The challenge of adolescence: hormonal changes and sensitivity to insulin

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Puberty is a period of rapid and radical physical, psychological and social change during which a child, in physiological terms, becomes an adult capable of reproduction. Adolescence refers as much to the psychosocial characteristics of development during puberty as to the physical changes. Adolescents with diabetes, who need to adhere to a complex medical regimen based around self-care throughout this period of development, face a series of particular and considerable challenges. In this article, Hala Tfayli and Silva Arslanian look at the hormonal, metabolic and behavioural changes that impact on diabetes care during the years of puberty, and outline strategies that could help young people to achieve good glycaemic control, and thus protect their health and well-being into adulthood.

The difficulties involved in maintaining good blood glucose control during adolescence were reflected in the findings of the Diabetes Control and Complications Trial (DCCT). In both the intensive and the conventional treatment groups, adolescents had 1% higher average long-term blood glucose levels (measured by HbA_{1c}) compared with the adults, despite similar therapeutic approaches – and despite receiving higher doses of insulin (units per kg of body weight).[1] This worsening in metabolic control is due to both physiological and behavioural changes.

Physiological insensitivity to insulin

Studies have demonstrated that insulin levels are higher during puberty than they are during adulthood or the years preceding puberty.[2] The direct evidence of this pubertal insensitivity to insulin became apparent only after experiments which measured *in vivo* insulin sensitivity.[3,4]

A decrease in insulin-stimulated glucose uptake in healthy adolescents compared with pre-pubertal children was demonstrated for the first time in the 1980s. While this effect is exaggerated in children with type 1 diabetes,[3] in children without diabetes, whose pancreatic beta cells function normally, puberty-related insensitivity to insulin is compensated by an increase in insulin secretion.[4]

Healthcare professionals should be aware of the evolution of insensitivity to insulin during puberty in children with type 1 diabetes, and appropriately increase insulin doses in order to prevent any deterioration in blood glucose control. Recently, a large cross-sectional study of children without diabetes found insensitivity to insulin to be lowest at age 12 to 14 years (Tanner stage 3 of puberty) in both sexes, and across ethnic groups, returning to almost pre-pubertal levels in young people above 16 years of age (Tanner 5).[5]

The cause of insensitivity to insulin during puberty has been under investigation. The major hormonal changes that are associated with the onset of puberty include a two-fold increase in the secretion of growth hormone and an increase in the sex steroids that lead to the development of secondary sexual characteristics, remarkable increase in height, and change in body composition. Thus, both growth hormone and sex steroids are likely hormonal candidates for inducing insensitivity to insulin during puberty.

However, while pubertal insensitivity to insulin is transient, in adulthood, the increasing levels of sex steroids remain elevated and insensitivity to insulin subsides. On the other hand, the secretion of growth hormone increases during puberty. Once the pubertal growth spurt is completed, growth hormone levels decline. Moreover, growth hormone is known to be an important factor in reducing insulin sensitivity – through several effects that are shared between insulin and growth hormone.

We now know that insulin-stimulated glucose metabolism correlates negatively with growth hormone and/or levels of insulin-like growth factor-1.[3,5,6] Additionally, a correlation between speed of growth and an increase in fasting serum insulin has been reported in pubertal adolescents without diabetes. Our studies show that the metabolic characteristics of pubertal insensitivity to insulin are decreased glucose oxidation and increased free fatty acid oxidation – known as the Randle cycle.[6,7] Thus, increased growth hormone secretion during puberty leads to increased breakdown of fat in fat cells (lipolysis) and increased flux of free fatty acids. These compete with glucose for glucose oxidation, resulting in decreased glucose uptake and insensitivity to insulin.

The question remains as to the significance of these physiological changes in metabolism and insulin sensitivity for children with type 1 diabetes. Deteriorating diabetes control in adolescents was thought to be merely the result of the behavioural and psychosocial factors that are characteristic in teenage years. However, it is now apparent that during puberty, insulin action decreases by between 30% and 50% – an important factor which may contribute to poor glycaemic control.

Therefore, healthcare providers working with children with type 1 diabetes should be aware that insulin requirements increase by between 30% and 50% during puberty, and unless this is appropriately addressed, a child's blood glucose control and HbA_{1c} levels will deteriorate. In our diabetes clinic, the average daily dose of insulin in pre-pubertal children is between 0.8 and 1.0 units/kg/day, while in adolescents it is between 1.2 and 1.4 units/kg/day. The Hvidore Study Group on Childhood Diabetes, which includes 18 countries in Europe and North America, and Japan, revealed a sharp increase in insulin requirements during pubertal years, particularly in girls with type 1 diabetes.[8]

Behavioural and psychosocial changes

In addition to the hormonal and metabolic changes that are characteristic of puberty, adolescence is associated with rapid behavioural changes that may impact on diabetes control. Adolescent behaviour typically involves challenging of authority figures, non-conformity, efforts at establishing autonomy, rebellious and pleasure-seeking behaviour, privacy, and heightened awareness of self-image and peer pressure, and the emergence of eating disorders in some girls.[9] This process of maturation both affects and is affected by the presence of a chronic illness like diabetes.

Adolescents with a chronic disease have generally been found to be at increased risk for depression, anxiety, and low self-esteem. In a number of studies, adolescents with type 1 diabetes have been found to suffer from anxiety and depression.[10] The prevalence of depression in young people with diabetes is reported to be two- to three-fold higher compared with their peers without diabetes. The combination of depression and diabetes in children and especially adolescents has serious consequences, including increased rates of suicide or suicidal tendencies, making diabetes management and self-care extremely difficult.

Lifestyle, diet, and exercise habits also tend to change during puberty. The Health and Behaviours in Teenagers Study

(HABITS), a school-based study in the UK, evaluated the association between puberty, smoking, food, and exercise. In both boys and girls, being more pubertally advanced was associated with a higher likelihood of smoking. In boys, puberty was linked to a less healthy diet, but higher levels of exercise; in girls, there was little association with either diet or exercise. Such findings constitute important barriers to achieving adequate blood glucose control.

Responding to the changes in puberty

Since the results of the DCCT were published in 1993, it has become widely accepted that good blood glucose control delays the onset and slows the progression of diabetes eye damage, nerve damage, and kidney disease. In order to maintain optimal glycaemic control, health professionals who provide care to children with diabetes during puberty should tailor therapy to counterbalance behavioural changes and physiological reductions in insulin sensitivity.

Children who are going through puberty require increased daily insulin. Diabetes outcomes are linked to the degree of adherence to medical regimens, blood glucose monitoring, and meal plans. Involving adolescents in decision making regarding the insulin regimen that best suits their daily schedules, meal plans, and exercise and sleep habits is potentially beneficial. Gradual transition of the responsibility to self-care from the parent(s) to the child is important.

A continued role for parents in providing collaborative support is associated with optimal health outcomes. Parents can also help prevent depressive symptoms by providing support and guidance, and encouraging positive coping strategies. Routine assessment and interventions to treat depression among adolescents with diabetes is strongly recommended; screening for anxiety and eating disorders may be necessary in certain situations.

Conclusions

In summary, the turbulent adolescent years are characterized by important hormonal, metabolic and psychological changes which impact on the management of type 1 diabetes. It is imperative that the healthcare team is aware of these changes. The decline in insulin sensitivity requires appropriate readjustment of insulin doses in order to prevent deterioration in blood glucose control. Psychosocial changes must be monitored in order to identify any depressive symptoms or behavioural problems, and provide supportive therapy and appropriate referral.

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