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SPECIAL ARTICLE

Evidence-based nutritional approaches to the treatment and prevention of diabetes mellitus

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Introduction

The Diabetes and Nutrition Study Group (DNSG) of the European Association for the Study of Diabetes (EASD) has issued a series of updated statements regarding the nutritional management of patients with diabetes (1-3). These have been based on the best available evidence derived from the scientific literature and the collective clinical experience of members of the group. Recently a more formal approach has been recommended for the development of evidence-based guidelines. This 2004 update has utilised the set of procedures suggested by the Agency for the Health Care Policy and Research and the Scottish Intercollegiate Guidelines Network (4). In brief this involves a formal search of the literature using an agreed set of descriptors and the relevant data banks (*eg* Medline, Embase). For each potential recommendation relevant research studies are assigned to 1 of 5 evidence classes (Table 1), according to type and quality of study (indicated by Roman numerals, in round brackets, after the reference number). A separate evidence class (IV) is reserved for statements from expert committees. The recommendations themselves are graded according to the strength of evidence. Grade A recommendations are based upon evidence classes Ia or Ib, grade B recommendations on evidence classes IIa, IIb or III, and Grade C on evidence class IV. Ideally evidence-based guidelines are based on clinical trials with fatal and non-fatal clinical endpoints. Where such information is not available recommendations are based on the agreed surrogate endpoints listed in Table 2. The criteria used for evaluating individual studies are shown in Table 3. The important role of regular physical activity as a component of lifestyle approaches to the treatment and prevention of diabetes is acknowledged but is not considered in this report. The report also does not include detailed issues relevant to the implementation of the nutritional recommendations in the different European countries, nor does it provide specific recommendations for diabetic patients in particular situations (*eg* pregnancy, critical illness). A recent Cochrane Collaboration [5 (Ia)] concluded that there were no high quality data regarding the efficacy of the dietary treatment of type 2 diabetes mellitus (T2DM). However this article included only those studies which continued for longer than 6 months. Many of these did indeed have design flaws or were characterised by poor compliance. However the DNSG considers that many appropriately designed studies of shorter duration are highly relevant in determining the potential of dietary modification to influence glycaemic control and risk of complications (Table 2).

Previous recommendations have dealt only briefly with the issue of reduction of diabetes risk. The publication of several recent randomised controlled trials has enabled firmer recommendations than were previously possible regarding the role of lifestyle change in the prevention of T2DM (6, 7).

Key words: Nutrition, diabetes, dietary fat, dietary carbohydrates, dietary protein, guidelines.

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TABLE 1
Evidence classes and grades of recommendations suggested by the Scottish Intercollegiate Guidelines Network (SIGN).

SIGN statements of evidence	SIGN grades of recommendations
Ia Evidence obtained from meta-analysis of randomised controlled trials. Ib Evidence obtained from at least one randomised controlled trial.	A Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation. (Evidence levels Ia, Ib)
IIa Evidence obtained from at least one well-designed controlled study without randomisation. IIb Evidence obtained from at least one other type of well-designed quasi-experimental study. III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.	B Requires the availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation. (Evidence levels IIa, IIb, III)
IV Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.	C Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level IV)

Energy balance and body weight

Recommendations

- For those who are overweight (BMI >25 Kg/m^2), caloric intake should be reduced and energy expenditure increased so that BMI moves towards the recommended range. Grade A
- Prevention of weight regain is an important aim once weight loss has been achieved (Grade A). Those who are overweight or obese and are unable to loose weight should be strongly encouraged to take measures to avoid further weight gain. Grade C
- For those with a body mass index (BMI) in the recommended range for adults (18.5-25 Kg/m^2), it is usually unnecessary to prescribe energy intake. Grade C
- The amount of physical activity needs to be taken into account when considering recommendations regarding total energy. Grade C
- Advice concerning the reduction of energy dense foods, in particular those high in saturated fat and free sugars, will usually help to achieve weight loss without the need for precise energy prescription. Grade C
- If these measures do not achieve the desired weight reduction, more precise advice may be required to achieve an energy deficit sufficient to loose weight at an appropriate rate. Grade C

Commentary

The mortality rates in diabetic individuals in the American Cancer Association Study [8 (III)] were dramatically increased when body mass index (BMI) exceeded 25 Kg/m^2. Data from the Nurses Health Study suggest a graded increase of risk as BMI rises above 22 Kg/m^2 which is exaggerated in those with diabetes [9 (III)]. Thus it seems reasonable to assume that the appropriate range for BMI in people with diabetes is similar to that (18.5-25 Kg/m^2) recommended for non-diabetic individuals [10-12 (Ia)]. Amongst the overweight, insulin sensitivity is decreased and there is a deterioration in most aspects of diabetes control [3 (IV), 13 (Ia)]. Even modest weight loss of under 10% body weight improves insulin sensitivity and glucose tolerance and reduces lipid levels and blood pressure [14, 15(Ib)]. The reduced life expectancy of overweight people with diabetes is improved in those who lose weight and may even be normalised without achieving a BMI under 25 Kg/m^2 [16, 17 (IIb)]. Maintenance of weight loss is an important goal of therapy (18, 19). Diabetic patients have a high proportion of intraabdominal fat and associated increased health risks related to insulin resistance and associated dyslipidaemia and hypertension (20). Weight loss may lead to greater improvements in cardiac risk factors in individuals with a high waist/hip ratio or waist circumference (21). Prevention and treatment of obesity have become a major public health issue, worldwide [22, 23 (IV)].

Overweight patients with type1 diabetes mellitus (TIDM) may also become insulin resistant and weight loss may lead to a reduction in insulin dose and improved glycaemic control (24, 25).

TABLE 2
Surrogate endpoints used in nutritional studies involving people with diabetes.

Glycaemia	Fasting plasma glucose Post-prandial plasma glucose Glycated haemoglobin (HbA_{1c})
Body composition	Adiposity Body weight Body mass index (BMI) Waist circumference
Lipoprotein profile	Total cholesterol LDL-cholesterol HDL-cholesterol Triglyceride
Blood pressure	
Insulin sensitivity	Fasting insulin Post-prandial insulin Insulin sensitivity index (ISI) Whole body glucose disposal
Renal function	Microalbuminuria Proteinuria Glomerular filtration rate

Protein

Recommendations

- In patients with no evidence of nephropathy, protein intake may provide 10-20% total energy. Grade B
- In patients with T1DM and evidence of established nephropathy, protein intakes should be at the lower end of the acceptable range (0.8 g/kg normal body weight/day). Grade A
- For patients with T1DM and incipient nephropathy (microalbuminuria) and those with T2DM and established or incipient nephropathy, there is insufficient evidence to make a firm recommendation regarding protein restriction. Grade C
- There is insufficient evidence to make recommendations about the preferred type of dietary protein. Grade C

Commentary

Protein intake in most western populations ranges between 10 and 20% total energy. In patients with both T1DM and T2DM protein contributes 15-20% total daily energy intake which corresponds to 1.3-2.0 g/Kg body weight. This represents an intake which exceeds requirements and is greater than the age-matched general population (26-29). Four cross sectional studies have not shown an association between protein intakes in the usual range and presence of microalbuminuria in T1DM [30-33 (III)]. However in T1DM patients with protein intake more than 20% total energy, the albumin excretion rate increases with increasing protein intake especially when hypertension and/or poor glycaemic control are also present [34 (III)]. Glomerular hyperfiltration is present in many T1DM patients at diagnosis but its significance as a risk factor for future diabetic nephropathy has not been established and furthermore in cross-sectional studies no correlation has been found between protein intake and glomerular filtration rate (GFR) (35, 36). Limited information is available concerning T2DM. Two cross sectional studies showed no association between protein intake and microalbuminuria or Albustix positive proteinuria [37, 38 (III)].

In T1DM patients with evidence of established renal disease several randomised controlled trials have confirmed the potential benefit of protein restriction. A metaanalysis of five randomised control trials (RCT's) in T1DM, of up to three years duration, showed that a low protein diet significantly slowed the development of albuminuria and the decrease of GFR [39 (Ia)]. In four RCT's, each one comprising from 15 to 35 T1DM patients with diabetic nephropathy and a follow-up ranging from 3 weeks to 3 years, a significant reduction in both albuminuria and the rate of GFR decrease has been documented (40-43). In the most recent randomised controlled trial involving 82 patients, the longest carried out thus far (4 years), the T1DM patients randomised to the low protein treatment (target intake: 0.6 g/Kg/day; achieved intake 0.89 g/Kg/day) had a strikingly improved outcome (relative risk for end stage renal disease or death, after adjustment for cardiovascular risk factors: 0.23) compared with those randomised to usual protein intake (1.2 g/Kg/day) [44 (Ib)]. Thus protein restriction is recommended for diabetic nephropathy in T1DM. However patients with diabetes, especially when poorly controlled or on haemodialysis, have increased protein turnover and their protein requirements may be greater than the recommended daily allowances (RDA) (45-48). Thus protein intake should not be reduced below 0.6 g/kg normal body weight/day because it may lead to malnutrition. Studies of protein restriction in patients with T1DM and incipient nephropathy (microalbuminuria) have shown inconsistent results. Small (5-7 μg/min), but significant decreases in albumin excretion rate (AER) were observed on low protein diets in two studies but no relation was found in another (49-51). In RCT's of a few

TABLE 3
Criteria for evaluating individual studies relevant to recommendations for people with diabetes.

• Surrogate endpoints must be appropriate (see Table 2) if fatal or clinical endpoint data not available
• Type of diabetes and treatment must be specified
• Subjects must be representative of relevant patient group
• In experimental studies, subjects should be randomised to control or experimental diets
• Experimental studies will usually involve parallel or cross over design, depending upon endpoint being investigated
• Nutrition intervention must be clearly specified and methods of assessing compliance stated when studies involve free-living individuals
• Duration must be appropriate to the endpoint under consideration. In general studies carried out for weeks or months are preferable to acute meal experiments
• Epidemiological studies (which will usually be cohort or comparative studies) must utilise validated dietary instruments and in the case of cohort studies should preferably be based on more than a single period of assessment
• Statistical methods must be clearly described and appropriate
• Methods for identifying appropriate studies (*eg* descriptors and search engines) must be specified

weeks duration, low protein diets reduced GFR in hyperfiltering patients with no effect on microalbuminuria (52, 53). In two RCT's in T2DM patients with microalbuminuria, proteinuria or overt nephropathy, protein restriction had no effect on albuminuria or GFR (54, 55), while in a randomised crossover study of 12 T2DM patients with microalbuminuria, a decrease of both GFR and microalbuminuria was observed (56). Although well planned and conducted, the above studies were of short duration and used surrogate endpoints (albuminuria, hyperfiltration) rather than end stage renal disease or death and thus their results cannot support valid recommendations.

Several studies have examined the source and quality of protein on renal function. In T1DM patients, a vegetable protein diet decreased GFR in one study (57) and albumin excretion rate in another (58). However in a RCT in T2DM patients with microalbuminuria, 6 weeks vegetable protein diet compared with animal protein diet had no effect on AER (59). In T1DM patients substitution of half of the protein intake with soy protein resulted in decrease of the urinary albumin excretion in one study (60), but showed no effect in another (61). In a case control study in T1DM patients, high fish protein intake was associated with a decreased risk of microalbuminuria (62). In randomised controlled crossover trials in T1DM patients, substitution of red meat with chicken for 4 weeks reduced GFR to the same extent as a low protein diet in hyperfiltering patients and in addition reduced the AER in patients with microalbuminuria (63, 64). However given the short duration of these studies and lack of clinical endpoints no recommendations are offered at present regarding nature of dietary protein.

Dietary fat

Recommendations

– Saturated and trans-unsaturated fatty acids should provide under 10% total daily energy. A lower intake (< 8% total energy) may be beneficial if LDL-cholesterol is elevated. Grade A
– Oils rich in monounsaturated fatty acids (MUFA) are useful fat sources and depending upon individual preferences MUFA may provide 10 to 20% total energy, provided total fat intake does not contribute more than 35% total energy. Grade B
– Polyunsaturated fatty acids (PUFA) should not exceed 10% total daily energy. Grade C
– Total fat intake should not exceed 35% total energy. Grade C
– For those who are overweight, fat intake below 30% may facilitate weight loss. Grade C
– Consumption of two to three servings of fish (preferably oily fish) each week and plant sources of n-3 fatty acids (*eg* rapeseed oil, soybean oil, nuts and some green leafy vegetables) will help to ensure an adequate intake of n-3 fatty acids. Grade B

– Cholesterol intake should not exceed 300 mg/day and be further reduced if LDL-cholesterol is raised. Grade A

Commentary

The recommendations on dietary fat intake in diabetes mellitus are mainly based on studies in non-diabetic subjects, including controlled dietary studies and epidemiological studies. There are no controlled dietary intervention studies in subjects with diabetes with sufficient power to demonstrate effects of dietary fat on cardiovascular or other disease endpoints, and very limited data from observational studies on the relationships between dietary fat intake and disease or death in subjects with diabetes. There are a number of studies comparing diets with a higher fat content (mainly due to an increased content of MUFA) with those containing a higher proportion of carbohydrates, and a number of controlled studies investigating the effect of the type of dietary fat in people with diabetes. Such studies which compare the effects of modifying fat intake on disease risk factors or surrogate endpoints (*eg* serum lipid or lipoprotein concentrations, adiposity, glycaemia, insulin sensitivity) complement the data from studies in non-diabetic individuals.

It is deemed to be appropriate to consider studies in "healthy" non-diabetic subjects when developing nutritional recommendations for people with T2DM as the delineation between healthy subjects with obesity and/or traits of the metabolic syndrome and T2DM is based on an arbitrarily chosen limit for blood glucose. All evidence indicates that the development of diabetes is a process which occurs over years or decades including a gradual impairment of insulin sensitivity and development of associated metabolic derangements. The risk for cardiovascular complications is high prior to the diagnosis of diabetes and the same risk factors are present before as after the diagnosis, although the importance of the risk factors is even more pronounced in diabetic patients. All available data suggest that the same dietary changes, which are documented to reduce the risk for cardiovascular disease in the non-diabetic population, are even more relevant in the diabetic population, as the risk factors are associated with an even higher risk in subjects with diabetes. Although the pathogenesis of T1DM differs from that of T2DM, most of the risk factors for cardiovascular disease shown to operate in healthy individuals and T2DM also appear to be relevant to T1DM. Thus broadly similar recommendations are given for T1DM and T2DM.

The major recommendation offered concerning total fat is that intake should not exceed 35% total energy due to the risk of increased body weight on high fat diets [65(Ia)]. In addition on a high total fat intake there may be an adverse effect on insulin sensitivity regardless of the nature of dietary fat, as suggested in a study of healthy individuals [66 (Ib)]. For most individuals a wide range of intakes is acceptable and will depend upon individual preferences and characteristics. For those who are overweight a total fat intake below 30% total energy may facilitate weight loss [3 (IV)].

Saturated fatty acids

There is convincing evidence from meta analyses of controlled trials in those without diabetes [67-69 (Ia)] that an exchange of dietary saturated fatty acids with unsaturated fatty acids (other than trans fatty acids – see below) or carbohydrates will reduce LDL-cholesterol. That an exchange of saturated fatty acids by unsaturated fatty acids will lower LDL-cholesterol has support also in a few controlled studies in subjects with diabetes [70 (Ib)] and glucose intolerance [71 (Ib)]. Recently, three controlled dietary intervention studies performed under isoenergetic conditions in healthy [72, 66(Ib)] and obese (some of them also with diabetes) subjects [73(Ib)] indicate that an exchange of saturated fatty acids with unsaturated fatty acids in the diet will significantly improve insulin sensitivity. Although little is known about the metabolic effects of the different saturated fatty acids in diabetes it has been clearly demonstrated that stearic acid, in contrast to other saturated fatty acids (lauric, myristic and palmitic) does not increase cholesterol (74). Furthermore it seems likely that those with diabetes, as is the case in those who do not have the condition, will show a greater increase in total and LDL-cholesterol when myristic and palmitic acids are compared with lauric acid (75).

Saturated fatty acids may also induce a detrimental postprandial lipid profile compared with monounsaturated fat in both normal (76) and diabetic [77 (Ib)] subjects. Saturated fatty acids and trans fatty acids induced an increase in postprandial insulinaemia in obese subjects with T2DM [78 (Ib)]. In two prospective studies of diabetic subjects [79, 80 (III)], the proportion of saturated fatty acids in the diet (or P/S-ratio) was significantly associated with the incidence of new coronary heart disease events. Several prospective studies [81-83 (III)] indicate that a high proportion of saturated fatty acids in the plasma lipid esters, compatible with a high dietary intake of saturated fatty acids, are related to an increased risk of developing T2DM. In observational studies [84-89 (III)] a clear association between saturated fat in the diet and diabetes development is, however, not found after adjustment for BMI.

Trans unsaturated fatty acids

A metaanalysis [90 (Ia)] and controlled dietary studies in those without diabetes demonstrate adverse effects by dietary trans fatty acids on LDL-cholesterol, HDL-cholesterol, LDL size and the Lp(a) levels. Trans fatty acids induced an increase in post-prandial insulinaemia in obese subjects with T2DM [78 (Ib)]. Some observational studies suggest that a high intake of trans fatty acids may increase the risk of developing T2DM [87 (III)]. However, the content of trans fatty acids of the diets in the observational studies are not well characterized.

Monounsaturated fatty acids

Substituting monounsaturated for saturated fatty acids has beneficial effects on serum lipid levels and on lipoprotein concentration and composition [67-69(Ia)] and also on insulin sensitivity in glucose intolerant (71) or healthy subjects provided that the total fat intake is not too high [66 (Ib)]. There are also controlled studies indicating that substituting a certain amount of monounsaturated fat (MUFA) for carbohydrates may confer some benefit regarding serum lipid levels, if the source of carbohydrates is mainly starch rich foods with a low content of dietary fibre and high glycaemic index [91 (Ia)]. This may mainly relate to normal weight diabetic subjects, possibly especially T1DM. There is, on the other hand, no convincing evidence that a shift from a diet high in carbohydrate rich foods with a high fibre content and low glycaemic index to a diet containing more MUFA will improve metabolic control in diabetes (72, 76, 92-95). Such a change might rather increase the risk of weight gain due to increased energy intake. Compliance with a low fat diet containing a high proportion of high-fibre, low glycaemic index carbohydrate may promote weight loss and metabolic improvement in subjects with T1DM (96), the metabolic syndrome (97) and glucose intolerance (98). In some intervention studies in T2DM a high intake of MUFA seems to be associated with a lower blood pressure than a diet with a higher proportion of PUFA (99) or carbohydrates (100). Oils rich in MUFA are thus useful fat sources and, depending upon metabolic features and individual preferences, MUFA may provide 10-20% total energy provided that fat intake does not exceed 35% total energy.

n-6 polyunsaturated fatty acids

Substituting PUFA for saturated fatty acids has beneficial effects on serum lipid levels and lipoprotein concentration and composition [67- 69 (Ia)] and insulin sensitivity [73 (Ib)]. With regard to both blood glucose and blood lipid levels in T1DM and T2DM, there appears to be little difference when sources of mono- and PUFA are compared (101). Prospective studies indicate that a high proportion of polyunsaturated vegetable (linoleic acid rich) fat in the diet [84, 85, 88 (III)], or a high proportion of linoleic acid in the plasma lipid esters [81-83 (III)] indicating a high dietary intake, is associated with a reduced risk of developing T2DM. A high P/S ratio has been associated with a low risk of fatal cardiovascular events in people with diabetes [79, 80 (III)]. However it has been suggested that the intake of linoleic acid in the diabetic diet be limited to less than 10% of the energy intake, because of the possibility that higher intakes might increase the risk of lipid peroxidation in the body. Direct evidence for such a recommendation [3 (IV)] is lacking, but it is offered as practical advice in the interests of safety. Furthermore a higher intake is unrealistic given the much lower intakes of PUFA in most European countries (102).

n-3 fatty acids

Observational evidence supports the recommendation that intake of fish and intake of n-3 fatty acids from plant sources (alpha linolenic acid) may reduce the risk of cardiac death and stroke [103, 104 (III)]. Supplementation with n-3 fatty acids in diabetes reduces serum triglyceride levels, but may simultaneously be associated with a moderate increase in LDL-cholesterol [105 (Ia)]. It has been suggested that supplementation with long-chain n-3 fatty acids may increase blood glucose levels, but recent meta analyses [106, 107 (Ia)] indicate that this effect is negligible. There are no published controlled studies to suggest that supplementation with n-3 fatty acids in humans will improve insulin sensitivity. Women with diabetes and a high regular fish consumption have a lower incidence of coronary heart disease and a decreased mortality rate compared with those with a lower intake [108 (III)]. Although current evidence supports the recommendations concerning the dietary intake of fish and n-3 fatty acids from plant sources, there is at present no consensus on the use of supplements containing n-3 fatty acids in diabetes (see section on Supplements). Furthermore there are insufficient data to make a precise recommendation regarding the optimal ratio of n-3/n-6 fatty acids. However an increased intake of dietary n-3 fatty acids is encouraged in line with current recommendations for the general population.

Dietary cholesterol

Data in non-diabetic subjects [109 (Ia)] and also in T1DM [110 (Ib), 111 (III)] support the recommendation to restrict the cholesterol intake in the diet, as the cholesterol levels in plasma increase with increasing intakes of dietary

cholesterol. In a prospective study of women with diabetes a high intake of cholesterol was related to an increased risk of cardiovascular disease [80 (III)]. In the EURODIAB Complications Study increased intakes of total fat, saturated fat and cholesterol were significantly related to higher prevalences of cardiovascular disease. These associations were, however, no longer significant after adjustment for dietary fibre intake for which an independent association with the serum cholesterol pattern and cardiovascular diseases (CVD) has been demonstrated [111 (III)].

Carbohydrate

Recommendations

- Carbohydrate intake may range between 45% and 60% total energy. Grade C
- Metabolic characteristics suggest the most appropriate intakes within this range for individuals with T1DM and T2DM. Grade A
- Vegetables, legumes, fruits and wholegrain cereals should be incorporated into the diet of people with T1DM and T2DM. When carbohydrate intake is at the upper end of the recommended range it is particularly important to emphasise foods rich in dietary fibre and with a low glycaemic index. (See recommendations on fibre, glycaemic index and micronutrients). Grade A
- There is no justification for the recommendation of very low carbohydrate diets in persons with diabetes (see recommendations on fat). Grade B
- Carbohydrate quantities, sources and distribution throughout the day should be selected to facilitate near-normal long-term glycaemic control (HbA1c-levels). In those treated with insulin or oral hypoglycaemic agents timing and dosage of the medication should match quantity and nature of carbohydrate. Grade C

Commentary

The recommended range of carbohydrate (CHO) intake (45-60% total energy) is based on the limits for total fat and protein intakes (see recommendations on protein and fat intake in this paper), [3, 28, 112-113 (IV)]. A meta-analysis [91 (Ia)] compared the effects of high carbohydrate diets (49-60% CHO, 20-32% fat, 7-13% MUFA) with diets higher in monounsaturated fat and lower in carbohydrate (36-40% CHO, 37-50% fat, 22-33% MUFA) on serum lipids and glycaemic control in persons with T2DM. Several of the studies involved high carbohydrate diets which were rich in starchy foods rather than fibre-rich low glycaemic index foods. Only randomised crossover trials [100, 114-121 (Ib)] using iso-energetic, weight-maintaining diets were considered. The trials involved 8 to 42 persons with T2DM (in- or outpatients on diet alone, different oral agents and insulin treatment); study length was 2-6 weeks.

Compared with a high carbohydrate diet, a high monounsaturated fat, lower carbohydrate diet resulted on average in a 19% reduction of serum triglycerides [significant in 5 studies, not significant in 3 studies (117, 120, 121), no change in 1 study (100)], a 4% increase in HDL-cholesterol [increase in 5 studies, no change in 4 studies (100, 118, 120, 121)], a 3% decrease in total cholesterol [decrease in 6 studies, no change in 1 study (121), increase in 2 studies (115, 117] and no net-change in LDL-cholesterol. The net-lowering of fasting blood glucose concentrations was -4 mg/dL with the high monounsaturated fat diet ($p<0.05$); no change was seen in fasting insulin concentrations. Effects on mean preprandial plasma glucose was either significantly reduced (114) or unchanged (116). Five studies reported a significant reduction of post-prandial blood glucose concentrations in the patients with a high MUFA lower carbohydrate diet, but none of the studies showed a significant reduction in HbA_{1c} or fructosamine compared with those on a high carbohydrate diet. Thus the long-term effect on glycaemic control was comparable on both the moderate to high carbohydrate diet (49-60%) and the low to moderate carbohydrate diet (37-50%) respectively. This meta-analysis shows that a wide range of carbohydrate intakes is compatible with overall comparable glycaemic control in persons with T2DM [91 (Ia)]. The untoward effects of relatively high starch intakes on fasting triglycerides and possibly on postprandial glucose concentrations observed in some of the studies included in this metaanalysis can be avoided if the carbohydrate-containing foods are rich in dietary fibre and/or have a low glycaemic index (122, and see sections on fibre and glycaemic index). The range of recommended carbohydrate intake is also suitable in T1DM [123 (Ib)], particularly when fruits, vegetables and whole grain cereal foods are a part of the diet [124 (III)].

Some persons with T2DM may show improved lipid levels when carbohydrate intake is at the lower end of the recommended range [114, 115, 116, 118, 119, 121, (Ib)] so that for those with persistently raised triglyceride levels a trial of intake at the lower end of the recommended intake range may be appropriate. This may also be tried in T1DM persons with hypertriglyceridemia [125 (Ib)].

There is no long-term evidence of benefit of low or very low carbohydrate diets. Such diets would be undesirably high in fat and could increase body weight and decrease

insulin sensitivity [66 (Ib), 96 (III), 126 (III)]. Low carbohydrate, high fat diets have not been shown to achieve long-term weight loss [127, 128 (Ib)]. Given the high percentage of saturated fatty acids (14% of total energy and more) in the diets of persons with diabetes throughout the European countries at present [28, 111(III), 112] such diets may induce raised levels of total and LDL-cholesterol (see recommendations on fat intake). In addition, there is no evidence on which to base a recommendation that protein intake should be more than 20% of total energy in order to reduce carbohydrate. Many foods high in protein are also high in saturated fat, and it seems inappropriate to promote a food pattern characterised by a high fat intake to persons with diabetes in European countries where high intakes of total and saturated fat predominate [29, 96, 102, 129, 130, (III)].

Besides ensuring desirable nutrient intakes in those with T1DM and T2DM it should be noted that appropriate quantities, sources and distribution of carbohydrate-containing foods can facilitate near-normal long-term metabolic control [124, 131-134 (III)]. The selection of carbohydrate quantities and sources as well as the distribution of these foods throughout the day may be guided by blood-glucose self-monitoring of the person with diabetes [3, 135, 136 (IV)]. Those who need oral hypoglycaemic agents in addition to nutritional therapy should be aware of the mode of action of their medication and the optimal timing of the intakes of tablets, meals and snacks. Persons with diabetes who are treated with insulin should be informed about the duration of action of their injected insulins to optimise the match between quantity and nature of carbohydrate and insulin dosage [113 (IV), 137 (III), 138, 139 (IV)]. For most patients those with T1DM and those with T2DM on insulin or oral agents it is usually possible to adjust therapy according to amount and type of carbohydrate so that it is possible for patients to include a variety of carbohydrate sources in their diet without deterioration in glycaemic control [124 (III)]. When choosing carbohydrate containing foods their effect on insulin sensitivity, serum lipids and energy balance should be considered [96, 97, 140, 141 (III)]. The effects of fibre, glycaemic index and content of sugars on these important predictors of health outcome are discussed in more detail in the sections which follow. However, it is relevant to note here that regular consumption of vegetables, legumes, intact fruits and wholegrain cereals should be part of the diet in people with T1DM and T2DM as these foods help to ensure adequate fibre and micronutrient intakes, do not promote hypertriglyceridaemia and may facilitate weight reduction by promoting satiety [142, 143 (III)]. Thus these foods should be especially emphasized for those who are overweight or obese, those with the metabolic syndrome and those who have a preference for relatively high intake of carbohydrate.

Dietary fibre

Recommendations

- People with T1DM and T2DM should be encouraged to consume naturally occurring foods that are rich in dietary fibre. Grade A
- Dietary fibre intake should ideally be more than 40 g/day (or 20 g/1000 Kcal/day), about half of which should be soluble. Beneficial effects are also obtained with lower, and for some, more acceptable amounts. Grade A
- Daily consumption of at least 5 servings of fibre-rich vegetables or fruit and at least 4 servings of legumes per week can help to provide minimum requirements for fibre intake. Grade C
- Cereal-based foods should, whenever possible, be wholegrain and high in fibre. Grade B

Commentary

In the 1980's short term randomised controlled studies (involving cross-over designs) were conducted in patients with T1DM and T2DM using two diets comprising naturally occurring foods but differing in the amounts of dietary fibre (16 g/day compared with 54 g/day, mainly soluble fibre). Average daily blood glucose levels were reduced by 10-15% and postprandial levels by 25% on the high fibre diet [144, 145 (Ib)]. Also during the 1980's other controlled trials in T1DM and T2DM compared the effects of high carbohydrate-high fibre diets (more than 50 g/day, at least 50% soluble fibre) with the then-conventional lower carbohydrate-low fibre diets. Again, the high carbohydrate-high fibre diets were associated with improved glycaemic control, including lower levels of HbA_{1c} [146, 147 (Ib)]. Since other studies carried out in the same time period showed no benefit or a detrimental effect on glycaemic control when a low carbohydrate diet was compared with a high carbohydrate-high starch-low fibre diet [148, 149, 150 (Ib)], the beneficial effect is attributed to the high fibre intake [151, 152]. Two recent randomised controlled trials of longer duration have been carried out in T1DM (parallel design) and T2DM (cross-over design). Sixty patients with T1DM were randomised to 2 diets which differed only with regard to amount of dietary fibre and followed as outpatients for 6 months. The high fibre diet was associated with a reduced number of hypo-

glycaemic events, improved mean daily and postprandial glucose levels, and in the 83% of compliant patients a reduction in HbA_{1c} [153 (Ib)]. Although 50 g fibre/day was recommended, in practice only 40 g/day (half of the soluble type, from legumes, fruit and vegetables) was consumed. The other study performed in patients with T2DM [154 (Ib)] shows very similar results: 10% reduction in the average blood glucose, 25% in postprandial blood glucose and also a significant decrease in daily insulin levels. Thus, the ideal amount of dietary fibre appears to be 40 g/day (about 20 g/1000 Kcal/day) or more, half of which is soluble. However beneficial effects are also obtained with lower, and for some, more acceptable amounts.

The few studies showing no effect of high fibre diets on blood glucose control utilised diets rich in insoluble fibre (155). Cross sectional epidemiological data based on the EURODIAB Complications Study which included over 2000 patients with T1DM in 31 European centres showed an inverse association between dietary fibre intake and HbA_{1c} which was independent of possible confounders. Risk of ketoacidosis was reduced in association with a high fibre intake [131 (III)].

Most of the randomised trials referred to above have also studied the effects of dietary fibre on lipids and lipoproteins. Several [143, 145, 146, 154 (Ib)], though not all (153), of the studies involving diets rich in soluble fibre have found lower levels of total and LDL-cholesterol on the high fibre diets. None have shown a deleterious effect. Cross sectional data from the EURODIAB Complications Study show an inverse association between dietary fibre and LDL-cholesterol (in men only) and a positive association between fibre intake and HDL-cholesterol (in both men and women) [156 (III)].

Dietary fibre intake has been inversely and significantly related to cardiovascular disease in a cross sectional study in T1DM [156 (III)] and in several prospective studies of non-diabetic individuals [157-160 (III)]. Dietary fibre is also associated with lower levels of BMI in T1DM (96) and prospectively in those without diabetes (161) and with higher insulin sensitivity in the non-diabetic population (162).

Glycaemic index

Recommendations

– Carbohydrate-rich, low glycaemic index foods are suitable as carbohydrate-rich choices provided other attributes of the foods are appropriate. Grade A

Commentary

The glycaemic index (GI) is defined as the incremental blood glucose area following ingestion of 25-50 g available carbohydrates expressed as a percentage of the corresponding area following ingestion of carbohydrate from a reference food (glucose or white bread). Both type and amount of carbohydrate influence the glycaemic response [133, 141 (III)]. Whether or not the cellular structure remains intact is also relevant (163). Thus in practice the actual carbohydrate load from a normal portion size varies considerably. In order to address this problem, the concept of glycaemic load (GL) was introduced. GL, calculated as the amount of carbohydrate in one serving multiplied by the GI of the food, allows comparisons of the likely glycaemic effects of realistic portions of different foods [164 (IV)]. There is, however, considerable variability within and between subjects in glucose response to the same glycaemic load on different days (165, 166).

A number of controlled dietary intervention studies comparing diets containing high GI and low GI foods have been undertaken with varying results [93, 153, 167-175 (Ib)]. A recent meta-analysis [176 (Ia)] reported an improvement of the mean blood glucose control, with an average reduction of HbA_{1c} by 0.43% on a low, compared with a high GI diet in diabetic subjects. Although the effect of a low GI diet on glycaemic control is smaller than that observed with other dietary interventions, it should not be considered trivial since it was achieved over and above that of other dietary changes such as reduction of total carbohydrates, increased fibre intake or body weight reduction [177, 178 (IV)]. It is similar to that achieved by some glucose-lowering medications and consistent with findings from the Eurodiab Complications Study, which showed that the GI of the diet was positively and independently related to HbA_{1c} levels [132 (III)].

When reviewing the results of intervention studies, there is no uniform evidence for beneficial effects on blood lipid levels by low GI diets. However in one well controlled study in T2DM subjects [174 (Ib)] there was a significant reduction of LDL-cholesterol, and of PAI-1 on the low GI diet indicating an improvement compared with a high GI diet. Another more recent 4- week study has shown additionally the potential for a low GI diet to enhance glucose utilisation and improve the capacity for fibronolysis in T2DM [179 (Ib)].

The GI concept should in principle be used to classify carbohydrate-rich foods, and is only meaningful when comparing foods within a comparable food group, *eg* breads, fruits, different types of pasta or rice. GI values should not

be used in isolation, but interpreted in relation to other relevant food characteristics, *eg* energy content, content of other macronutrients, available carbohydrates, and dietary fibre [132 (III), 180 (IV)]. For example, some foods may be rich in saturated fat and free sugars and have a low GI. Provided all qualities of the food are taken into account, available evidence supports the suggestion that the GI content of food may be a helpful additional indicator regarding the appropriate carbohydrate-containing foods for inclusion in the diet. Despite this qualified support for the use of the GI concept as it relates to natural foods, it should be noted that most studies showing beneficial effects have been relatively short term.

Sucrose and other free sugars[1]

Recommendation

– If desired and if blood glucose levels are satisfactory, moderate intakes of free sugars (up to 50 g/day) may be incorporated within the diet of individuals with T1DM and T2DM. Grade A
– As for the general population intake of total free sugars should not exceed 10% total energy. More restrictive advice concerning free sugars may be useful for those needing to lose weight. Grade C

Commentary

In the 1980's several randomised controlled trials with crossover designs demonstrated no adverse effects on glycaemic control, lipids and lipoproteins when diets containing small amounts of sucrose (usually around 50 g) were compared with virtually sucrose-free diets in T1DM and T2DM [181-183 (Ib), 184]. These studies led to a more liberal approach than that adopted previously when sucrose restriction as far as possible was advised.

While there is clear evidence for the acceptability of moderate intakes of sucrose for most people with diabetes, there are fewer data from which to derive acceptable upper limits. It is necessary to extrapolate recommendations from studies of healthy individuals, overweight and obese subjects and those with the metabolic syndrome using lipid levels and energy balance as surrogate endpoints (185). In non-diabetic individuals [186 (Ib)] and those with the metabolic syndrome [97 (III)] diets high in sugars have been associated with hypertriglyceridemia when compared, in randomised controlled trials, with diets higher in starches and non-starch polysaccharides. In subjects with the metabolic syndrome the high starch, relatively high fibre diet was associated with weight loss when compared with a diet high in sugars [97 (III)].

Diets including high sucrose containing drinks have been shown to be associated with an increase in energy intake, body weight, fat mass and plasma lipids when compared with diets in which the drinks were artificially sweetened [187 (Ib)]. It appears that humans may have a weak innate ability to recognise sweet drinks and to appropriately down regulate the consumption of such foods in order to maintain energy balance. The resultant overcompensation of energy, regardless of sources, without concomitant increase in energy expenditure will lead to weight gain, reduced insulin sensitivity and associated abnormalities including dyslipidaemia and hypertension. Thus it is clear that excessive consumption of free sugars may indirectly contribute to disturbances which predispose to adverse clinical outcomes. However the recommendation regarding a maximum intake of 10% total energy is somewhat arbitrary and is derived from recommendations of other expert consultations including the Expert Consultation on Diet, Nutrition and the Prevention of Chronic Diseases [23(IV)].

In healthy subjects, high intakes of fructose (17% total energy) are associated with hypertriglyceridaemia [188 (Ib)]. However a moderate intake of fructose (up to 30 g/day) appears to have no deleterious effects in terms of plasma insulin and lipids when included in the diet of people with T2DM [189 (Ib)].

Antioxidant nutrients, vitamins, minerals and trace elements

Recommendation

– Foods naturally rich in dietary antioxidants (tocopherols, carotenoids, vitamin C, flavonoids, polyphenols, phytic acid), trace elements and other vitamins should be encouraged. Grade C
– The daily consumption of a range of vegetables and fruit is encouraged since these are rich sources of many vitamins and antioxidant nutrients. Grade C
– Regular intakes of wholegrain breads, cereals and oily fish facilitate recommended intakes of the remaining water and fat soluble vitamins. Grade C

[1]Free sugars are defined as: all monosaccharides and disaccharides added to foods by the manufacturer, cook or consumer, plus sugars naturally present in honey, syrups and fruit juices.

– As in the general population people with diabetes should be advised to restrict salt intake to under 6 g/day. A further restriction may be appropriate for those with elevated blood pressure. Grade A

Commentary

There is a considerable body of evidence from prospective studies in non-diabetic individuals to suggest that a range of antioxidant nutrients and vitamins, and foods rich in them: fruits, vegetables, nuts and berries, protect against cardiovascular disease [190-200 (III)]. Furthermore, regular consumption of wholegrain breads, cereals and oily fish facilitate appropriate intakes of the remaining vitamins [157, 201-204 (III)]. Short-term studies which involve the consumption of foods rich in these nutrients and supplemention with a range of synthetic micronutrients confirm in diabetic and non-diabetic individuals that markers of oxidative stress can be favourably influenced by substantial intakes (205-208). However studies with clinical endpoints (principally carried out in people who do not have diabetes) have thus far not demonstrated beneficial effects. Thus in people with diabetes it seems appropriate to recommend foods rich in such nutrients, but not supplements (209).

Moderate dietary sodium restriction has been shown to produce substantial reduction in systolic blood pressure in mildly hypertensive patients with T2DM [210 (Ib)] and to enhance the blood pressure lowering effect of other dietary manipulations (low fat dairy products, fruits and vegetables) in non-diabetic individuals [211-213 (Ib)].

Between 20 and 25% of people with diabetes have been reported to have low levels of circulating magnesium, especially those with T1DM and poor glycaemic control (214, 215) and those with reduced absorption in autonomic neuropathy or associated autoimmune disease (216). Magnesium depletion of muscle (217) and bone (218) has been observed and linked to retinopathy (219) and polyneuropathy (220). A role for magnesium supplementation in halting the progression of neuropathy and retinopathy, and possibly for all patients with poorly controlled T1DM, has been suggested (221). Magnesium-rich foods may also be considered in this context. However firm recommendations must await confirmation of these observations.

Low levels of zinc and chromium and high levels of copper have been reported in people with diabetes, but there is no evidence to suggest that such observations should influence nutritional recommendations.

Alcohol

Recommendations

– Moderate use of alcohol (up to 10 g/day for women and 20 g/day for men) is acceptable for those with diabetes who choose to drink alcohol. Grade B
– When alcohol is taken by those on insulin it is most appropriately consumed with a meal including carbohydrate-containing food because of the risk of potentially profound and prolonged hypoglycaemia. Grade B
– Alcohol should be limited by those who are overweight, hypertensive or hypertriglyceridaemic. Abstention is advised for women during pregnancy and those with a history of pancreatitis or alcohol abuse, appreciable hypertriglyceridaemia, advanced neuropathy, and erectile dysfunction. Grade C

Commentary

A high proportion of adults in the general population, and many people with diabetes, drink alcoholic beverages. Alcohol may have both untoward and beneficial effects. Many ecological, case control and cohort studies based on people who do not have diabetes suggest that moderate intake of a range of alcoholic drinks is linked to reduced risk of coronary heart disease [222 (IIb)] and stroke [223 (III)]. A limited amount of information based on four studies in individuals with T2DM confirms this association. The benefit appears to be principally derived from the alcohol rather than other components of the various types of beverages [224 (III)]. Moderate intakes of alcohol may confer benefit by elevating levels of high density lipoprotein, reducing coagulability and decreasing lipid oxidation through antioxidant nutrients. Regular but moderate consumption of alcohol (at least 3 to 4 days/week) has a more beneficial effect than drinking occasionally higher quantities [225 (III)]. Neither the timing of alcohol intake in relation to meals nor the type of beverage consumed alters the expected benefits [225 (III), 226 (IIb)].

Alcohol may be an important energy source to an extent that is relevant in those who are overweight. Furthermore a high alcohol consumption is associated with a greater waist-hip ratio independently of body mass index [227 (III)]. On the other hand, moderate amounts of alcohol might be associated with improved insulin sensitivity [228 (Ib), 229 (IIb), 230 (III)]. Alcohol can also be associated with raised levels of blood pressure, increased triglycerides and an increased risk of hypoglycaemia [231, 232 (III)]. There are no conclusive data regarding an appropriate upper limit of alcohol intake for people with diabetes. Thus the recommendation is

based upon that suggested for the general population (233).

Abstention from alcohol should be advised for women during pregnancy and those with a history of pancreatitis or alcohol abuse, appreciable hypertriglyceridaemia, advanced neuropathy and erectile dysfunction. Recommendations regarding alcohol for people with diabetes must therefore depend upon the characteristics of the individual patient, and the socioeconomic consequences of overconsumption should not be forgotten. There is insufficient information to encourage patients who do not drink alcohol to start.

The recommendation regarding the need to consume carbohydrate when alcohol is taken is made because of the potential serious consequences of severe alcohol-induced hypoglycaemia. While a modest amount of alcohol can usually be taken without directly causing hypoglycaemia, the risk increases with the quantity consumed [3 (IV)].

Prevention of diabetes

Recommendations

- Avoidance of overweight and regular physical activity provide a means of reducing the risk of developing T2DM. Grade A
- Weight reduction and maintenance of weight loss in overweight individuals is a critical component of the lifestyle modification programme which may be expected to reduce the risk of developing T2DM. Grade A
- Appropriate macronutrient composition for diets aimed at reducing risk of T2DM is as follows: total fat intake <30% energy intake, saturated fat intake <10% energy intake, fibre intake >15 g/1000 kcal. Grade A

Commentary

An impressive series of longitudinal studies show a reduced risk of T2DM in those who are not overweight, have a high intake of dietary fibre (especially cereal fibre) and low GI foods or consume relatively little saturated fat and partake of regular activity [85, 234-243 (III)]. A high consumption of sugar sweetened beverages has been associated with weight gain and an increased risk of T2DM in women [244 (III)]. A well-designed randomised controlled study has demonstrated enhanced insulin sensitivity when saturated fatty acids are replaced by unsaturated vegetable oils in the context of a diet containing moderate amounts of total fat, *ie* less than 37% total energy [66 (Ib)]. Three randomised controlled trials conducted in China, Finland and the United States in individuals with impaired glucose tolerance (IGT) have shown a nearly 60% reduction of progression from IGT to T2DM over an approximately 3 $^{1}/_{2}$ year period in association with modest weight loss [245, 6, 7 (Ib)]. The benefit appears to have been sustained in the Finnish study [246 (Ib)]. In two of the three studies (6,7) weight loss was achieved by a combination of diet and exercise, the recommended diet being reduced in total and saturated fat and high in dietary fibre. In the third (245) randomisation was to clinics where participants received advice to increase level of activity, to modify their diet, to alter both diet and exercise, or no specific lifestyle advice. Comparable benefit was seen in each of the intervention groups. The benefit appears to be principally explained by weight loss and physical activity [247 (IB)]. Thus for those who are overweight or obese, especially if there is a strong family history of T2DM or if they have impaired glucose metabolism, weight loss should be strongly encouraged. A BMI within the recommended range is the goal for those who are overweight or obese, but a more practical approach, and the one used in the Finnish Study, is to advise a weight reduction of 5-7% of initial body weight or a weight loss of 5-10 kg depending upon degree of obesity. In both the Finnish and US intervention studies frequent ingestion of wholegrain products, vegetables, fruit, low fat milk and meat products, soft margarines and vegetable oils rich in MUFA were the means of facilitating the appropriate macronutrient composition. In addition the traditional Mediterranean diet and other traditional dietary patterns may be equally appropriate. Physical activity of at least moderate intensity (eg brisk walking) for at least 30 minutes per day is an important component of lifestyle modification aimed at reducing risk of T2DM and together with an increase in dietary fibre has been shown to make a contribution to risk reduction which is independent of weight loss. A similar exercise and dietary regimen has been shown to improve insulin sensitivity in insulin resistant individuals prior to the development of impaired glucose tolerance (248). There is currently no published evidence that weight loss achieved by diets high in fat or protein and low in carbohydrate will achieve similar results in those with insulin resistance or impaired glucose tolerance.

Regular vitamin D supplementation or a high dietary intake among young children has been shown to be associated with a lower risk of T1DM [249 (III)]. Three prospective studies have shown a consistent inverse association between magnesium intake and fasting insulin levels as well as risk of developing T2DM (250-253). Low magnesium levels have also been linked to other features of the metabolic syndrome in non-diabetic individuals (254). A high intake of magnesium in drinking water (>2.61 mg/l) appears to be protective against the development of T1DM in childhood

(255). A negative association has been reported between coffee consumption and risk of T2DM (256-260). However the absence of clinical trials precludes definitive recommendations regarding the roles of vitamin D or magnesium in the prevention of diabetes at present. Clinical trials have not confirmed an earlier suggested beneficial effect of nicotinamide in the prevention of T1DM (261).

Supplements and functional foods

– No recommendations are offered regarding supplements and functional foods. A number of such products is now available.

Commentary

Many functional foods and supplements are currently being promoted as beneficial for the management of people with diabetes or for reducing the risk of developing diabetes and its complications. These include fibre-enriched products and margarines containing plant sterols or stanols, and supplements containing various dietary fibres, n-3 fatty acids, minerals, trace elements and some herbs. Many of these products have been shown to have potentially relevant functional effects but have not been tested in long term clinical trials. The DNSG considers that, in the light of current evidence, the principal benefits of nutritional approaches to the treatment and prevention of diabetes are derived from the appropriate intake of usual foods. Because functional foods and supplements have not been a component of any traditional dietary pattern the Group believes that longer term evaluation in formal clinical trials is required before offering firm recommendations.

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