Weight gain and metabolic side effects with antipsychotic drugs in children
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Background
Weight gain and metabolic side effects are some of the most troublesome side effects of atypical antipsychotics, especially when used in children and adolescents. There have been few studies on these side effects in children in Arab countries.

Objectives
To determine weight gain and metabolic side effects in a group of children and adolescents on antipsychotic drugs (APDs) and to compare different group of atypical antipsychotics and typical APDs in terms of these side effects.

Methods
Sixty-four patients younger than 18 years of age with different psychiatric diagnoses and different types of APDs were assessed in terms of weight, height, BMI at the start of the study, and then after 3 and 6 months. Estimation of the BMI \(z\)-score and metabolic profile including fasting blood glucose, fasting lipid profile, and liver transaminases was carried out.

Results
Significant weight gain and increase in BMI were found after 6 months (mean 3.5 ± 3 and 1.7 ± 1.2, respectively). In addition, 50% of our patients were either overweight or obese and 4.7% fulfilled the criteria of metabolic syndrome and 46.9% had one to two symptoms of metabolic syndrome. Weight gain was more common at a younger age and metabolic side effects were associated significantly with obesity. Although olanzapine led to the greatest weight gain 6.1 ± 5.6 kg, there were no significant differences in weight gain and metabolic side effects between different drugs.

Conclusion
All groups of APD showed significant weight gain and increase in BMI; in addition, obesity was associated significantly with metabolic side effects. Therefore, prescription of APD to children should be revised and done only by professional child psychiatrists, with careful monitoring of weight and metabolic profile.

Keywords:
APD, in children, metabolic syndrome, weight gain

Introduction
The use of atypical antipsychotic (AAP) drugs has increased in the last decade such that it is gradually replacing typical antipsychotics such as haloperidol, aiming for better tolerance and a more benign side effect profile. In a recent Canadian survey of child psychiatrists and developmental pediatricians [1], 12% of all AAP prescriptions were for children 8 years of age and younger, which is of particular concern. However, in adults, there has been a clear link between AAPs and metabolic adverse effects for some time. Many studies in adults confirm that AAPs can precipitate weight gain [2], hyperlipidemia [3], and insulin resistance [4], and that their use is associated with the development of metabolic syndrome [5,6] and type 2 diabetes [7,8]. There have been recent reports [9,10] of similar metabolic effects in children and adolescents. Meanwhile, the third National Cholesterol Education Program Adult Treatment Panel (ATP III) [11] defines the metabolic (or insulin resistance) syndrome as the presence in an individual of at least three of the following five risk factors: central or abdominal obesity, hypertriglyceridemia, hypertension, low high-density lipoprotein (HDL) cholesterol, and high fasting blood glucose (FBG) levels. However, there is no agreement on the definition of the metabolic syndrome as a whole in children. Some researchers use definitions that follow the ATP III guidelines (having at least three of five components) [12,13], whereas others have included an elevated fasting insulin level as a component of the syndrome [14]. Central obesity, which is considered a key component of the metabolic syndrome, is a good example of the problem of defining risk levels in children. Although there are accepted risk cut points for waist circumference in adults, there are no accepted normative values for children. Some researchers have used the BMI \(z\)-score, a measure of overall overweight, rather than a more specific indicator of central overweight, such as waist circumference [15]. Recently, there have been a few FDA-approved indications for some of the typical and
AAP drug; although recently, many of AAPs prescriptions to youth may lack evidence. This raises the importance of the fact that child and adolescent psychiatrists should be aware of the possible serious metabolic side effects of these drugs on young children, and indicates the importance of monitoring of our patients for possible side effects. In developing countries, the situation is more serious because of lack of information gathered from local researches on the possible side effects of these drugs and insufficient monitoring because of the shortage of resources in many areas. This is why we tested the hypothesis that, similar to developed countries, AAP drug may predispose to weight gain and serious metabolic side effects in children. Therefore, our objectives were to describe the pattern of weight gain and metabolic side effects in a group of children and adolescents who took antipsychotic drug (APD) in a naturalistic setting and also to compare those side effects between different groups of APDs.

Methodology

This study was a prospective naturalistic study carried out in Al Aml Complex of Mental Health in Saudi Arabia in the period between December 2009 and June 2010. Patients were recruited from the Child Psychiatry Outpatient Clinic with the following inclusion criteria:

1. age younger than 18 years;
2. patients on any type of APD or had decided to use APD for at least 6 months;
3. any diagnosis.

The exclusion criteria were as follows:

1. age older than 18 years;
2. did not use APD;
3. any medical illness that may affect weight or metabolic profile secondary to illness or its medications such as DM, other endocrinial disorders, and chronic use of corticosteroids.

Tools

1. Oral informed consent from the care giver;
2. full medical history and general examination;
3. psychiatric history and examination by KSAD-PL [16];
4. assessment of body weight and height by a digital scale;
5. measurement of fasting lipid profile [total cholesterol, low-density lipoprotein, HDL cholesterol, and triglyceride (TG)] FBG and liver enzymes (SGPT, SGOT, and alkaline phosphatase);
6. data on drug history including the type, the mean dose received during the period of the study, any change or addition of another drug, and the duration of treatment.

Study proper

After approval by the ethical committee of the complex, a group of 82 patients with different psychiatric diagnosis were selected according to our inclusion and exclusion criteria and provided consent (diagnosis made according to the DSM-IV criteria). Upon enrollment, vital signs were obtained; in addition, height was measured to the nearest 0.1 cm while patients were standing erect and weight was recorded to the nearest 0.1 kg using a digital scale. That procedure was repeated after 3 and 6 months, with an estimation of BMI each time in order to construct the growth curve and obtain the percentile. Weight, height, and BMI (kg/m²) measurements were converted into z-scores using the 2005 growth charts for Saudi children and adolescents [17]. In our study, we did not depend on waist circumference as a measurement of central obesity or triceps skin fold and blood pressure measurement as advised by the International Diabetic Federation [18] in the assessment of metabolic syndrome in children as there were not sufficient data on the normal reference points in the Gulf area. Therefore, we used percentiles of weight and BMI z-score as an indication of overall weight as in some previous studies [15]. For children younger than 16 years of age, we further divided our sample according to weight and BMI percentile into overweight, which is defined as a BMI at least 85th percentile, obese, defined as at least 95th percentile for age and sex [19], and a normal group if the BMI was less than 85% as in Carlage et al. [20]. For adolescents older than 16 years of age, we divided the sample into overweight if the BMI was between 25 and 30, as obese if the BMI was more than 30, and normal if the BMI was less than 25 [18].

A morning blood sample was obtained after at least a 10-h overnight fast; assessment of the metabolic profile (FBG, liver enzymes, lipid profile in the form of total and HDL cholesterol, and TG) was carried out at the start of the study and reassessment was carried out after 6 months. In children younger than 16 years of age and according to the reference point of our laboratory and IDF, we considered the TG level as abnormal if more than 1.7 mmol/l, HDL cholesterol as abnormal if less than 1.03 mmol/l, and FBGs abnormal if more than 100 mg/dl. Metabolic syndrome was diagnosed if the child was overweight or obese in addition to any two of the previous findings [18].

Statistical analysis

Analysis of the data was carried out using SPSS, version 15 (statistical program for social science, Chicago, Illinois, USA), with descriptive statistics, χ², and cross stab for analysis and relation of categorical variables. A paired-sample t-test was carried out to compare repeated measures within the same group; in case of violation of the t-test assumption for normality, the Wilcoxon sign rank test was carried out. The Mann–Whitney and Kruskal–Wallis tests were used to compare the quantitative variables in the same group instead of an independent group t-test and one-way between-groups analysis of variance because of the nonparametric criteria of the data (SD > 50% mean). Spearman's rank correlation was used to find an association between obesity, metabolic syndrome, and possible related quantitative variables.
Weight gain and metabolic changes
The mean weight of the entire sample at the onset of the study was 33.7 ± 19.1 kg and the mean weight after 6 months was 39.1 ± 20.2 kg. The mean weight gain in the entire sample was 3.5 ± 3 kg; there was significant weight gain as df, was 63 and \( P = 0.000 \). Furthermore, the mean BMI at the onset of the study was 19 ± 5.5 kg/m² and the mean BMI after 6 months was 20.6 kg/m²; the mean increase in BMI was 1.7 ± 1.2 kg/m². Comparison of the BMI z-score at the onset of the study with that after 6 months (mean was 0 ± 1 and 0.5 ± 1.1, respectively) showed a significant increase as df, was 63 and \( P = 0.000 \), with an increase of 0.5 points in 6 months.

A greater duration was associated with less weight gain and less increase in BMI; however, there was no statistical significance as \( r = -0.191, P = 0.131 \) and \( r = -0.184, P = 0.188 \), respectively.

Furthermore, three (4.7%) patients fulfilled the criteria of metabolic syndrome, 30 (46.9%) patients had one or two symptoms of metabolic syndrome, and 31 (48.4%) patients were normal. In terms of overweight and obesity, 32 (50%) patients were normal, whereas 16 (25%) patients were overweight and another 16 (25%) were obese. On comparing the overweight/obese group with the normal group in terms of the BMI z-score (the mean was \(-0.6 ± 0.4\) and \(0.6 ± 1.1\), respectively) a highly significant difference was found as df, was 52 and \( P = 0.000 \).

Weight gain was more in those who were younger, although there was no statistically significant difference as \( P = 0.767 \). Furthermore, there was a high significant correlation between obesity and metabolic syndrome symptoms and disorder as \( r = 0.951 \) and \( P = 0.000 \).

Sex difference in weight gain and metabolic abnormalities
The mean weight gain among males was 3 ± 2.4 kg and the mean weight gain in females was 4.2 ± 3.6 kg. The mean increase in BMI was 1.5 ± 1.2 kg/m² in males and 2.1 ± 1.1 kg/m² in females; however, there was no statistically significant difference as \( P = 0.196 \) and \( 0.060 \), respectively.

Although 61.6% of females were either overweight or obese versus 42.2% of males, there were no statistically significant differences as \( P = 0.312 \). There were tendency of BMI change and cholesterol abnormalities to be significantly more among females as \( P = 0.060 \) and 0.051. In addition, there was a direct correlation between BMI percentile, TG, and total cholesterol level as \( r = 0.250, P = 190 \), and \( r = 197, P = 0.305 \), respectively. There was an indirect correlation between BMI percentile and HDL cholesterol as \( r = -0.115, P = 0.661 \).

Table 1 shows some sociodemographic variables among normal, overweight, and obese patients.

As shown in the table, there was no significant sex difference in weight gain and metabolic abnormalities.

Weight gain and change in body mass index with different drugs
Comparison of weight gain, increase in BMI, and metabolic changes between both sexes indicated no statistically significant difference as shown in Table 2. At the same time, comparison of different drugs in the diagnosis of obesity when dividing patients into either a normal group or an overweight/obese group showed that patients who took risperidone had the smallest percentage of overweight/obese patients among them than the other groups of APDs; however, the number in each subgroup was small and no significant difference was found. Furthermore, the diagnosis of metabolic syndrome symptoms and disorder was significantly less among patients on risperidone as \( P = 0.047 \) as shown in Tables 3 and 4.

As Table 3 show Olanzapine had the greatest increase in BMI and weight gain while Risperidone had the lowest increase. However no significant difference in weight gain and BMI increase between different drugs.

Comparison of different groups of drugs in terms of the presence of obesity and metabolic syndrome showed significant difference in metabolic syndrome as it was more with risperidone and other atypical drugs rather than haloperidol (Table 5).

No significant difference was found between different groups of drugs in metabolic abnormalities as shown in the table.

In terms of other metabolic changes with APD, 17 patients on risperidone were found to have an increased
level of one or more enzymes above the normal value (alkalin phosphatase, SGPT, and SGOT); three of the patients required replacement of the drug as the enzyme level was rising.

**Monotherapy versus combination therapy**

Comparison of weight gain and change in BMI in patients under monotherapy \(N = 31 (48.4\%)\) versus those under combination therapy \(N = 33 (51.6\%)\) showed no statistically significant difference, although weight gain and change in BMI were greater among the patients under combination therapy (Table 6). Furthermore, there were no significant correlations between weight gain, metabolic changes, and any of the combined drugs including (carbamazpine, methyl phenidate, Na valproate, and aripiprazole) as \(r = 0.025\) and \(P = 0.889\) and \(r = 0.232\) and \(P = 0.224\), respectively.

There was no significant difference between monotherapy versus combination therapy in terms of metabolic changes.

There was no significant difference between monotherapy versus combination therapy in terms of weight gain and metabolic syndrome.

**Discussion**

**Sociodemographic and clinical variables**

Weight gain is one of the most troublesome side effects of AAPs when used in children and adolescents. It is especially of concern because obesity may lead to the development of serious medical problems including diabetes, hyperlipidemia, and cardiovascular disease [21]. In this study, the mean weight gain among the entire sample after 6 months was 3.5 ± 3, with a significant weight gain as \(P = 0.000\). In addition, the mean increase in BMI in our sample was 1.7 ± 1.2; there was a significant increase in BMI from the onset of the study as \(P = 0.000\). Similar to our study, Arango et al. [22], comparing olanzapine and quetiapine in adolescent patients with a first psychotic episode, reported the mean incremental weight gain to be 15.5 and 5.4 kg, respectively, during the 6-month study [22]. Similar to our results, Correll et al. [23] reported that within 12 weeks of treatment, there was an increase in the BMI \(z\)-score of more than 0.5 in 62% of olanzapine-treated, 36% of quetiapine-treated, 47% of risperidone-treated, and 22% of aripiprazole-treated young patients.

The mean age of our sample was 9.8 ± 4.5 years; younger age patients showed affected greater weight gain, although this was not statistically significant. As our study was carried out in a naturalistic setting, the mean duration of APD use was 16.7 ± 15 months, greater duration associated with less weight gain and less increase in BMI; however, there was still a significant weight gain and change in BMI at the end of the study after 6 months. That was similar to previous studies that have reported that weight gain eventually plateaus; during extended treatment, patients continue to maintain an elevated weight compared with their same-age peers [24,25]. There are limited long-term studies of AAPs in which weight gain is a primary or a secondary outcome measure [26].

**Overweight and metabolic syndrome**

A total of 4.7% of our sample fulfilled the criteria of metabolic syndrome in children and 46.9% of patients had one or two symptoms of metabolic syndrome; in addition, 50% of our sample were either overweight or obese. Our findings were similar to those of Panagiotopoulos et al. [27] as they reported that the cross-sectional prevalence rates of obesity/overweight were more than double in AAP-treated youth (57%) compared with AAP-naive youth (23%) [27]. However, we do not have data on the prevalence of obesity among Saudi children and adolescents. In our study, there were significant associations between obesity and the symptoms of metabolic syndrome as \(P = 0.000\); also, there was a significance increase in the BMI \(z\)-score after 6 months as \(P = 0.000\) and the mean increase was at least 0.5 point. This was similar to previous studies that have reported that an absolute increase in the BMI \(z\)-score of at least 0.5 point has been proposed to be significant because this degree of growth-adjusted weight gain was found to increase the risk for metabolic syndrome by more than 50% [15,28]. In terms of sex differences in weight gain and metabolic abnormalities, although females were more affected by weight gain and metabolic side effects in terms of the number of patients (61.6% of females were obese vs. 42% of males) or the extent of weight gain and change in BMI, this was not statistically significant. Similar results have been reported in adults by Koga [29], who carried out a retrospective investigation of BMI in patients who had been treated with antipsychotic agents over extended periods. The odds ratio for weight gain was significantly higher in women than in men (4.94).

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**Table 2 Comparison between both sexes in weight gain, BMI change, and metabolic abnormalities**

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight gain (kg)</td>
<td>3 ± 2.4</td>
<td>4.2 ± 3.6</td>
<td>0.198</td>
</tr>
<tr>
<td>BMI change (kg/m²)</td>
<td>1.5 ± 1.2</td>
<td>2.1 ± 1.1</td>
<td>0.060</td>
</tr>
<tr>
<td>TG (n)</td>
<td>4</td>
<td>1</td>
<td>0.271</td>
</tr>
<tr>
<td>Cholesterol (n)</td>
<td>1</td>
<td>4</td>
<td>0.051</td>
</tr>
<tr>
<td>HDL cholesterol (n)</td>
<td>4</td>
<td>5</td>
<td>0.309</td>
</tr>
<tr>
<td>Glucose (n)</td>
<td>0</td>
<td>1</td>
<td>0.285</td>
</tr>
<tr>
<td>Enzyme increase (n)</td>
<td>12</td>
<td>12</td>
<td>0.474</td>
</tr>
</tbody>
</table>

HDL, high-density lipoprotein; TG, triglyceride.

**Table 3 Weight gain and change in BMI with different drugs**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Weight increase (kg)</th>
<th>BMI change (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risperdone</td>
<td>3 ± 2.3</td>
<td>1.5 ± 0.9</td>
</tr>
<tr>
<td>Olanzapin</td>
<td>6.1 ± 5.6</td>
<td>1.9 ± 1.7</td>
</tr>
<tr>
<td>Aripiprazol</td>
<td>3.7 ± 2.4</td>
<td>2.1 ± 1.9</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>4 ± 3.1</td>
<td>2.2 ± 1.5</td>
</tr>
</tbody>
</table>

P value: 0.273 and 0.381.
Type of antipsychotic drug
At the same time, in our study, comparing different APD in terms of weight gain, increase in BMI, metabolic changes, and metabolic syndrome as shown in Tables 4 and 5, olanzapine induced the greatest increase in weight and BMI as they were 6.1 ± 5.6 and 1.9 ± 1.7, respectively, followed by haloperidol as weight gain was 4 ± 3.1 and BMI was 2.2 ± 1.5. The third drug was aripiprazole as the increase in weight was 3.7 ± 2.4 and the increase in BMI was 2.1 ± 1.9, whereas risperidone exerted the least effect as weight gain was 3 ± 2.3 and the increase in BMI was 1.5 ± 0.9. However, our results need some explanations in terms of haloperidol and aripiprazole as most of the patients on haloperidol in our study had previously received risperidone and shift from risperidone to haloperidol occurred because of lack of efficacy; thus, weight gain in this group may not be attributed only to haloperidol. Similarly, with aripiprazole, three out of five patients who used it in our study also received risperidone; thus, weight gain here may be because of the combination. However, similar findings have been reported in previous studies, with olanzapine producing the greatest weight gain [23,30–32].

The same findings were reported in another study [33] in which a significant increase in BMI was found (P<0.001) from the baseline to the endpoint in both treatment groups; however, the change in BMI was not significantly different between the olanzapine and the risperidone groups (P = 0.425).

Metabolic symptoms and metabolic syndrome
In our study, Table 5 shows the number and pattern of metabolic symptoms that occur during APD treatment, the most common being overweight and obesity, about 50% of the sample, followed by reduced HDL cholesterol in nine (14.1%) patients, and the least was impaired FBG in one patient in the olanzapine group. There were positive associations between the BMI z-score, TG, and total cholesterol level as r = 0.250, P = 190 and r = 197, P = 0.305, respectively. There was a negative association between the BMI z-score and HDL cholesterol as r = −0.115 and P = 0.661. This was similar to the study of Woods et al. [34], who reported that BMI z-scores were associated positively with total cholesterol, TGs, and low-density lipoprotein and correlated negatively with HDL. Our results were less than that of the CAPE unit at BCCH, where the mean duration of AAP treatment at the time of assessment was 12 months, the prevalence of metabolic syndrome was nine times higher in AAP-treated (27%) compared with AAP-naive (2.9%) children, and adolescents (P<0.001) had an increased prevalence of the following components, respectively; elevated waist circumference (49.1 vs. 17.9%; P<0.0001); hypertriglyceridemia (42.6 vs. 22.4%; P = 0.015); impaired FBG (16.1 vs. 2.6%; P = 0.005); and hypertension (54 vs. 18%; P<0.0001). In addition, low HDL cholesterol was seen in 16% of AAP-treated youth compared with 11% of AAP-naive youth; however, this result was not statistically significant [27]. The differences between our study and the previous studies may be attributable to the different study designs, durations, and drugs.

Table 4 Obesity and metabolic syndrome with different drugs

<table>
<thead>
<tr>
<th>Type of antipsychotic drug</th>
<th>Obesity [n (%)]</th>
<th>Metabolic syndrome [n (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Overweight</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No</td>
</tr>
<tr>
<td>Risperidone</td>
<td>27 (57.4%)</td>
<td>20 (42.6%)</td>
</tr>
<tr>
<td>Other atypical</td>
<td>2 (22.2%)</td>
<td>7 (77.8%)</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>3 (37.5%)</td>
<td>0.115</td>
</tr>
</tbody>
</table>

P value 0.585 0.464 0.288 0.278 0.834

*P was significant.

Table 5 Metabolic changes with antipsychotic drug

<table>
<thead>
<tr>
<th>Type of antipsychotic drug</th>
<th>TG (n)</th>
<th>Cholesterol (n)</th>
<th>HDL cholesterol (n)</th>
<th>Glucose (n)</th>
<th>Enzyme increase (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risperidone</td>
<td>4</td>
<td>3</td>
<td>6</td>
<td>0</td>
<td>17</td>
</tr>
<tr>
<td>Other atypical</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>0</td>
<td>0</td>
<td>0.288</td>
<td>0.278</td>
<td>0.834</td>
</tr>
</tbody>
</table>

HDL, high-density lipoprotein; n, number of cases with abnormal changes; TG, triglyceride.

Table 6 Comparison of monotherapy versus combination therapy in weight gain, change in BMI, and metabolic changes

<table>
<thead>
<tr>
<th>Type of therapy</th>
<th>TG (n)</th>
<th>Cholesterol (n)</th>
<th>HDL cholesterol (n)</th>
<th>Glucose (n)</th>
<th>Enzyme increase (n)</th>
<th>Weight gain (kg)</th>
<th>BMI change (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monotherapy</td>
<td>4</td>
<td>2</td>
<td>7</td>
<td>0</td>
<td>10</td>
<td>2.9 ± 2</td>
<td>1.7 ± 1.1</td>
</tr>
<tr>
<td>Combination</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>14</td>
<td>4.1 ± 3.5</td>
<td>1.8 ± 1.3</td>
</tr>
</tbody>
</table>

P value 0.271 0.337 0.098 0.336 0.591 0.129 0.800

HDL, high-density lipoprotein; TG, triglyceride.
Although elevated hepatic transaminases were not part of metabolic syndrome, they still represented a controversial finding in previous studies and were found commonly during the monitoring of our patients on AAP drug. In our study, 37.5% of patients had elevated hepatic enzymes; other studies [34,35] have reviewed the FDA MedWatch Drug Surveillance System in terms of olanzapine and found significantly higher risk ratios for hepatic transaminase abnormalities in children (under 10 years of age) (RR 3.4, 95% CI: 1.9–6.1) and adolescents (10–19 years of age) (RR 1.9, 95% CI: 1.5–2.4) compared with adults. However, in risperidone-treated youth, data are conflicting. One case series [36] identified steatohepatitis in two of 13 children treated with risperidone, whereas other prospective studies [37,38] have reported low rates of clinically significant hepatic transaminase elevation.

**Monotherapy versus combination therapy**

Combination therapy has been used recently by many child psychiatrists because of the heterogeneity of the childhood disorders and the lack of efficacy of monotherapy in many cases; thus, it is important to ensure the safety of such combinations. In our study, 51.6% of our patients used combination therapy despite the fact that weight gain and increase in BMI were greater among patients who received combined treatment as shown in Table 7, but still not statistically significant. In addition, none of the combined drugs were significantly associated with any of the metabolic symptoms. This was different from some other studies in adults such as the study of Correll et al. [39], who reported that compared with antipsychotics, polytherapy was associated with elevated rates of metabolic syndrome (50.0 vs. 34.3%, \( P = 0.015 \)) and TG/HDL (50.7 vs. 35.0%, \( P = 0.016 \)) [39]. However, in the same study, they concluded that antipsychotic polytherapy is not associated independently with the prevalence of these abnormalities, which are related to known demographic, clinical, and anthropometric risk factors [39]. Further researches on a larger sample with control of possible confounding factors may be required.

**Strengths and limitations**

This study was one of the few studies on the metabolic side effects of APD in children in Arab countries. The prospective nature of the study allowed follow-up of anthropometric measures regularly three times so that we could construct the growth curve of the patients and obtain the percentile and z-scores, which were found to be more accurate in the estimation of overweight in children rather than crude values. This study was carried out in a naturalistic setting and provided insights into the possible side effects of APD in real life. However being naturalistic study, that may lead to contamination of our results due to combination therapy or due to past history of different APD use before the patients joined the study. Our study did not use waist circumference or triceps skin fold as the measurement of central obesity and body fat as in previous studies in developed countries because of lack of data on normal values in Gulf area; the same held true for estimation of blood pressure. In order to overcome small number in each subgroup of drugs we choose suitable statistical method. However, we found no statistically significant difference between different APD in terms of weight gain and metabolic symptoms in contrast to previous studies.

**Table 7 Comparison of monotherapy versus combination therapy in obesity and metabolic syndrome**

<table>
<thead>
<tr>
<th></th>
<th>Obesity [( N )] (%)</th>
<th>Metabolic syndrome [( N )] (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Overweight</td>
</tr>
<tr>
<td>Monotherapy</td>
<td>18 (58.1%)</td>
<td>13 (41.9%)</td>
</tr>
<tr>
<td>Combination</td>
<td>14 (42.4%)</td>
<td>19 (57.6%)</td>
</tr>
<tr>
<td>( P ) value</td>
<td>0.211</td>
<td>0.320</td>
</tr>
</tbody>
</table>

**Recommendations and conclusion**

We had a stable finding in our study and previous studies in different countries that AAP drug was associated with weight gain and metabolic syndrome at different ratios between different drugs and different studies. What is new in our study was that even typical APD was not totally safe; however, further studies are required. So revising indications of APD use in children and limit it to absolute indications that had strong evidence base and made consensus between child psychiatrists in each country on that indications. Education of junior psychiatrists and pediatricians on indications of APDs and its metabolic side effects should be provided. Regular monitoring of all children and adolescents on APDs should be carried out even by simple anthropometric measures, with more detailed investigations for those with overweight. Strategies for the management of metabolic syndrome in children should be developed.

**Acknowledgements**

Conflicts of interest

There are no conflicts of interest.

**References**

Weight gain and metabolic side effects with APDs


39 Correll CU, Fredericksen AM, Kane JM, Manu P. Does antipsychotic polypharmacy increase the risk for metabolic syndrome? Schizophr Res 2007; 89:91–100.
دور مضادات الذهان في زيادة الوزن وخلل الأيض عند الأطفال

لقد شاع استخدام العقاقير المضادة للذهان في الأطفال في السنوات الأخيرة لأهداف متعددة بعضها توافق عليه وبين المجالين دمشق والمخصصين.

كما يلاحظ بالتزامن زيادة ملحوظة في الوزن وارتفاع في دهون الدم ومستوى السكر بالدم عند هؤلاء الأطفال في بعض الدراسات في الدول الغربية.

لذا يهدف هذا البحث لدراسة تأثير مضادات الذهان على الوزن والأيض لدى مجموعة من الأطفال والراهقين من 18 سنة في المملكة العربية السعودية ومقارنة تأثير مضادات الذهان المختلفة.

وقد تم فحص 64 مريض سعودي الجنسية وتم قياس الوزن والطول مع فحص عضوي ونفسى وتحليل نسبة الدهون في الدم ومستوى السكر وأنزيمات الكبد وأعيدت القياسات بعد 3 شهور و6 شهور كما أعيدت التحاليل في نهاية البحث.

وقد وجد أن مضادات الذهان باعتمادها المختلفة تؤدي إلى زيادة ملحوظة في الوزن ( معدل زيادة الوزن 3.5 كجم) كما وجد أن 50% من عينة البحث تعاني من السمنة وكذلك وجد مظاهر خلل في الأيض عند 46.9% من المرضى. ولم نجد فارق ملحوظ بين مضادات الذهان المختلفة في أي من هذه المظاهر.

ومن خلال هذه الدراسة أثارت ضرورة مراجعة أسباب علاج الأطفال بمضادات الذهان مع حصرها في أهم الأسباب المتفق عليها وضرورة متابعة هذه الحالات وعمل قياسات وتحليل لها بصفة منتظمة.