipulation is in marked contrast to the relative responsiveness of plasma TG concentrations. The reason for the difference is not clear. There is evidence that HDL cholesterol concentrations are inversely related to the fractional catabolic rate (FCR) of apo lipoprotein A-1 in patients with Type 2 diabetes (31), the more rapid the FCR of apo A-1, the lower the HDL cholesterol concentration. Furthermore, the higher the plasma insulin response to an oral glucose challenge, the faster the apo A-1 FCR (31). Perhaps the changes in circulating insulin concentration resulting from relatively minor variations in macronutrient composition in patients with Type 2 diabetes are not sufficient to modulate the FCR of apo A-1. Irrespective of the explanation, it appears that dietary manipulations have relatively little effect on HDL cholesterol concentrations in patients with Type 2 diabetes.

**Dyslipidaemia and CHD Risk**

As discussed above, there is evidence that drug-induced decreases in LDL cholesterol concentration decrease risk of CHD. Although there is ongoing debate as to whether or not hypertriglyceridaemia is an ‘independent’ risk factor in non-diabetic individuals (32), the importance of increases in plasma TG for predicting CHD in patients with Type 2 diabetes seems less controversial (32–34). There is little reason to question the importance of a low HDL cholesterol as a CHD risk factor, and there is increasing evidence in non-diabetic subjects of the atherogenic potential of postprandial lipaemia (the accumulation of RLPs throughout the day), and the appearance of smaller and denser LDL particles (35–37). Thus, it seems prudent to suggest that dietary recommendations for patients with Type 2 diabetes should take into account the predictable effects on lipoprotein metabolism.

**METABOLIC EFFECTS OF VARIATIONS IN THE KIND OF CARBOHYDRATE IN ISOCALORIC DIETS**

Evidence presented to this point has focused on the effects of variations in the relative amounts of dietary fat and CHO in isocaloric diets, and emphasised the
untoward effects of replacing SF with CHO versus PUFA/MUFA. Another possible approach to this issue would be to continue the practice of replacing SF with CHO, but doing this with the kind of CHO that would maintain the beneficial effects of low SF–high CHO diets on LDL cholesterol concentration, without leading to the harmful impact on glucose, insulin and lipoprotein metabolism that has been observed with CHO-enriched diets. In this context, two different, but somewhat related, approaches have been evaluated – emphasising either the glycaemic index of the high CHO diets, or their fibre content.

**VARIATIONS IN GLYCAEMIC INDEX**

Perhaps the best example of the ability of differences in glycaemic index of CHO-enriched diets to modify glycaemic control and lipoprotein metabolism in patients with Type 2 diabetes is the report by Jarvi and colleagues (38). These investigators compared the metabolic effects of two diets, each containing 55% of total calories as CHO, in 20 patients, consuming each of the test diets for 24 days. The glycaemic indices were calculated to vary from 57 to 83 as compared to white wheat bread. The two test diets were compared to each other, as well as to baseline values obtained on an uncontrolled diet. Of considerable interest was the observation that fasting plasma glucose, TG, and LDL cholesterol concentrations fell on both diets, supporting the general belief that essentially any prescribed diet is better than no diet plan. On the other hand, the degree of improvement in all of these variables was the same, irrespective of the difference in glycaemic index of the diet. Furthermore, the improvements in day-long plasma glucose and insulin concentration appeared to be of somewhat lesser magnitude than in the study in which the CHO intake was reduced, and unsaturated fat intake increased (20). Brand and associates (39) conducted a somewhat similar study in 16 patients with Type 2 diabetes, comparing the metabolic effects of two diets, differing in their glycaemic index from 77 to 91. However, both of the diets were relatively low in CHO (~45%). The fasting plasma glucose concentrations were similar after the high glycaemic index and low glycaemic index diets, as were the fasting concentrations of plasma insulin, TG, LDL cholesterol and HDL cholesterol. However, the total integrated postprandial plasma glucose response following the low glycaemic index breakfast and lunch was lower by 14% as compared to the high glycaemic meals.

Two other papers are often cited as showing the benefits of differences in the glycaemic index of CHO-rich foods: in one of these (40), only six patients with Type 2 diabetes were studied, and their data were not presented separately; while in the other paper the patients were only followed for two weeks (41).
VARIATIONS IN FIBRE CONTENT

In the most general sense, it is deemed useful for patients with Type 2 diabetes to increase their dietary fibre intake, particularly of soluble fibre. At the same time, the clinical utility of this intervention is not clear. For example, the recommendation of the American Diabetes Association is for patients to increase their dietary fibre intake to 20–35 g/day, without clear evidence of the importance of this amount of fibre on glycaemic control (42). Chandalia and associates (43) have pursued this issue further, and evaluated the metabolic effect of essentially doubling the daily fibre intake of 13 patients with Type 2 diabetes. In this study they compared two diets, each containing ~55% of daily calories as CHO, with one test diet having twice as much total fibre (50 vs 24 g/day), and threefold the soluble fibre content (25 vs 8 g/day). The patients were studied at the end of two randomly assigned diet periods of six weeks in duration. Even if it is assumed that patients will be willing to consume diets made up almost entirely of oranges (300 g/day), green peas (110 g/day), zucchini (195 g/day), papaya (250 g/day), peaches (300 g/day), fruit cocktail (200 g/day) and cherries (100 g/day), the improvement in day-long plasma glucose concentrations was no greater, and the decline in plasma TG concentration of lesser magnitude, than when the low fat–high CHO diet was compared to a diet in which MUFA was increased and CHO decreased (20).

When put into the context of results of earlier studies evaluating variations in fibre content, it appears that the clinical benefit is closely related to the increment in daily fibre intake. More specifically, increases in fibre intake of ~15 g/day did not lead to any significant metabolic changes (44,45), whereas dietary increases up to 23 g/day (46) and 30 g/day (47) resulted in a modest improvement in glycaemic control, without any decrease in plasma TG concentration. Thus, there appears to be no study in which the untoward metabolic effects of CHO-enriched diets have been shown to be attenuated to the degree seen when MUFA/PUFA fat is used to replace SF (20), and the only instance in which the effects were even comparable involved the daily intake of 50 g fibre (43).

SUMMARY AND SUGGESTIONS

The most useful dietary intervention, by far, is the initiation of a calorie-restricted diet in patients with Type 2 diabetes who are overweight: the beneficial effects of weight loss on both glucose and lipid abnormalities in patients with Type 2 diabetes are both unequivocal and dramatic. Although there may be something to be gained by avoiding the use of low fat–high CHO diets in this context, the major benefits will depend upon the decrease in total calories, not in variations in kind of macronutrient.
There is also substantial evidence in support of the view that SF should be decreased in patients with Type 2 diabetes. The major lifestyle variable regulating total and LDL cholesterol is the intake of SF, and the lower the SF intake, the lower the LDL cholesterol concentration.

Given the above considerations, the only unresolved question that remains in dietary recommendations for patients with Type 2 diabetes is what to substitute for SF. It is difficult to find any scientific justification for continuing to recommend the continued use of low SF–high CHO diets in patients with Type 2 diabetes. As discussed in this chapter, several alternative approaches are possible. Based on published data, it is suggested that replacing SF with MUFA/PUFA is the simplest and most effective way to maximally improve glycaemic control, and attenuate the lipoprotein abnormalities characteristic of patients with Type 2 diabetes. In this context a diet containing (as per cent of total calories) approximately 15% protein, 45% CHO and 40% fat, with SF intake < 10% of total calories, does not require a substantial change in eating habits, while effectively minimising abnormalities of CHO and lipid metabolism. However, there are alternative approaches that have as their goal the continued use of CHO-enriched diets, but minimising the untoward manifestation of such a diet by increasing fibre intake and/or decreasing the glycaemic index of CHO-rich foods. The view that these dietary manipulations do not seem to be as effective as simply increasing the MUFA/PUFA content does not mean that recommendations to increase dietary fibre intake should be ignored, or that efforts to decrease the glycaemic index of CHO-rich foods have no utility. On the other hand, there seems to be little justification for placing entire reliance on these more complicated, and seemingly less effective, solutions for overcoming the untoward metabolic effects of CHO-enriched diets.

REFERENCES


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