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Obesity and Diabetes

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INTRODUCTION

Obesity has recently been highlighted as having a substantial human cost, by contributing to the onset of disease and premature mortality, as well as having serious financial consequences for the health service and the economy (1). There is a strong relationship between diabetes and obesity, and excess body fat has been shown to affect both the development and progression of this chronic endocrine condition. Obesity is most closely associated with Type 2 diabetes and evidence suggests that a substantial number of the cases of Type 2 diabetes could be avoided if individuals were to stay within a healthy weight range (2). The mean body mass index (BMI) at diagnosis of Type 2 diabetes is $29\,kg/m^2$ (3), with the risk of developing the disease increasing exponentially with an increase in BMI. For example, the risk is 80-fold greater in an individual with morbid obesity ($BMI > 40\,kg/m^2$) compared with an individual with a $BMI \leqslant 22\,kg/m^2$ (4). Several studies have also shown that even modest degrees of overweight in early age are predictive of diabetes risk in middle age (4,5).

The prevalence of obesity in the UK has almost tripled since 1980, and this trend shows no sign of reversing (1). It follows, therefore, that there has been an increase in the incidence of Type 2 diabetes, with 180 million cases predicted world-wide by the year 2010 (6). Alarmingly, as the levels of obesity have increased, a greater number of cases of Type 2 diabetes have emerged in both children and young adults. No longer can Type 2 diabetes be considered as a 'late-onset' condition. The management costs of diabetes are already exceptionally high (7) and this shift in the age of onset of Type 2 diabetes will have

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devastating implications for both the medical and social costs of diabetes. While such statistics are alarming, it is important to recognise that obesity is also the most modifiable risk factor for Type 2 diabetes. It must be remembered, however, that correlation does not prove causation and that obesity is not obligatory for the development of diabetes. Obesity must interact to a variable degree with other environmental and genetic factors that determine insulin resistance and β-cell dysfunction, in order to lead to Type 2 diabetes in an individual (8).

There is a substantial disease burden associated with obesity and overweight. However, in the presence of diabetes, the devastating metabolic consequences of insulin resistance further expose the obese individual to cardiogenic risk factors such as dyslipidaemia and hypertension. Atherosclerosis and ischaemic heart disease are more likely to develop, and the risk of premature death is 10-fold greater in a diabetic person with a BMI $> 36\,kg/m^2$ compared with a similarly obese non-diabetic patient (9). While many of the complications associated with diabetes are linked to the metabolic consequences of increased adipose tissue mass, it is important to remember that other sequelae in the guise of obesity-related co-morbidities are common in diabetic patients. Most notable are: musculoskeletal disease, sleep apnoea, cancer, gall bladder disease, impaired mobility, respiratory problems, foot ulcers and perhaps most significantly for the individual, low self-esteem and poor quality of life. In addition, obese persons suffer from marked discrimination in society and often face prejudice from both the public and health professionals (10,11).

It is clear that weight management should form an integral part of the management of diabetes, with a strong emphasis on the prevention of obesity. It should be recognised however that obesity is a complex condition, the treatment of which is far from simple and requires the support of skilled helpers. Obesity treatment should be regarded as a long-term procedure, which is threaded into the management of diabetes. The primary focus of this chapter is to consider the mechanisms which link obesity and diabetes, the benefits of weight loss in diabetes, and how to manage obesity within a model of life-long diabetes care.

DEFINING OBESITY

Obesity is a condition in which there is excessive reserves of body fat. Clinically, obesity is classified in terms of the BMI (kg/m^2). The different classifications of

Table 8.1 Categories of BMI [weight (kg)/height (m^2)]

Normal weight	Overweight	Pre-obese	Obese Class 1	Obese Class 2	Obese Class 3
18.5–24.9	$\geqslant 25$	25.0–29.9	30.0–34.9	35.0–39.9	$\geqslant 40$

BMI are outlined in Table 8.1, with obesity defined as a BMI > 30 kg/m^2 and morbid obesity as a BMI > 40 kg/m^2.

OBESITY AND TYPE 1 DIABETES

The strong association between obesity and Type 2 diabetes has generally overshadowed obesity in relation to Type 1 diabetes. Obesity is relevant, however, as increases in body fat stores generally dictate an increase in insulin requirements, mainly as a result of a further decline in insulin sensitivity. Conversely, excessive dosages of insulin can lead to weight gain, presumably through the lipogenic effects of hyperinsulinaeima and possibly compounded by overeating during the hypoglycaemic episodes, which become more frequent as insulin therapy is intensified. Weight gain, following intensive treatment of those with Type 1 diabetes, has been shown to induce unfavourable changes in lipid levels and blood pressure, similar to those observed in the insulin resistance syndrome (12). However, if intensive therapy results in improvements in glycaemic control, this can reduce the impact of weight gain on such cardiovascular risk factors (13).

Of concern also is that obesity, or the fear of it, can have detrimental effects, particularly in young (predominantly female) patients with Type 1 diabetes. The desire to remain thin can lead these patients to reduce or omit insulin dosages and/or to engage in purging and laxative abuse (14–16). This particular form of 'eating disorder' is probably one of the prevailing causes of 'brittle' or unstable diabetes, and often leads to recurrent episodes of diabetic ketoacidosis with an increased risk of developing chronic diabetic complications and of premature death (17). Consideration should therefore be given to the management of those with Type 1 diabetes who are obese or at risk of becoming obese, and to vulnerable individuals who are in danger of adversely controlling their own treatment for fear of becoming obese. It remains true, however, that the prevalence of being overweight in Type 1 diabetes is lower than that in the general population (13).

THE ASSOCIATION BETWEEN OBESITY AND TYPE 2 DIABETES

The link between obesity and Type 2 diabetes has long been established and a visit to any diabetes clinic will confirm the alarming statistic that 90% of those with Type 2 diabetes are also estimated to be obese (18). It is not currently known whether insulin resistance is the cause of obesity, the result of obesity, or whether the two conditions arise independently from each other (19). It is known that the prevalence of insulin resistance is greater among the obese, however, there are normal weight individuals who are equally insulin resistant

(20). Without question, reduction in weight is associated with improvements in insulin sensitivity (21,22). It is also clear that regular physical activity improves insulin action, although the exact mechanisms involved are not clear.

Several mechanisms have been proposed to explain how excessive body weight is associated with Type 2 diabetes. In general, the accumulation of fat mass is associated with a decline in whole body insulin sensitivity. The distribution of obesity is important, with resistance to the action of insulin and glucose intolerance most closely associated with excess abdominal adipose tissue. As visceral adipose tissue increases plasma triglyceride (TG) concentrations are elevated, high-density lipoprotein (HDL) cholesterol decreases and low-density lipoprotein (LDL) cholesterol increases with a greater proportion of the more atherogenic small dense LDL particles (LDL subclass III). Other associated characteristics include an elevated plasma non-esterified fatty acid (NEFA) concentration, an increased plasminogen activator inhibitor 1 (PAI-1) concentration, hyperuricaemia and hypertension. Abdominal obesity is also associated with specific changes in skeletal muscle morphology, namely a reduction in capillary density and an increase in the proportion of 'white' or 'glycolytic' fibres which are less insulin sensitive than the red (oxidative) fibres (23). Within the adipocyte an increase in the expression of products such as tumour necrosis factor-α (TNF-α) and leptin may also contribute to the deterioration in insulin sensitivity. More recently a novel protein known as resistin has been reported as providing the missing link in explaining the molecular link between diabetes and obesity. Resistin is secreted by adipocytes. Its circulating levels correlate with obesity and it has been shown to cause insulin resistance in target tissues (24).

BENEFITS OF WEIGHT LOSS

Despite the expectations of the individual, the likelihood that an obese person will achieve sufficient weight loss to reach an 'ideal' body weight is remote (25). However, this does not imply that treating obesity is fruitless, as there is evidence that even a modest weight loss of 5–10% in obese diabetic subjects can produce clinical benefits. Improvements have been noted in all modifiable risk factors such as HbA_{1c} levels, hypertension, dyslipidaemia, self-esteem and overall quality of life. Moreover, improvements in these risk factors have a favourable effect on mortality. A retrospective study of Type 2 diabetic patients receiving standard dietetic advice showed a mean weight loss of 2.6 kg for those with a BMI 25–30 kg/m^2 and a loss of 6.8 kg for those with a BMI > 30 kg/m^2 after 1 year. For the average patient each kilogram of weight loss was associated with a three- to four-month prolonged survival and a 10 kg weight loss predicted the restoration of about 35% in life expectancy (26).

GLYCAEMIC CONTROL

A reduction in body weight has a direct influence on glycaemic control by improving both hepatic and peripheral insulin sensitivity and decreasing insulin resistance (27). HbA_{1c} is the accepted measure of longer-term glycaemic control with a level $< 7\%$ as the desired target (28). While several studies of Type 2 diabetic subjects have demonstrated improvements in fasting blood glucose, HbA_{1c} and plasma insulin after weight loss, it has been observed that the benefits are proportional to the amount of weight lost. A study by Wing *et al*. (29) showed that a weight loss of 10% of total body weight reduced HbA_{1c} levels by 1.6%. Correspondingly, there was a reduction in the need for oral diabetic agents. In fact, those losing 15% of their body weight were able to discontinue medication for diabetes altogether.

HYPERTENSION

Hypertension is a feature of Type 2 diabetes and is thought to result from a failure of insulin-induced vasodilation to counteract both renal sodium reabsorption and activation of the sympathetic nervous system (30). Indeed the UKPDS emphasised the importance of tight blood pressure (BP) control in Type 2 diabetes to reduce the risk of cardiovascular and macrovascular complications, with a recommended target BP of 140/85 mmHg (31). For the obese Type 2 diabetic patient, weight loss is pivotal to achieving this target as a weight loss of more than 10 kg has been shown to reduce the risk of hypertension by 26% (32). A more realistic intervention may be to prevent further weight gain, as it is estimated that a 1 kg increase in weight is associated with a 5% increase in risk of hypertension (32).

DYSLIPIDAEMIA

Adverse lipoprotein concentrations are commonly observed in those with Type 2 diabetes, with 40–50% of subjects having an abnormal profile (33). The most characteristic lipid pattern in diabetes is a high serum triglyceride level and a low HDL cholesterol level. Raised serum triglyceride levels lead to the synthesis of TG-enriched VLDL from the liver, promoting an unfavourable lipid exchange between lipoproteins. This results in an increased clearance of the more protective HDL cholesterol from the circulation and an increase in the more atherogenic LDL cholesterol. Weight loss can help to reverse this TG-driven atherogenic process and promote a more favourable shift in the LDL cholesterol profile of an individual, through the generation of larger and less dense LDL particles, which are less of an atherogenic threat (34). Lean *et al*. (26) investigated the effects of weight loss in newly diagnosed diabetic subjects. Their results support the benefit of modest amounts of weight loss

and at 6 years they found that an initial and sustained weight loss of 9 kg had associated improvements in lipid and lipoprotein levels.

QUALITY OF LIFE

Although the evidence of the physical benefits of weight loss is sustained and unequivocal, arguably, it is improvements in the quality of life that are more significant for the obese individual with Type 2 diabetes. Diabetes itself is a chronic condition, which severely affects daily living. It is estimated that the average person with diabetes is willing to trade away 12% of his remaining life in return for a diabetes-free health state (35). For many with Type 2 diabetes, this is further compounded by the burden of obesity. Compared to the general population, obese subjects report significantly worse physical, social and role functioning and worse perceived general health, with the morbidly obese experiencing greater distress than the moderately to severely obese. In addition, the obese also report significantly greater disability due to bodily pain than patients with other chronic medical conditions (36). Encouragingly, a trial of 13 weeks weight loss treatment resulting in a mean weight loss of 8.6 ± 2.8 kg showed significant improvements in all of these domains.

APPROACHES TO WEIGHT MANAGEMENT

In theory, the management of the obese diabetic patient should not differ from that of the obese non-diabetic patient. However, it has been reported that weight loss is much more difficult for Type 2 diabetic subjects than obese non-diabetic subjects. For example, 12 overweight diabetic patients treated in a behavioural weight loss programme for 20 weeks lost significantly less weight than their non-diabetic spouses on the same programme (29). Although it appears that dietary adherence alone may account for the difference, a small sample size and family dynamics may be confounding factors in these results. Indeed a more recent study using larger numbers and unrelated subjects showed that, on the contrary, Type 2 diabetic subjects can lose as much weight as their non-diabetic peers during active treatment but that the diabetic subjects regain significantly more weight at 1 year follow-up (37). This suggests that weight loss maintenance rather than initial weight loss is the main problem for these individuals. Both studies demonstrate the complex interplay between obesity and diabetes. Indeed the many physical, social and psychological burdens of these two chronic conditions make it important from the outset to build a trusting and non-judgemental relationship with the patient. The aim of the initial assessment should be to gather information needed to make a decision about the direction of future treatment (38). The general goals of weight management can be considered as follows:

1. To prevent further weight gain
2. To reduce body weight
3. To promote long-term maintenance of weight loss

ASSESSMENT OF OBESITY

Measurement of height and weight, in order to determine the BMI, is the initial step in the clinical assessment of obesity. Waist and hip circumference measurements provide information as to the distribution of weight, with a waist circumference measure of >102 cm in men and >88 cm in women associated with increased risk of CHD (39). More sophisticated measures of body fat can be made using other techniques such as bioelectrical impedance, dual energy X-ray absorptiometry, densitometry and isotope dilution, although these techniques tend to be expensive, complex and are generally confined to a research setting.

RISK FACTORS FOR OBESITY

The patient's age is important in determining risk from obesity and generally there is greater risk from obesity in those under 40 years of age. Taking a weight history can ascertain the onset and duration of obesity as well as the pattern of weight gain and weight loss throughout the individual's life. Longitudinal studies have shown that weight gain confers a greater risk of cardiovascular disease than an unchanging level of obesity (40). In addition, the longer the duration of obesity the more difficult treatment may be. Gender is another variable that impacts on the development of obesity, with women generally having a higher prevalence of obesity compared to men, especially in middle age (41). Reproductive function can be affected in younger women, with menstrual disorders including irregular bleeding and amenorrhea being more common among obese females.

Various medical/genetic causes of obesity must also be considered. Endocrine conditions associated with weight gain include hypothyroidism, Cushing's syndrome, hypogonadism in the male, polycystic ovary syndrome (PCOS) in the female and growth hormone deficiency (42). Rare genetic causes of obesity include Prader–Willi syndrome, Bardet–Biedl syndrome and Cohen's syndrome. Diabetes can be an obvious consequence of the severe obesity associated with such syndromes.

FAMILY HISTORY

It is important also to establish a family weight history. Estimates of the heritability of obesity vary, with some early estimates as high as 70% (43) to

more recent estimates of 30–40% (44,45). The children of those with diabetes are at an increased risk of developing the condition and the involvement of the whole family in treating and preventing obesity should be encouraged.

ASSESSMENT OF CO-MORBIDITY

It is important to determine the presence of any cardiac risk factors such as hypertension, hyperlipidaemia and cigarette smoking and to provide appropriate advice and therapy. The physical symptoms of obesity include reduced mobility, joint pain, chest pain, breathing difficulties and sleeping difficulties, and these should also be assessed. Conditions such as osteoarthritis and gastrointestinal disorders such as gastric reflux can also be exacerbated by excess weight. As well as measures of glycaemic control, measurements of biochemical indices such as lipid levels and thyroid levels are advisable.

DIETARY HISTORY

A history of eating behaviour and if appropriate a current diet history can provide information as to the eating patterns and food preferences of the individual and can be used to begin to identify the changes needed. Encouraging patients to monitor their own food intake and activity patterns can be helpful in providing feedback to the patient on how to improve the nutritional quality of the diet and how to identify and overcome barriers that lead to overeating. Consideration should also be given to socio-economic and cultural factors that influence the eating patterns of an individual, particularly since diabetes is strongly associated with the Asian and African–Caribbean populations in the UK.

Eating disorders and in particular binge eating are common among the obese, with prevalence estimates of 23–46% in those seeking treatment (46). Binge eating disorder has also been reported to be associated with Type 2 diabetes, but would appear to precede Type 2 diabetes in most patients. The prevalence of binge eating disorder in those with Type 2 diabetes was recently estimated as 10% among a sample of 322 German patients (47). Other forms of disordered eating, including night eating syndrome, should also be considered when assessing an obese individual.

ASSESSING MOTIVATION TO LOSE WEIGHT

When conducting an assessment of obesity, it is important to establish the ability and motivation of the individual to make lifestyle changes at that time. The style of the therapist can be crucial in facilitating behaviour change (48) and enhancing the confidence of the individual to be able to sustain changes. Key skills include the core counselling skills of listening and reflecting,

motivational interviewing techniques, as well as strategies such as cognitive behavioural therapy (CBT).

OBESITY TREATMENT

It is a basic fact that excess body fat results from an imbalance between energy input and energy output. Any obesity treatment will therefore have to attempt to reverse this imbalance so that energy intake is less than energy expenditure. However, obesity is a complex condition that involves the integration of social, behavioural, cultural, physiological, psychological, metabolic and genetic factors. It follows therefore that no single treatment option is likely to address all components. Treatments need to be interwoven so that dietary counselling, physical activity, behavioural therapy, pharmacotherapy and even surgical treatment are provided in tandem. A multidisciplinary approach to weight management is generally advocated, although where resources are limited this may not always be achievable.

DIETARY MANAGEMENT

The dietary management of diabetes is focused on measures that will improve glycaemic control. The high-fibre, high-carbohydrate and low-fat advice advocated is a type of dietary regimen which should also encourage weight loss. Increasingly, attention has also been given to the glycaemic index (GI) within the dietary management of diabetes. It is interesting to note that diets based on low glycaemic foods have been shown not only to improve blood glucose control but also to cause greater weight loss than diets based on high GI meals (49).

Ultimately, in order to lose weight, a reduction in overall energy intake is required. A useful first step, therefore, is to calculate the energy requirements of an individual based on their current body weight, age, gender and activity levels using prediction equations such as those recommended by Lean and James (50). Aiming for a weight loss of 0.5–1 kg/week involves reducing energy intake by 500–1000 kcal/day. In conjunction with the individual, it is possible to devise an eating plan which will provide a modest reduction in energy intake and be more achievable than standard prescribed energy diets. Blanket energy prescription, usually 1200 kcal for women and 1500 kcal for men, has been shown to produce significant weight loss in several studies (51–53). For those most overweight, however, a standard energy prescription can be several thousand calories below their requirements. Frost *et al*. (54) compared a 1200 kcal dietary prescription to a daily energy deficit of 500 kcal in a group of patients attending a dietetic weight management clinic. Their results showed that those in the daily deficit group achieved a greater weight loss than those in

the standard prescribed diet group, suggesting a greater compliance to a more modest energy reduction. As well as aiming for a realistic reduction in energy intake, the nutritional quality of the diet is important and it should provide all of the essential nutrients in order to maintain health.

Several studies have looked at the effect of very low calorie diets (VLCDs) in the treatment of diabetes (55,56). VLCDs are 'nutrient-enriched' regimens, usually in the form of liquid drinks, which aim to provide less than 3300 kJ/800 kcal of dietary energy per day. Mean weight losses with a VLCD range from 1.5–2.5 kg/week, so that use over 12–16 weeks should produce close to a 20 kg weight loss. In practice, however, such weight loss is not always observed, indicating that as with other dietary regimes, this change is difficult to sustain. Maintenance of weight loss may be of particular concern with a VLCD regimen, due to the significant calorie reduction from actual energy requirements and the sharp divergence from normal eating patterns (57). Following the termination of severe energy restriction, subsequent overeating could be a compensatory response to the physiological or psychological effects of food deprivation (58). VLCD regimens have been used in many short-term studies with considerably fewer examining their long-term use. Often improvements in glycaemic control in the obese diabetic patient are seen within days of caloric restriction, suggesting that calorie restriction as well as actual weight loss is responsible for improvements in blood glucose control. The mechanisms for improved glycaemic control through calorie restriction are unclear, but are thought to relate to a reduction in hepatic glucose output. Wing *et al*. (59) studied a group of 93 obese Type 2 diabetic patients who were randomised to receive two different degrees of calorie restriction, i.e. 400 or 1000 kcal/day. The study showed that the degree of calorie restriction, independent of differences in the magnitude of weight loss, affected fasting glucose levels and insulin sensitivity. It is recommended that VLCDs are carried out under medical supervision only, with consideration given to long-term maintenance of weight loss.

Whichever type of dietary regimen is adopted it is important to remember that dissemination of information and direct persuasion alone are unlikely to bring about sustained dietary change (60). Adopting a counselling approach and developing skills in communication that facilitate behaviour change are recommended to help people through the process of change necessary in obesity treatment (61).

BENEFITS OF ACTIVITY

Regular physical activity has been shown to confer a protective effect against the development of diabetes, particularly in those individuals who are at greatest risk of developing the condition (62–65). For the obese individual who has already developed diabetes, regular physical exercise also has several

clinical benefits. In any weight management programme, therefore, it is essential that consideration be given to increasing physical activity. Treatment strategies that combine physical activity with dietary changes are generally much more effective than treatments which are exclusive to one or other strategy (66). In general, any measure that increases modest daily activity, such as avoiding lifts, or getting off the bus one stop earlier, is beneficial in increasing energy expenditure. A sedentary obese individual performing 3 h of any activity standing up rather than sitting down will increase his 24-h energy output from 40% to more than 75% above the BMR (67). However, for the obese individual with Type 2 diabetes, increasing daily activity patterns may not be enough, and more intensive degrees of exercise need to be considered on an individual basis.

Physical activity has a positive effect on insulin action, thus improving glucose control and insulin sensitivity (68). In addition, exercise improves lipid profiles by reducing serum TG and VLDL and raising HDL concentrations. Improvements in blood pressure have also been observed, independent of weight loss. Cardiac fitness is improved, with the risk of myocardial infarction reduced by 35–50% (69). Evidence suggests that these benefits are not uniform and that, in general, younger (40–54 years) individuals with Type 2 diabetes, in the early stage of disease, are more likely to benefit from the effects of exercise (70). In addition, the greatest benefits from physical activity may be in the weight maintenance phase of obesity management (71).

The psychological benefits of exercise are equally important for the obese individual with Type 2 diabetes. Reductions in anxiety levels, improved body image and higher self-esteem promote greater self-efficacy and help the individual to cope with stressful situations which often result in overeating and relapses (71,72).

While exercise improves insulin action, the effects of physical training disappear within days when discontinued, so consideration must be given to the nature and duration of the activity. Programme activities need to be regular and of at least moderate intensity (73). Aerobic activities, e.g. walking, swimming, cycling, for 20–60 min at moderate or greater intensity for 3–4 days/week will benefit glycaemic control and at least 5 days a week will assist weight loss (74,75). The value of walking as an exercise strategy for those with Type 2 diabetes should not be overlooked. Those asked to walk 10 000 steps a day, and maintain a 1000 kcal deficit diet, lost more weight and had greater improvements in insulin sensitivity than those on diet alone (76).

Unfortunately, obese persons with Type 2 diabetes identify more barriers to exercise than to any other aspect of the diabetes self-care regimen, with specific complaints of physical discomfort, fear of hypoglycaemia, being too overweight to exercise and lack of family support (77). Physical discomfort as a limiting factor has to be considered from the perspective of both obesity and diabetes. Obese women report higher degrees of perceived pain and exertion

when walking than non-obese, suggesting that this moderate intensity activity is actually more intense for the obese due to the greater relative oxygen cost of walking (78). In addition, the myriad of macrovascular and microvascular complications associated with diabetes may increase discomfort during activity and limit endurance and flexibility (71). Patients with proliferative retinopathy or hypertension, for example, should avoid resistance training and high-intensity exercises and those with peripheral neuropathy are advised to pursue activities such as swimming, where the ankle and foot are not under stress. Advice regarding appropriate footwear, foot inspection and adequate hydration should be given and those at risk of hypoglycaemia should take care to adjust insulin doses and consume sufficient carbohydrates (79). The emergence of exercise referral schemes may be an important development for the treatment of obesity in Type 2 diabetes (1).

BEHAVIOURAL THERAPY

Behavioural treatments for obesity originated in the 1960s and were founded on the concept that altering behaviours associated with eating and activity could be central to weight loss. Specific strategies include self-monitoring of both eating habits and physical activity, stress management, stimulus control, problem solving, contingency management, cognitive restructuring and social support. Treatments employing cognitive behavioural therapy (CBT) generally achieve levels of between 5–10% weight loss. A notable fact with regard to studies which have investigated CBT as a treatment strategy is that drop-out rates are very low. Over 80% of subjects who enter behavioural treatments complete the programme and are available for follow-up (80). It is recognised that CBT may produce the best results when combined with other treatments (81).

PHARMACOLOGICAL MANAGEMENT

There is incontrovertible evidence to show that early pharmaceutical intervention achieves better glycaemic control and reduces macrovascular and microvascular outcomes for Type 2 diabetic subjects (82). However, the conflict for obese diabetic patients between the need to achieve glycaemic control whilst minimising weight gain poses a challenging dilemma, as weight gain is an unfortunate consequence of several diabetic medications, a summary of which is provided in Table 8.2 (83).

Despite the undoubted ability of insulin to influence glycaemic control and microvascular outcomes, the mean weight gain by insulin-treated Type 2 obese subjects after 6 years is 10.4 kg. Sulphonylureas have a similar, but less pronounced effect, with a mean gain of 4.9 kg (84). For this reason, there is a general reluctance to use insulin in particular with the obese, although there is

Table 8.2 Anti-diabetic agents and their impact on body weight

Anti-diabetic agent	Effect on body weight
Sulphonylureas (e.g. gliclazide)	+
Biguanides (e.g. metformin)	−
α-Glucosidase inhibitors (e.g. acarbose)	−
Thiazolidinediones (e.g. pioglitazone, rosiglitazone)	+
Insulin	+ +

Source: Adapted from Hauner (83).

some evidence that the use of basal insulin as opposed to meal-time insulin will lessen the weight gain effect (85). Newer agents such as the thiozolidinedione insulin sensitisers remain controversial, as the impact of undesirable subcutaneous weight gain, despite reductions in the more harmful visceral fat, continues to be debated (8).

α-Glucosidase inhibitors such as acarbose, although generally less effective hypoglycaemic agents, may have some value in the management of the obese Type 2 diabetic patient. Although they generally have a neutral effect on weight, some studies suggest they cause modest weight loss and are thought to act by reducing the energy available from carbohydrates by delaying fermentation in the gut (86).

Biguanides such as metformin, on the other hand, have a weak anorectic action, and were shown by the UKPDS to be the treatment of choice for the obese Type 2 diabetic patient, causing no weight gain relative to conventional policy and demonstrating a cardio-protective effect by reducing the rates of mortality and myocardial infarction (87).

Furthermore, there is some evidence that the combination of metformin with intensive insulin therapy can negate the weight gain caused by insulin (88). However the effects of metformin on microvascular outcomes are less favourable than insulin, and for many patients its side-effects and contra-indications mean that it is not a viable option.

Clearly there is no easy way for an individual with diabetes who is obese to improve glycaemic control, reduce microvascular and macrovascular complications and lose weight at the same time. A more rational approach may be to address the problem of obesity first, using agents that cause weight loss as a primary effect and achieve reductions in hyperglycaemia as a desirable consequence. One such agent is orlistat, an intestinal lipase inhibitor, which acts enterically to inhibit the absorption of approximately 30% of dietary fat (89). Orlistat is recommended for use in those aged 18–75 years with a BMI 28–30 kg/m^2, in the presence of significant co-morbidities and in those with a BMI > 30 kg/m^2 with no associated co-morbidities. Patients are required to demonstrate a weight loss of at least 2.5 kg in the month prior to the drug being prescribed. The NICE (90) guidelines in the UK have also recently

recommended that continuation of this therapy beyond three months should be supported by evidence of a loss of at least a further 5% of body weight, and beyond six months by evidence of at least 10% weight loss. Several clinical trials have been conducted to examine the efficacy of this drug treatment in obese diabetic and non-diabetic patients (89,91). While over a one-year period, Type 2 diabetic subjects taking sulphonylureas and orlistat lost less weight than non-diabetic subjects taking orlistat (mean 6.2 kg vs 9.5 kg), the subsequent improvements in HbA_{1c} reduced the need for diabetic medication and had favourable effects on lipid profiles and hypertension. In addition, improvements in the insulin resistance index of obese non-diabetic subjects, proportional to the degree of weight lost, suggest that orlistat may have a valuable role in the delay of onset or perhaps the prevention of Type 2 diabetes in the obese (92).

Sibutramine is a selective serotonin and noradrenaline reuptake inhibitor, which promotes weight loss. The blocking of serotonin reuptake has a satiety enhancing effect and inhibition of noradrenaline uptake promotes thermogenesis. Sibutramine has only recently been licensed in the UK, the drug having been available on prescription in the USA for considerably longer. The results of the clinical trials show that obese non-diabetic patients are more able to achieve a 5–10% weight loss with sibutramine than with placebo, although the positive effects are dose-related. A 10 mg dose results in a mean weight loss of 5.5% and a 15 mg dose a loss of 7.2% (93). For the Type 2 diabetic patient who loses weight with sibutramine, the ensuing improvements in all modifiable risk factors are proportional to the degree of weight lost, with significant improvements, specifically a reduction in HbA_{1c} of 0.4%, seen in those who lost $> 5\%$ of body weight (94). As a word of caution, slight increases in pulse and blood pressure (2–3 mmHg) are associated with sibutramine, but in the long term, weight loss results in a net decrease in blood pressure.

SURGICAL INTERVENTION

Surgery is a treatment option which is usually only advised for patients with severe obesity ($BMI > 40\ kg/m^2$), although some centres are now opting to use this in patients with a $BMI > 35\ kg/m^2$ if significant co-morbidity is present. There are two types of obesity surgery: (1) restrictive procedures and (2) combined restrictive and malabsorptive procedures. Restrictive surgery uses bands or staples to create a stomach pouch, thereby producing a restriction in food intake. Examples of restrictive procedures include the vertical banded gastroplasty (VBG) and the laprascopic banding procedure. Combined restrictive and malabsorptive surgery involves a combination of restrictive surgery with bypass or malabsorptive surgery, in which the stomach is connected to the jejunum or ileum of the small intestine, bypassing the duodenum. Roux-en-Y gastric bypass is the most commonly performed gastric bypass procedure.

In terms of the percentage of excess weight loss, results range from 50% for restrictive procedures to 60–70% for malabsorptive procedures.

Results from the surgical treatment of obesity provide the most convincing evidence of the benefit of weight loss in Type 2 diabetes. The Swedish obese subjects (SOS) study is a recent prospective trial, which has demonstrated the effect of surgically induced weight loss on the incidence of diabetes mellitus (95). The intervention consists of a surgically treated group of severely obese individuals and a matched group of weight-stable obese controls. This study provides overwhelming evidence that weight loss not only helps reduce, treat and eliminate diabetes, but also that losing weight can prevent the onset of diabetes. The surgically treated patients lost an average of about 60% of their body weight, with the incidence of hyperinsulinaemia and high blood glucose significantly decreased compared with the medically treated group. For the 8 years these patients have been followed, one consistent factor has held up – weight loss maintains improvements in insulin sensitivity, helps decrease the incidence of diabetes, and effectively treats Type 2 diabetes. Pories *et al.* (96) followed 608 patients who had undergone gastric bypass surgery for up to 14 years. At 1 year, there was an average weight loss of 100 lb, which was maintained by the majority of patients at 5 years. About 83% of the 146 patients with diabetes experienced a return to normal levels of plasma glucose, glycosylated haemoglobin and insulin. In 152 patients with impaired glucose tolerance, more than 98% achieved normal glucose tolerance post-surgery. It is interesting to note however that even before a large weight loss was obtained, post-surgery glycaemic control improved.

Surgical intervention requires long-term follow up to help patients adjust to the surgery and change their eating habits. Vitamin supplementation, particularly vitamin B_{12}, will be necessary in patients who have undergone malabsorptive surgery.

While the results from the studies of obesity surgery are impressive, as pointed out by Pinkney *et al.* (97), it should be remembered that no trials have been designed with diabetes as the central focus and moreover few patients on oral agents or insulin have been reported on. There is a need therefore for more large-scale, long-term prospective studies specific to diabetes before firm conclusions can be drawn as to the role of obesity surgery in diabetes management.

CONSIDERATIONS IN MANAGING OBESITY WITHIN DIABETES CARE

It would be unusual to find the overweight patient with diabetes who has not at one time or another been advised to ‘lose some weight’. For the patient faced with the prospect of attempting to achieve this it can be helpful first of all to quantify the amount of weight loss which we now know can bring clinically

significant benefit, i.e. 5–10% of current body weight. Although the results of obesity surgery provide compelling evidence that an even greater amount of weight loss can significantly reduce the need for medication and in some cases eliminate the need for any further treatment, obesity surgery will not be appropriate for or accessible to many people with diabetes. It is important therefore that an achievable degree of weight loss is promoted and that a greater understanding of the benefits of a more modest amount of weight loss in the treatment of those with Type 2 diabetes is gained. In addition, with many studies demonstrating weight regain following a period of weight loss, the importance of weight maintenance needs to be more strongly emphasised.

Also in advising patients to 'lose some weight' it is to be questioned whether current services are designed to help patients to achieve this. Obesity, like no other condition, is considered to be solely under the control of the individual, and as such can lead to the view that there is little that can be done by the health professional to alter this. This belief could easily impact upon the priority given to weight management within the realm of diabetes care. It could be argued however that the 'medical' treatment of obesity is in effect still in its infancy, with only 50% of the health authorities surveyed in the National Audit Office report of England and Wales (1) indicating that they had a dedicated obesity strategy in place. Weight loss achieved through changes in lifestyle is not impossible and perhaps before we dismiss weight loss as an unattainable ideal we need to consider whether we offer adequately funded, comprehensive and effective weight management programmes.

In the pharmacological management of diabetes it has already been highlighted that finding a regimen which complements both glycaemic control and weight loss is a challenge. With a greater number of anti-obesity drugs emerging there is a need to investigate more fully their potential as front-line treatments in the management of the obese Type 2 diabetic patient. While it is not questioned that treating hyperglycaemia reduces complications in diabetes, the long-term benefit of reacting to what is in effect the consequence of obesity rather than reacting to the obesity itself is controversial. At a certain level of obesity, or if weight continues to increase, there will inevitably be a finite limit to the effectiveness of anti-diabetic agents and we need to consider whether a 'reactive' approach is the most effective in the long term.

Finally, more and more evidence is emerging to suggest that prevention strategies are extremely important, particularly since the escalation in the levels of obesity has seen a corresponding increase in the incidence of diabetes. Indeed in Europe alone, the number of diabetic patients is predicted to increase from 16 million in 1994 to 24 million in 2010 and indicates that the 21st century will herald an astounding increase in both the financial and social costs of diabetes (98). Impaired glucose tolerance is in effect the first stage of Type 2 diabetes and consideration must be given to (a) how such individuals can best be identified and (b) whether more rigorous intervention at this stage would be

a more cost-effective method of tackling the impending diabetes epidemic in the long term. Modest weight loss, for example in high-risk subjects, could help to prevent a substantial number of cases of diabetes from ever developing (64, 65). The studies which have highlighted the benefits of weight loss in preventing progression to diabetes from IGT involved reductions in body weight of on average < 5 kg. These findings again lend credence to the message that weight loss does not have to be extensive in order to modify the risk of diabetes.

SUMMARY

- Obesity is a chronic condition that impacts greatly upon the development, the progression and the consequences of diabetes.
- Weight management should form an integral part of the management of diabetes, with a strong emphasis on the prevention of obesity.
- The traditional emphasis on achieving pharmacologically driven glycaemic control can make weight loss difficult. Consideration should be given to the provision of a multi-skilled weight management service as part of the front-line therapy in diabetes treatment.

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