Severe weight gain in 2 boys treated with risperidone

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Abstract:

Weight gain is a frequent side effect of treatment with atypical antipsychotics in adults as well as in children, but the prevalence and severity are still far underestimated. We here report on 2 boys who developed severe overweight during treatment with risperidone. An 8.5 years old boy more than doubled his weight during 4 years of treatment with risperidone resulting in a BMI increase from 17.0 kg/m² (+ 0.6 SDS) to 29.6 kg/m² (+ 2.9 SDS) at the age of 12.4 yrs. A 12.3 years old boy, treated since the age of 9.1 years with risperidone, also doubled his weight during 3 years of treatment with an increase in BMI from 16.4 kg/m² (+ 0.1 SDS) to 26.0 kg/m² (+ 1.9 SDS). Auxological and metabolic parameters should carefully be followed-up in all children treated with atypical antipsychotics and weight stabilising or reducing actions should be taken as soon as indicated.

Keywords:

atypical antipsychotics – obesity – risperidone – weight gain

Introduction

Atypical or second-generation antipsychotic medications, amongst which risperidone, are increasingly prescribed to children and adolescents with neuropsychiatric disorders [1, 2]. Their use has been associated with various health risks including obesity, diabetes mellitus, and dislipidemia [2, 3, 4]. The seriousness of these potential side-effects is, however, often underestimated and the recommended monitoring of these children neglected. We here report on 2 boys who developed overweight during treatment with risperidone and stress the severity of the weight gain.

Case reports

Case 1

This boy was initially referred to the paediatric endocrinologist at the age of 5.9 years because of short stature. He is the 2nd child of healthy parents (father's height: 170.5 cm (- 1.5 SDS); BMI: 37.8 kg/m²; mother's height: 147.0 cm (- 3.3 SDS); BMI: 27.8 kg/m²). The family history reports overweight at the paternal side, but is negative for diabetes mellitus or other obesity related diseases. The patient was born at the gestational age of 36 weeks with a birth weight of 2800 g (+ 0.1 SDS) and length of 49.5 cm (+ 0.8 SDS). At the age of 5.9 yrs his height was 99.8 cm (- 3.4 SDS [5]) and his weight 15.8 kg (- 2.4 SDS); BMI = 15.8 kg/m² (+ 0.3 SDS). All biochemical and hormonal tests were normal. The diagnosis of familial short stature was withheld. The patient was seen yearly at the outpatient clinic. Height followed the – 3.4 SD line and weight the – 2.0 SD line.

At the age of 8.5 yrs (height: 112.3 cm (- 3.6 SDS); weight: 21.4 kg (- 2.0 SDS); BMI: 17.0 kg/m² (+ 0.6 SDS)) the boy developed behaviour problems (aggression, psychosis). Treatment with risperidone (2 mg/day) was started by the child psychiatrist. After the start of risperidone appetite increased tremendously and the boy showed a rapid weight gain. Over 4 yrs his weight more than doubled to 54.4 kg (+ 1.1 SDS) at the age of 12.4 yrs. Height increased to – 2.6 SDS and BMI increased to 29.6 kg/m² (+ 2.9 SDS; severe obesity according to the IOTF criteria [6]) (Fig. 1a). An extensive evaluation could not retrieve any metabolic or endocrine disorder (fasting glucose: 86 mg/dl; insulin: 15.3 µU/ml; free T4: 0.9 ng/dl; TSH: 5.3 mIU/L; total cholesterol: 183 mg/dl; triglycerides: 135 mg/dl; ASAT: 25 U/l; ALAT: 21 U/l). The diagnosis of iatrogenic obesity due to risperidone use was withheld. Dietary advice was given and the psychopharmacological treatment was changed to quetiapine, clotiapine, and valproate. Following these changes the weight decreased to 49.6 kg (- 0.3 SDS) and BMI decreased to 23.6 kg/m² (+ 1.6 SDS) (Fig. 1a).

Case 2

This boy was referred at the age of 12.3 yrs by the child psychiatrist for the evaluation of overweight. The family history is negative for overweight and overweight related diseases. At the age of 6.5 yrs (height: 117.0 cm (- 0.8 SDS); weight: 22.4 kg (0.0 SDS); BMI: 16.4 kg/m² (+ 0.6 SDS)) attention deficit disorder was diagnosed and treatment with methylphenidate was started. During the following years growth decreased slowly. At the age of 9.1 yrs (height: 127.0 cm (-1.5 SDS); weight: 26.5 kg (- 0.8 SDS); BMI: 16.4 kg/m² (+ 0.1 SDS)) the boy developed a disruptive behaviour disorder with aggression and treatment with risperidone (2 mg/day) was started. During the following 3 yrs his weight doubled to 54.6 kg (+ 1.2 SDS) at the age of 12.3 yrs, while his height increased normally to 145.0 cm (- 1.3 SDS) resulting in a BMI of 26.0 kg/m² (+ 1.9 SDS; obesity according to IOTF criteria) (Fig. 1b). The laboratory evaluation could not reveal any metabolic or hormonal abnormalities (fasting glucose: 90 mg/dl; free T4: 1.0 ng/dl; TSH: 2.6 mIU/L; total cholesterol: 178 mg/dl; triglycerides: 79 mg/dl; ASAT: 30 U/l; ALAT: 27 U/l). The patient did no return after the initial evaluation and further follow-up data are not available.

Discussion

Overweight and obesity are serious health problems in children affecting respectively 15 and 3 % of the pediatric population [7]. Most of the cases are due to an unhealthy lifestyle and no underlying disease can be found by routine endocrine and metabolic evaluation. We here reported on 2 normal weight boys who developed severe overweight during treatment with risperidone, an atypical antipsychotic drug.

Prescription of atypical antipsychotics, mainly risperidone, has become a widely accepted practice in the treatment of children and adolescents with psychotic disorders and other neuropsychiatric conditions [1, 2]. In Belgium, risperidone figures in the top 10 of most prescribed drugs in school-aged children [2]. Atypical antipsychotics have less neurological side effects (e.g. extrapyramidal symptoms, tardive dyskinesia) but there is concern about metabolic side effects as weight gain (including obesity), hyperglycaemia (including diabetes mellitus), and dislipidemia [2, 3, 4]. Pronounced weight gain early in life and changes in glucose levels and lipid profiles may have ominous long-term health implications [4]. In our patients the investigations did not reveal any disturbances in the glucose or lipid metabolism, probably due to the relatively short duration of the obesity.

Several mechanisms contribute to the weight gain induced by atypical antipsychotics: appetite stimulation, excessive fat deposition and adipocyte hyperplasia, and to a lesser extent reduced energy expenditure [8, 9]. It is hypothesized that atypical antipsychotics interfere with the appetite regulating system by interrupting the pathways between peripheral signals from the fat tissue and the gastrointestinal tract, and the hypothalamic appetite controlling centres [9]. There is, however, a large interindividual variability: some patients do not gain weight, whereas other become rapidly severely obese [10]. Genetic and non-genetic factors play a role in this variability [11]. Among the genetic factors polymorphisms of the serotonin 5-hydroxytryptamine (5-HT2C) receptor and leptin genes have been reported to play a crucial role [12]. Among the non-genetic factors it has been shown that familial obesity, lower baseline body weight, younger age, male gender and longer treatment are associated with larger body weight gain [11].

Hence, careful monitoring of weight and metabolic parameters is mandatory in all children and adolescents before and after prescription of atypical antipsychotics. Drugs which potentially cause weight gain should be avoided in overweight patients. Consensus guidelines (Table) have been developed as to how patients should be monitored

for the development of metabolic adverse effects [13, 14] but it is not known whether clinicians who prescribe these medications to children and adolescents adhere to these guidelines. Therapeutical strategies for the management of drug-induced obesity include life style changes and pharmaceutical intervention [10]. Eating habits and daily activities should be targeted as they may also have a significant impact on overall health. However, children and adolescents with mental health problems often have multiple risk factors, including poor nutrition and inadequate exercise, and have lack of compliance with behavioural interventions. Short-term trials with metformin, an insulin sensitiser, showed that this drug was effective in abrogating weight gain, decreased insulin sensitivity and abnormal glucose metabolism resulting from treatment with atypical antipsychotics [10, 15]. More long-term studies are needed to evaluate the efficacy of this medication.

In conclusion, in this era of obesity epidemics we have to be very careful with the use of new psychopharmaca, which can cause iatrogenic overweight. A careful cost-benefit analysis needs to accurately gauge both short-term and long-term risks. Auxological and metabolic parameters should carefully be followed-up in all children treated with atypical antipsychotics and weight-reducing strategies should start as soon as possible.

Acknowledgements

This study was supported by a grant from the Belgian Study Group for Paediatric Endocrinology.

Table Monitoring protocol for patients on atypical antipsychotics (adapted from references 13 & 14).

	baseline	4 weeks	8 weeks	12 weeks	quarterly	annually
Personal/ family history	X					X
Weight (BMI)	X	X	X	X	X	X
Waist circumference	X					X
Blood pressure	X			X		X
Fasting blood glucose	X			X		X
Fasting lipid profile	X			X		X

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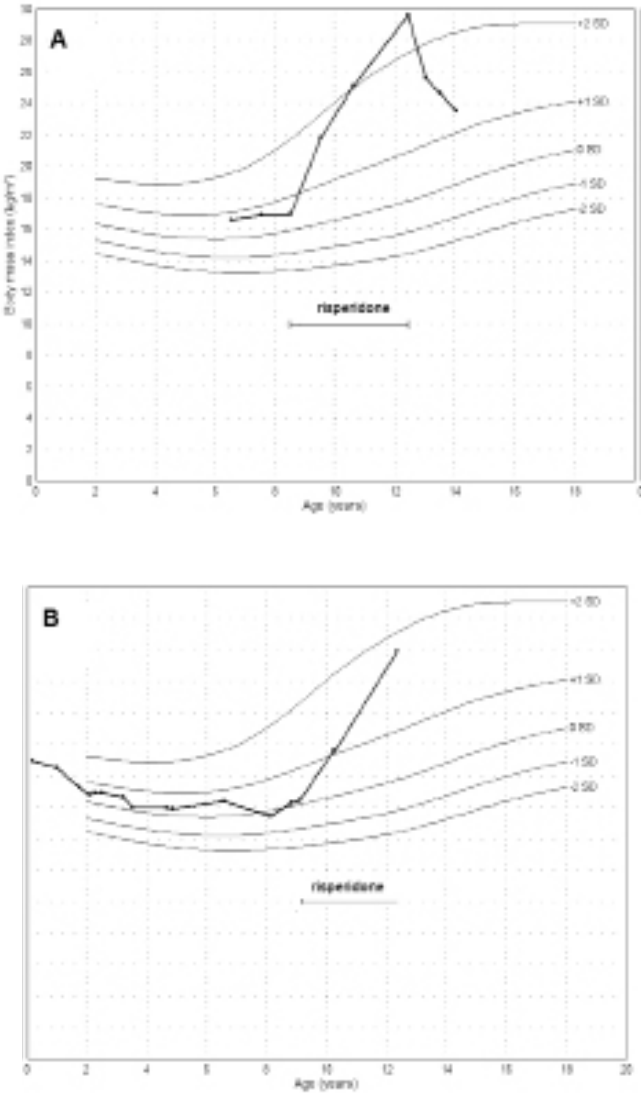

Figure 1: Evolution of BMI in 2 boys before, during (and after) treatment with risperidone. SD-lines represent BMI references for flemish boys [5]