Paediatrics

Managing weight gain and metabolic risk in children taking antipsychotic medication

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The prevalence of overweight and obesity is increased in children and young people with learning disabilities: one study of autistic children found that 30.4% were obese compared to 23.6% of children without autism (Curtin et al, 2010). The aetiology is likely to be complex with genetic and environmental risk factors being important.

Second generation antipsychotics (SGA) are increasingly being prescribed to manage aggressive and disruptive behaviours that are not uncommon in children with learning disabilities. Medications such as risperidone are used in certain clinical scenarios such as aggression in conduct disorders, autism and attention deficit hyperactivity disorder yet most SGA are not licensed in children so data regarding both short- and long-term safety are sparse.

A recent systematic review (De Hert et al, 2011; summarised alongside) has examined the metabolic side-effects of SGA. The paper was limited by a lack of good-quality studies of significant numbers of subjects. Yet the data do highlight a number of significant metabolic or endocrine side-effects and a hierarchy of risk. Using a pooled analysis, the mean weight gain during short-term studies (with an average duration of 8 weeks) varied from 0.5±0.5 kg for ziprasidone, 1.0±0.6 kg for aripiprazole, 2.4±0.9 kg for risperidone and 3.8±0.5 kg for olanzapine.

The mechanisms of weight gain are not completely understood but may include disease-related factors such as changes (improvements) in appetite or drug-related factors (for example, changes in metabolism). Interestingly, the data did suggest that weight gain was likely to be greater in those with a lower BMI at baseline but there does not appear to have been a study that has examined the metabolic effects of SGA in children and young people who are overweight or obese when first started on antipsychotic medication.

Although there is no universally accepted definition of metabolic syndrome in childhood, using the IDF criteria for children (Zinmet et al, 2007) the odds of developing metabolic syndrome was three times greater in those young people started on second- versus first-generation antipsychotics. The development of type 2 diabetes has also been described although it is rare and it is not clear if it may or may not be reversible on discontinuing treatment. Therapies that have been used to mediate weight gain when on SGA include orlistat, topiramate, sibutramine and metformin, but only two out of 32 studies from another review (Maayan et al, 2010) were performed in children. There appears to be no consensus in terms of screening or management of these people with complex needs.

What is striking from this review is the rapid weight gain that can occur in some of these young people over a short period of time. Weight change is difficult in most young people with significant overweight or obesity, and the added complications of a significant psychiatric disorder and antipsychotic treatment is very daunting. Although it may be difficult to manage weight in this scenario it would seem prudent to consider suitable strategies for monitoring and managing metabolic risk and could be a rewarding area of research.

Curtin C, Anderson SE, Must A, Bandini L (2010) The prevalence of obesity in children with autism: a secondary data analysis using nationally representative data from the National Survey of Children's Health. *BMC Pediatr* **10**: 11

Maayan L, Vakhrusheva J, Correll CU (2010) Effectiveness of medications used to attenuate antipsychotic-related weight gain and metabolic abnormalities: a systematic review and meta-analysis. *Neuropsychopharmacology* **35**: 1520–30

Zimmet P, Alberti G, Kaufman F et al (2007) The metabolic syndrome in children and adolescents. *Lancet* **369**: 2059–61

EUROPEAN PSYCHIATRY

Weight gain in children using second-generation antipsychotics

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 In this systematic review, the authors critically evaluated the literature on cardiometabolic and endocrine side-effects of second-generation antipsychotics (SGA) in children and adolescents.

2 A total of 31 randomised, placebo-controlled trials of SGA in children aged <18 years until February 2010 were identified, including 3595 participants.

3 A review of these data confirmed that SGA are associated with cardiometabolic and endocrine side-effects.

4 Further analysis of weight change data from 24 trials of 3048 participants showed that ziprasidone was associated with the lowest weight gain (−0.04 kg; 95% confidence interval [CI], 1.17–1.69), followed by aripiprazole (0.79 kg; 95% CI, 0.54–1.04).

5 Intermediate weight gain was associated with quetiapine (1.43 kg; 95% CI, 1.17–1.69) and risperidone (1.76 kg; 95% CI, 1.27–2.25). Olanzapine was associated with the most weight gain (3.45 kg; 95% CI, 2.93–3.97).

6 In participants with an autistic disorder who were also younger and had less previous exposure to antipsychotics, significant weight gain was more prevalent.

7 The authors concluded that the least cardiometabolically problematic SGA should be used first whenever possible.

De Hert M, Dobbelaere M, Sheridan EM et al (2011) Metabolic and endocrine adverse effects of second-generation antipsychotics in children and adolescents: A systematic review of randomized, placebo controlled trials and guidelines for clinical practice. *Eur Psychiatry* **26**: 144–58

DIABETOLOGIA

Seasonal changes in HbA~1c~ level in children are associated with weather conditions

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

1 The association of weather conditions with seasonal changes in HbA_{1c} was assessed in 589 children ≥7 years of age and in 88 children ≤7 years of age with T1D.

2 A total of 3935 HbA_{1c} readings from a 3-year period or longer were analysed in children with T1D who were <18 years of age and had a diabetes duration of >12 months. The readings were then correlated with measures of weather conditions (such as temperature and hours of sunshine).

3 Patterns of metabolic control and meteorological data were evaluated using Spearman rank correlation after comparison of autocorrelation patterns.

4 Mean HbA_{1c} level over the whole study period was 7.65±1.12% (60±12 mmol/mol) with highest levels observed in winter and lowest in summer. Differences consistently exceeded 0.44% (4.8 mmol/mol).

5 In the children aged ≥7 years, HbA_{1c} level had a strong negative correlation with ambient temperature ($R=-0.56$; $P=0.0002$) hours of sunshine ($R=-0.52$; $P=0.0007$) and solar irradiance ($R=-0.52$; $P=0.0006$) but not in children aged ≤7 years ($P≥0.29$ for each correlation).

6 The authors concluded that seasonal changes in HbA_{1c} in children are significant enough to be taken into consideration when using HbA_{1c} levels in clinical trials or for diagnosis of diabetes.

Mianowska B, Fendler W, Szadkowska A et al (2011) HbA(1c) levels in schoolchildren with type 1 diabetes are seasonally variable and dependent on weather conditions. *Diabetologia* **54**: 749–56

JOURNAL OF PEDIATRICS

Growth failure in children with coeliac disease and T1D

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

1 This multicentre survey aimed to evaluate the influence of biopsy-proven coeliac disease on development and metabolic parameters in children with T1D.

2 Data were collected from 297 centres in Germany and Austria between 1995 and 2009, which included 41 951 people with T1D aged <20 years.

3 The prevalence of biopsy-proven coeliac disease increased over time (from 0.6% in 1995 to 1.3% in 2008).

4 The standard deviation score for weight and height were significantly lower in people with coeliac disease compared with people without ($P<0.001$ for both).

5 The authors concluded that it is important to screen for coeliac disease in children with T1D to prevent growth failure.

Fröhlich-Reiterer EE, Kaspers S, Hofer S et al (2011) Anthropometry, metabolic control, and follow-up in children and adolescents with type 1 diabetes mellitus and biopsy-proven celiac disease. *J Pediatr* **158**: 589–93

DIABETES TECHNOLOGY & THERAPEUTICS

Overnight closed-loop is feasible in young children

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓✓

1 Automated overnight closed-loop glucose control (AOCL) was evaluated in eight children (mean age, 9.4±2.7 years) with T1D.

2 At a clinical research facility on two separate occasions, participants had a meal at 18:00 and a snack at 21:00 both with a prandial insulin bolus.

3 Participants randomly started AOCL at 18:00 on one occasion and 21:00 on another occasion and the AOCL ran until 08:00 the next day.

4 Time spent with plasma glucose levels in the target range (3.9–8.0 mmol/L) was 50.7% and it did not differ on the two occasions (42% vs 58%; $P=0.093$).

5 The authors concluded that AOCL is feasible in young children and results were comparable on both occasions.

Elleri D, Allen JM, Nodale M et al (2011) Automated overnight closed-loop glucose control in young children with type 1 diabetes. *Diabetes Technol Ther* **13**: 419–24

LANCET

Results of phase III trial of teplizumab

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 An antibody that may preserve beta-cell function has been trialled in 516 people with T1D who randomly received either a 14-day full dose, 14-day low dose, 6-day full dose or placebo.

2 The primary composite outcome (the percentage of people with insulin use of <0.5 U/kg per day and an HbA_{1c} level of <6.5% [<48 mmol/mol] at 1 year) did not differ between groups in year 1.

3 Of those taking teplizumab, 5% were not taking insulin at 1 year compared with none in the placebo group ($P=0.03$).

4 Analysis showed that among children aged 8–11 years and those randomised within 6 weeks of diagnosis, the proportion of participants who achieved an HbA_{1c} level of <7% (<53 mmol/mol) and used <0.25 units/kg/day was greater in the 14-day full dose group compared with placebo.

5 The authors concluded that immunotherapeutic intervention might be most effective if targeted in people who have recently been diagnosed or in children.

Sherry N, Hagopian W, Ludvigsson J et al (2011) Teplizumab for treatment of type 1 diabetes (Protégé study): 1-year results from a randomised, placebo-controlled trial. *Lancet* **378**: 487–97

> "*The authors concluded that seasonal changes in HbA~1c~ in children are significant enough to be taken into consideration when using HbA~1c~ levels in clinical trials or for diagnosis of diabetes.*"