The management of obesity in children with type 2 diabetes

Mars Skae

Type 2 diabetes in children and young people is commonly associated with obesity and is increasing in prevalence globally. Weight loss is key to improving glycaemic control and reducing insulin resistance in such individuals, with the potential to reverse the disease. Many therapeutic interventions in children and young people are adapted from interventions used in adults; however, due to a lack of research evidence and concerns in the growing child, clinicians need to consider and adopt a number of evidence-based strategies to tackle the condition. These could include approaches such as calorie capping, low-glycaemic-index foods, eating patterns consistent with circadian rhythms, energy-restriction diets and newer medical therapies, as well as bariatric surgery.

Type 2 diabetes in children and young people (CYP T2D) is becoming an increasing public health concern and continues to increase in prevalence in many countries globally (Pinhas-Hamiel and Zeitler, 2005). In the USA alone, numbers of CYP T2D have doubled between 2001 and 2017 (Lawrence et al, 2021).

CYP T2D is a complex metabolic disorder associated with inadequate glycaemic control due to a mismatch between insulin secretion and the relatively increased demands caused by insulin resistance (Giannini and Caprio, 2012). The increasing rates of CYP T2D have correlated directly with escalating rates in childhood obesity, which is a major risk factor for developing insulin resistance.

In obese individuals, problems with glycaemic control are coupled with impaired insulin secretion (Bacha et al, 2010). CYP T2D, like in adults, is also characterised by an absence of identified autoimmune-triggered islet cell degeneration; nevertheless, it has a multifaceted aetiology linked with genetic predisposition and obesogenic environmental and social factors.

Management intentions

The ultimate management intention in T2D is the normalisation of glycaemic status, with a reduction in HbA_{1c} to a treatment target of 53 mmol/mol (7.0%; Zeitler et al, 2018). In the first instance, lifestyle changes to improve diet and encourage physical activity are recommended to improve glycaemic status.

In T2D associated with obesity, interventions causing a significant net reduction and negative energy balance cause several physiological changes to restore glycaemic control. Weight loss leading to reductions in liver fat content result in normalisation of hepatic insulin insensitivity and can effect normalisation of fasting glucose levels within weeks of treatment (Taylor et al, 2018). Subsequent to this, reductions in pancreatic fat content will lead to restoration of normal first-phase beta-cell insulin secretion, with resultant

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Article points

1. Type 2 diabetes in children and young people (CYP T2D) is a complex metabolic disorder that is linked with obesity in the majority of cases.
2. CYP T2D is caused by a mismatch between a level of impaired insulin secretion and the relatively increased demand for insulin due to insulin resistance.
3. CYP T2D requires intensive dietary strategies to reduce insulin resistance, particularly in postpubertal individuals.
4. Patterns of eating are important to improve glycaemia status and reduce insulin resistance.
5. Setting age-appropriate caloric consumption thresholds (calorie capping) may helpfully underpin some of the dietary principles used to reduce obesity in CYP with T2D.

Key words

- Children and young people
- Obesity
- Type 2 diabetes
- Weight loss interventions

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1. As weight management in those with obesity-driven type 2 diabetes (T2D) is key to improving glycaemic outcomes, creating a negative calorie balance by way of limiting caloric input and maximising caloric burn is key to improving T2D.
2. The use of calorie counting has been traditionally seen as controversial when used in younger cohorts due to concerns around promoting eating disorders; however, it is no different in reality to counting carbohydrates in other forms of diabetes.

normalisation of plasma glucose control over weeks and months (Taylor et al, 2019).

Nutritional interventions for weight loss and improved glycaemic control

In adult-onset T2D, there is a body of evidence that demonstrates that T2D reversal is achievable through significant weight loss, using bariatric surgery, low-calorie diets (LCDs) and carbohydrate restriction (Hallberg et al, 2019). However, all of these interventions are approached with caution in CYP as there are safety concerns about long-term outcomes and growth. It is, therefore, essential that we engage with nutritional principles that relieve the pancreatic burden of insulin production from a scientific perspective, bearing in mind the pre- and post-pubertal status of CYP.

Principles behind calorie management

As weight management in those with obesity-driven T2D is key to improving glycaemic outcomes, creating a negative calorie balance by way of limiting caloric input (through food and drink consumption) and maximising caloric burn (through physical activity) is key to improving T2D. Different food groups have different energy densities, with fat being twice as energy-dense as carbohydrate and protein (1 g fat = 9 kcal; 1 g protein = 4 kcal and 1 g carbohydrate = 3.75 kcal). Therefore, providing individuals with guidance around their daily caloric requirements to discourage excessive caloric intake and create a caloric deficit for weight maintenance or loss is essential. In the Diabetes Prevention Program, calorie capping was the major predictor of weight loss and ultimate reduction in diabetes risk (Hamman et al, 2006).

Energy requirements generally increase up to the age of 15–18 years, with males generally having slightly higher requirements than females due to increased body size and muscle mass. Based on values from the report *Dietary Reference Values for Food Energy and Nutrients for the United Kingdom* in 1991 by the Committee on the Medical Aspects of Food and Nutrition Policy, while accounting for increased sedentary lifestyles of children through the use of screen-based technologies for work, learning and play, a rough age-related guide for setting caloric caps for children is shown in *Table 1*.

Calorie counting has traditionally been seen as controversial when used in the younger cohorts, due to concerns around promoting eating disorders; however, it is no different in reality to counting carbohydrates in other forms of diabetes. In reality, access to calorie information in food labels, particularly for purchased foods and prepared meals, is readily available nowadays, and understanding maximum allowances can help individuals to know exactly how much they can consume in one meal.

The use of paediatric obesity treatment regimens, including calorie restriction, improves self-esteem and body image in the short and medium term. Unsupervised dieting to reduce weight may exacerbate eating disorder risk; however, supervised and structured weight management and weight loss programmes are likely to reduce eating disorder risk for most young people (Jebeile et al, 2019a; Gow et al, 2020).

Table 1. Age-related guide for caloric caps.

Age (years)	Daily energy requirements for boys (kcal)		Daily energy requirements for girls (kcal)	
	Weight maintain	Weight loss	Weight maintain	Weight loss
2–3	1000–1200	1000	900–1100	1000
4–6	1400–1550	1200	1300–1500	1100
7–10	1650–2050	1500	1500–2000	1300
11–13	2100–2400	1800	2000–2200	1500
14–18	2600–3200	2000	2300–2500	1800

Glycaemic index

Insulin response is also dependent on glycaemic index (GI), which is the glycaemic response elicited by a portion of food containing 50 g (or in some cases 25 g) of available carbohydrate. High-GI foods (GI >70 on the glucose scale) are foods containing carbohydrates that are digested, absorbed, and metabolised more quickly; while low-GI foods (GI <55 on the glucose scale) are those containing carbohydrates that are absorbed more slowly, take longer to break down and are processed by the body more slowly. These include most fruits and vegetables, unsweetened milk, nuts, pulses, some wholegrain cereals and bread (Augustin et al, 2015). Lower-GI foods cause slower rises in blood glucose and are weaker drivers for insulin production. Cooking methods and food processing can also alter GI; for example, rolled oats have a higher GI than steel-cut quick-cook oats. The ripeness of a fruit can also increase GI, whereas fibre-rich foods, such as those containing wholegrains, have a lower GI because they act as a physical barrier that slows down the absorption of carbohydrate.

The effects of high-GI foods in driving up blood insulin levels, and eventual resistance to insulin, are thought to induce hunger and overeating. Therefore, lower GI is thought to have a positive effect on obesity through its effect on reducing food consumption and hunger while improving glycaemic responses to food. Several large epidemiological investigations have shown that the combination of low-GI and high-fibre intake reduced T2D risk (Livesey et al, 2019: Chiavaroli et al, 2021). Although there is a lack of data around the efficacy of low-GI diets in CYP, the physiology and evidence for their use in T2D management across all age groups is compelling.

Eating patterns

Patterns of eating are also pivotal to glycaemic status and insulin resistance. Circadian rhythms that inherently affect human and animal biology and behaviours are controlled by the suprachiasmatic nucleus in the hypothalamus, which acts as the "central master clock" in the brain. This signals peripheral circadian clocks in the liver and musculoskeletal system and has an impact on metabolism throughout the day.

In most individuals, insulin sensitivity decreases throughout the day and is lowest during the night, due to circadian patterns in insulin secretion and the suppressive effects of growth hormone, which has increased secretion in the night. Therefore, meals consumed at night are more likely to be associated with greater postprandial glucose and insulin exposure, leading to increased blood glucose levels and risk of type 2 diabetes over time (Panda, 2016; Stenvers et al, 2019). Therefore, in CYP with increased risk of hyperglycaemia, considering the timing of feeding regimens and avoiding overnight feeds is important to prevent driving insulin resistance and hyperglycaemia.

In addition, promoting eating patterns such as time-restricted eating, by ensuring a food-free window of 12–16 hours to encourage a fasted state in the latter half of the day and night, will promote not only weight loss but also better cardiometabolic outcomes. This may dramatically reduce energy intake in the evening and allow a diurnal rhythm of food intake aligned with our biological clocks and lead to improvements in insulin resistance (Melkani and Panda, 2017). Such habits can easily be adhered to by most individuals through bringing forward the timing of the evening meal and delaying the first meal of the next day, hence creating a time-limited food-free window. For example, not eating between 6 pm and 8 am creates a 14-hour fasting window.

Energy-restriction diets

The most aggressive form of energy restriction diet is the very-low-calorie diet (VLCD), which is a form of continuous energy restriction. This can result in significant improvements in glycaemic control and lead to full remission of T2D without the need for surgical interventions such as bariatric surgery. VLCDs are hypocaloric diets that limit daily caloric intake to 400–800 kcal/day. These are usually used for a maximum duration of 12–16 weeks, primarily to cause weight loss. There is a wide range of VLCD protocols, which causes variability in known data on the efficacy and longitudinal outcomes of VLCDs in T2D remission (Juray et al, 2021). However, a systematic review of such studies

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2. Patterns of eating are pivotal to glycaemic status and insulin resistance.
3. The most aggressive form of energy-restriction diet is the very-low-calorie diet, which is a form of continuous energy restriction. This can result in significant improvements in glycaemic control and lead to full remission of type 2 diabetes.

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1. A less aggressive energy-restrictive approach is intermittent energy restriction.
2. Pharmacological treatments for obesity alone have historically been limited; however, some newer therapies such as GLP-1 analogues are now being used in some children with type 2 diabetes.
3. Other type 2 diabetes treatments for adults, such as SLGT2 inhibitors, are not licensed for use in children.
4. Although seen as an extreme method of obesity control, metabolic bariatric surgery should be considered in children and young people with severe obesity who are not responding to standard therapeutic interventions in order to reduce weight and improve glycaemic control.

indicated a mean reduction in HbA_{1c} of 1.4% (range, 0.1–3.1%; Sellahewa et al, 2017).

While this is suitable in adults, there is caution around using such interventions in CYP due to concerns around effects on growth and mental health, particularly in relation to eating disorders. Nevertheless, there is growing evidence of the positive efficacy of VLCDs in CYP with weight loss as great as 30.4 kg at 5 months (Andela et al, 2019).

VLCDs are associated with several side effects, albeit fairly minimal. These include fatigue, hunger, dizziness and headache. There is a paucity of data, however, on the long-term effects on the growing child and a need to investigate the use of VLCDs in the prepubertal child and postpubertal adolescent who has completed growth (Sothern et al, 2000; Andela et al, 2019). In general, when calculating caloric requirements in CYPs, the general principle of reducing the total caloric cap by 25–30%, which is consistent with a low-calorie diet (LCD), may be more suitable. Nevertheless, if this approach is to be adopted, it must be used in a research setting or adopted with caution.

A less aggressive approach to energy restriction is intermittent energy restriction. This approach involves intermittent fasting and is another nutritional intervention for treatment of obesity. Jebeile et al (2019b) reported that BMI changes achieved at 26 weeks were -5.1 ± 1.9 kg/m^2 (P=0.013) compared with baseline. This approach involves using a LCD approach on 2–3 days a week by extending the fasting window on those days, so that only one, or at the most two, small meals are consumed, with adherence to the caloric target set. On the remaining days, an individual is allowed to eat their normal food intake.

In adult studies, remission rates of T2D using calorie restriction are reported to be similar to those reported in bariatric surgery, provided a weight loss of >10% of total body weight is achieved (Jacob and Avery, 2021). Intermittent energy restriction, however, has demonstrated equivalent effects in weight loss to continuous energy restriction (such as VLCDs), with 5% body weight loss achieved over a similar time course, with superior improvements in insulin resistance and lipidaemia in intermittent energy restriction regimens (Antoni et al, 2018; Rynders et al, 2019).

Medical interventions for weight loss and improvement in glycaemic status

In the UK, traditionally metformin has been the mainstay of treatment of CYP T2D. The use of subcutaneous insulin in CYP T2D is generally reserved for those initially presenting with ketoacidosis or ketonuria, or those with a persistent higher glycaemic status (HbA_{1c} >53 mmol/mol [7.0%]) despite metformin therapy for 16 weeks (Zeitler et al, 2018).

Pharmacological treatments for obesity alone have been limited to no more than orlistat, a fat uptake inhibitor, according to NICE (2014) obesity guidance; however, newer therapeutic agents are becoming available for treating both obesity and T2D in CYPs. These agents require further evaluation but appear to demonstrate good efficacy for tackling both obesity and hyperglycaemia.

Newer therapies include glucagon-like peptide-1 (GLP-1) receptor agonists. GLP-1 is a hormone belonging to the incretin family, which connects the stimulation of the gastrointestinal system through glucose ingestion to insulin release. GLP-1 is released from L-cells in the intestine in response to the ingestion of food and enhances glucose-stimulated insulin secretion. In addition to its insulin–glucoregulatory mechanisms, activation of GLP-1 receptors regulates appetite and caloric intake, and delays gastric emptying while promoting weight loss (Page and Freemark, 2020). GLP-1 analogues, such as liraglutide, have been demonstrated to reduce HbA_{1c} by 0.72% in prediabetes and 0.30% in T2D in young people. Treatment effects pertaining to weight are also seen, with BMI z-score reduction as great as 0.22 SDs in adolescents. Adverse effects have generally been reported to include gastrointestinal symptoms and minor hypoglycaemic episodes (Page and Freemark, 2020; Chadda et al, 2021). In the US, liraglutide is approved for the treatment of T2D in ages 10 years and older.

Other T2D treatments in adults such as sodium–glucose cotransporter 2 (SLGT2) inhibitors are not licensed for use in children. Nevertheless, there is promise of potential dual gastric inhibitory polypeptide (GIP)/GLP-1 receptor agonists, known as a "twincretins", that are on the horizon for the treatment of obesity and T2D in the near future and which may bring potential further therapies for paediatric patients.

Surgical intervention

Although it is seen as the more extreme end of intervention for obesity, metabolic bariatric surgery is currently the most successful strategy for significant and sustained weight loss and improvement of associated comorbidities in CYP with morbid obesity. Roux-en-Y gastric bypass and vertical sleeve gastrectomy are the most commonly performed forms of bariatric surgery in CYP (Bolling et al, 2019). Current data demonstrate that surgery has the greatest efficacy in terms of significant weight loss (pooled estimate, 14.04 kg/m^2) and achieves this in relatively short periods of time (Selvendran et al, 2018). Nevertheless, there is a growing body of evidence for new treatments and dietary strategies that may change opinion in years to come. Due to the invasiveness of bariatric surgery and its associated risks and long-term complications, all other weight loss routes should be considered before opting for this treatment.

Nevertheless, due to the rapid decline in beta-cell mass in T2D CYP (as much as 4% per month; Dabelea et al, 2012), metabolic bariatric surgery should be considered in CYP with severe obesity who are not responding to standard therapeutic interventions to reduce weight and improve glycaemic control. ■

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