



Managing obesity and glycemic control in insulin-using patients: clinical relevance and practice recommendations

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Abstract

In a number of large-scale studies, intensive therapy regimens have improved glycemic control while reducing the microvascular complications of type 2 diabetes. However, insulin use has been associated with weight gain, thereby hampering patient compliance with intensive insulin therapy. As the prevalence of type 2 diabetes and obesity continues to increase worldwide, health care providers must incorporate the management of weight gain in therapeutic strategies that promote glycemic control. The central component in any such strategy is a tailored program of medical nutrition therapy (MNT), which includes a healthy diet, physical activity, and education. This article reviews several dietary options within a MNT program, including the uses of liquid meal replacements, low-glycemic index carbohydrates, and foods rich in monounsaturated fatty acids. It also provides several practice recommendations to encourage compliance in patients with type 2 diabetes who wish to manage their weight while receiving insulin therapy.

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1. Glycemic control and weight management for diabetes: achieving a balance

In the past four decades dramatic worldwide increases have occurred in the prevalence of type 2 diabetes [1] and obesity [2]. These two pandemics are inexorably linked, as excess adipose tissue promotes insulin resistance [3,4], an underlying feature of the metabolic syndrome and of type 2 diabetes. Weight gain, whether modest or excessive, significantly increases the risk of developing type 2 diabetes and comorbidities such as coronary heart disease and

hypertension [5]. For example, a person's risk of developing type 2 diabetes doubles with a weight gain of 11–18 lb (≈ 5 –8 kg) and quadruples with a gain of 44 lb or more (20 kg) [5]. It has been estimated that women who have a body mass index (BMI) above 35 kg/m^2 have a 93-fold increased risk of developing diabetes, while men in this category are at a 42-fold increased risk relative to individuals with BMI values that are less than 23 kg/m^2 [6]. The close relationship between obesity and diabetes underscores the need for effective strategies that establish glycemic control while managing weight.

The results of large studies such as the Diabetes Control and Complications Trial (DCCT) [7] and the

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United Kingdom Prospective Diabetes Study (UKPDS) [8] have demonstrated that glycemic control is an essential factor for improving clinical outcomes for people with diabetes. Intensive therapy strategies designed to lower blood glucose concentrations reduce microvascular complications, such as retinopathy and nephropathy. However, the UKPDS demonstrated that intensive therapy in type 2 diabetes, especially with insulin, increases the risk of hypoglycemia and promotes weight gain [8], as in the DCCT which studied type 1 diabetes [7]. Weight gain was significantly greater in the cohort of patients receiving intensive treatment with insulin or sulfonylureas relative to the cohort receiving dietary and conventional treatment [8]. These results suggest that the health care provider must strive to maintain a balance between achieving glycemic control and controlling weight when designing a treatment regimen for an individual patient.

This balance can be difficult to achieve in practice, as numerous environmental factors encourage weight gain and physical inactivity [9]. Contemporary lifestyles are often sedentary, and people are surrounded by a plethora of calorically-dense “convenience” foods, many of which are high in fat content, and increasingly larger portion sizes. Television, computers, and other passive recreational activities promote spectatorship rather than participation in physical activities. As a result, the contemporary environment often discourages a caloric balance and promotes storage of energy by the deposition of fat. Weight gain thus becomes a risk associated with intensive therapy, and many people with diabetes opt for less intensive glycemic control to minimize weight gain.

2. Glycemic control and risk reduction through medical nutrition therapy

A tailored program of medical nutrition therapy (MNT), consisting of a healthy diet, physical activity, and education, is endorsed by all diabetes-related professional associations as the cornerstone of any diabetes management program [10–13]. The primary goal of an MNT program is to control blood glucose levels, with weight loss and reduction in risk for comorbidities representing secondary benefits. A well-designed MNT regimen also has preventative

benefits for people at high risk of developing type 2 diabetes; the incidence of diabetes in people with impaired glucose tolerance can be reduced by as much as 58% with lifestyle changes alone [14]. A MNT program must be designed in accordance with the needs of the individual and should be continued in the event of subsequent therapeutic interventions, such as oral antidiabetic agents or insulin.

In obese people with type 2 diabetes, weight loss clearly improves hyperglycemia and lowers risk for comorbidities such as hypertension and dyslipidemia [15]. The UKPDS demonstrated that dietary therapy can reduce fasting blood glucose levels in overweight type 2 diabetic patients, although the degree of improvement is determined more by the restriction in caloric intake than by body weight [16]. Moreover, evidence suggests that caloric restriction has an important regulatory effect on metabolism in obese patients with type 2 diabetes that is independent of weight loss; reducing caloric intake often improves glycemic control more rapidly than weight loss [17]. However, fostering adherence to successful caloric restriction regimens requires a strategy that addresses convenience and compliance.

3. Dietary management issues in diabetes: compliance and convenience

Contemporary lifestyles may deter compliance with a MNT program. Convenience foods often lack a nutrient balance, and people have increased difficulty maintaining a diet while away from home. Complex diet plans may be time-consuming or difficult to follow on a daily basis. People who use insulin face additional challenges to their dietary management, as a quick meal or snack is often necessary to prevent nocturnal or daytime hypoglycemia, to spread the nutritional load, or to match the energy demand of exercise.

One popular solution to enhance dietary adherence and practical convenience is the use of specially-designed nutritional drinks and meal replacements. The use of such therapy to promote weight loss on a daily basis is endorsed by professional societies including the American Diabetes Association [11] and the Canadian Diabetes Association [12]. Benefits to the use of these products include convenience,

portion size and calorie control, and their compatibility with calorie-controlled diets.

The use of liquid meal replacements as one component of a structured meal plan has been shown to be effective for long-term maintenance of weight and reduction in risk factors obese people [18]. Although the sugar content of many commercial meal-replacement products has fostered concern about their use in management regimens for obese patients with type 2 diabetes, recent data suggest that these concerns may be unfounded [18,19]. In one study, 75 obese subjects with type 2 diabetes followed a 1200–1500 kcal/day, American Diabetes Association-approved diet for 12 weeks. Subjects were randomized into three categories: diet with no meal replacements, diet using two meal replacements per day sweetened with oligosaccharides, and diet using two meal replacements per day fortified with sucrose, fructose, or lactose. Weight loss was comparable between the two meal-replacement cohorts and was greater than the loss achieved through diet alone. Moreover, the subjects using meal replacements demonstrated significant reductions in levels of fasting blood glucose, total cholesterol and low-density lipoprotein as compared to those who received no meal replacements [19].

4. Diet and glycemic control

Appetite may be influenced by a variety of physiological, psychological, emotional, and cultural factors. It has long been established that a transient decline in blood glucose is recognized by the central nervous system and influences hunger and meal-seeking behavior [20]. Blood glucose dynamics and diet are linked in a complex relationship, and strategies to regulate blood glucose levels must be designed with diet in mind.

After a meal, digestion of complex sugars produces a temporary “spike” in the blood glucose concentration. This postprandial glycemic response is influenced by a number of controllable factors, including the dietary carbohydrate profile and the schedule of meal ingestion. Studies have shown that a diet high in monounsaturated fatty acids and low in carbohydrates improves peripheral insulin sensitivity in people with type 2 diabetes [21], and high-carbohydrate diets have been shown to cause more deterioration of glycemic

control, accentuation of hyperinsulinemia, and a rise in plasma triglyceride and very-low-density lipoprotein levels relative to comparable diets that are high in monounsaturated fatty acids [22]. There is also evidence to suggest that a diet rich in low-glycemic index foods can improve glycemic control in diabetic patients, reduce serum lipids in hyperlipidemic individuals, and reduce the risk of developing obesity, diabetes and cardiovascular disease [23–29].

At present, the American Diabetes Association does not recognize a role for glycemic index in the treatment or prevention of disease. Based on their evidence-based review, diets low in glycemic index may reduce postprandial glycemia but may be difficult to maintain long term [11]. The ADA claims that additional evidence to support the glycemic and lipid benefits of low-glycemic index diets is needed [11].

Based on the mounting evidence regarding diet and glycemic control, several generalized dietary recommendations can be made. When possible, low-glycemic index carbohydrates, such as those contained in pasta, should be ingested in favor of high-glycemic index carbohydrates as contained in rice and baked potatoes. A diet rich in monounsaturated fatty acids is recommended in favor of one with a high-carbohydrate content. Glycemic control can also be promoted by spreading of caloric intake throughout the day via regular spacing of meals, and, when possible, through smaller, more frequent meals. For convenience, nutritionally-fortified liquid meal replacements can be substituted for up to two meals per day to enhance compliance. However, it must be noted that any diet designed for the person with type 2 diabetes must be tailored to the needs and requirements of the individual, and it is recommended that the health care provider and the patient develop and monitor the diet in consultation with a dietitian.

5. The role of insulin

Weight gain is associated with a reduction in mean blood glucose concentration and is a feature of insulin use in people with type 2 diabetes [30]. In the UKPDS, treatment groups that received intensive therapy (diet plus insulin or a sulfonylurea) demonstrated significant weight gain relative to the cohort that received conventional dietary therapy alone [8]. Moreover,

patients who received insulin demonstrated a greater weight gain than those on sulfonylureas. Although this weight gain results largely from reversal of hyperglycemia-related glycosuria rather than insulin therapy itself [30,31], most patients will gain some weight following initiation of insulin therapy. Furthermore, the progressive decline in pancreatic beta-cell function associated with type 2 diabetes, when combined with insulin's proven efficacy at achieving glycemic control, suggests that insulin will ultimately play a role in the therapeutic regimens for many people with type 2 diabetes.

Insulin may be taken alone [32] or in combination with oral antidiabetic drugs, including metformin and agents from the sulfonylurea and thiazolidinedione classes [33]. The combination of insulin and oral agents has been shown at times to be more effective than insulin alone at lowering hemoglobin A_{1c} levels [34,35], while also allowing a lower dose of insulin. Such combination therapy is less likely to promote weight gain and hypoglycemia. Combination therapy with metformin is recommended when appropriate in overweight or obese people with type 2 diabetes, as metformin has been associated with less weight gain than other oral agents [35,36]. In contrast, despite lower insulin levels, thiazolidinedione agents may promote fluid retention and encourage weight gain in patients who display a marked improvement in glycemic control [36–38].

Many varieties of insulin are available, from short- and rapid-acting insulins that have an onset of action in 30 min or less, to intermediate-acting insulins such as NPH (isophane), to long-acting insulins such as human ultralente and insulin glargine, the latter providing an almost-constant supply of basal insulin over 24 h [39]. Various combinations of insulins have been compared to minimize hypoglycemic episodes and achieve appropriate postprandial peaks of insulin. A common combination is the once-daily dose of intermediate or long-acting insulin combined with an injection of a rapid-acting insulin before meals. When designing a regimen for an individual patient, the health care provider must consider the relative complexity afforded by the number of daily injections and blood glucose measurements. However, in all cases, the primary goal of insulin therapy is to improve control of blood glucose without promoting hypoglycemia. Once glycemic control has been established,

adjustments of insulin dose may be made to maintain control while avoiding weight gain.

6. Conclusions

The intensive treatment of type 2 diabetes in overweight or obese patients presents many challenges, including establishing glycemic control, controlling weight and plasma lipid levels, and designing compatible, practical treatment regimens. The central component of all treatment plans is a tailored program of medical nutrition therapy. Dietary considerations for a MNT regimen include the use of low-glycemic index carbohydrates and monounsaturated fatty acids, and adherence may be enhanced through the use of fortified meal replacements. In insulin-treated patients, several options are available to manage weight and/or enhance compliance, including combination therapy with metformin, the use of once-daily long-acting insulins, and by ingesting frequent small meals throughout the day. Numerous tools are available to help the patient to achieve a balance between glycemic control and weight management, and the health care provider must teach the patient how to use these tools to promote good health and improve quality of life.

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