Amisulpride-associated Hyperglycemia and Hyperlipidemia in a Patient with Mental Retardation and Schizophrenia

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Objective: The authors are reporting a case of hyperglycemia and hyperlipidemia after amisulpride use in treating a patient with schizophrenia and mental retardation. Case Report: A 38-year-old woman suffers from schizophrenia and mild mental retardation developed hyperglycemia and elevated serum triglyceride level after being treated with amisulpride. Conclusion: Fasting sugar and lipid profiles should be closely monitored in schizophrenia along with mental retarded patients receiving amisulpride treatment in order to facilitate early detection and intervention to prevent further metabolic complications.

Key words: amisulpride, mental retardation, hyperglycemia, hyperlipidemia

Introduction

The authors would like to report a case of hyperglycemia and hyperlipidemia after amisulpride use in a patient of mild mental retardation comorbid with schizophrenia, who had family history of diabetes mellitus and hypertension. Then, we would like to discuss the changes of patient’s metabolic profile and to speculate the possible causes of those side effects.

Case Report

A 37-year-old, unmarried lady patient, Miss X, came to our hospital with poor insight, auditory hallucinations and over-weight (body mass index = 25.2). She had restricted facial expression and anxious about the environment. Past history revealed that she had poor academic performance at primary and high schools. She graduated from school with poor grades and began to work as a laborer worker. She first experienced auditory hallucinations (third person) and persecutory delusions when she was 30 years old. She lost her job. Since her elder sister had actively sought psychiatric help. She first came to our psychiatric outpatient clinic two years ago and was diagnosed to have mild mental retardation (full intelligence quotient = 69) and schizophrenia. No systemic disease was recorded at that time except hypertension which was treated by her internist. She was
referred to our hospital on September 8, 2011 because her elder sister could no longer take care of her during the day time and had difficulty to supervise her medications. Routine biochemistry checkup revealed nothing particular.

Since the patient was overweight and her family had history of diabetes mellitus and hypertension, she received aripiprazole first, but she complained of headache and the increased frequency of auditory hallucinations. Antipsychotic drug, aripiprazole was then changed to amisulpride and was gradually increased to the dosage of 300 mg/day. Two months after her receiving amisulpride, she gained 4 kg in body weight (Table 1) and biochemistry follow-up showed abnormal findings. She and her elder sister claimed that no particular diet or lifestyle changes before and after patient’s amisulpride treatment. Metformin, 500 mg/day, was also added to her regimen and we doubled the dose to 1,000 mg/day later. Miss X got improved in her high fasting sugar level but not in her triglyceride (TG) level (Figure 1).

The patient has consulted an internist who explained that her high TG level was not due to medication use but to impaired liver function and no additional medication was suggested. Since we had monitored her metabolic profile more frequent than suggested treatment guideline and her liver function (Figure 1 and Table 1).

Although Miss X’s psychotic symptoms were under control with amisulpride 300 mg/day, we decided to shift this antipsychotic drug to aripiprazole because of the uncontrollable high level of lipid. She was not happy about taking aripiprazole, and we then changed to ziprazidone after having a detailed discussion with the patient and her sister (Figure 1). Dyslipidemia still existed but became much better than that when amisulpride was used. She was discharged after her staying in the day hospital for five months.

Discussion

The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study has confirmed the differences in metabolic impact among second-generation antipsychotic medications even during brief periods of exposure [1]. About 28.7% to 60.0% of patients with schizophrenia-related disorders have metabolic syndrome. Most studies show that the prevalence of metabolic syndrome in patients with schizophrenia-related disorder is higher than that in the normal population [2]. A meta-analysis of the published randomized, double-blind studies demonstrated that amisulpride treatment was significantly associated with relatively low weight gain [3]. Leucht et al., (2004) reported that amisulpride has minimal detrimental effects on lipid profiles [4]. In Taiwan, significantly decreased fasting triglyceride, total cholesterol, glucose, and insulin resistance levels and a significant increase in high-density lipoprotein cholesterol levels have been reported after switching to amisulpride from other second-generation antipsychotic drugs [5]. All these findings suggest that amisulpride may be a good choice for schizophrenic patients with metabolic problems. For patients who developed metabolic abnormalities or gained more than 5% of the baseline body weight from antipsychotic therapy, switching to another antipsychotic drug is a logical treatment strategy.

Miss X has a family history of diabetes mellitus and hypertension but not dyslipidemia, she may be vulnerable of having diabetes mellitus after antipsychotic used. That is why the authors selected the antipsychotic with least metabolic effects and clarified with the care-giver of the patient about particular diet or lifestyle changes. Although we could not have fully control of her diet because of the day care setting, at least we
Figure 1. Changes of blood sugar, cholesterol, triglyceride, high density lipid and HbA1c during the treatment course.
T1: 2012/2/3, Glucophage 500 mg/day; T2: 2012/3/15 Glucophage 1000 mg; T3: 2012/4/12 Glucophage 1000 mg + Glimepiride 2 mg
A: quetiapine 50 mg/day; B: 2012/10/31, amisulpride 50 mg/day; 2012/11/3, amisulpride 100 mg/day; and 2012/11/30, amisulpride 300 mg/day; C: 2012/3/23, aripiprazole 7.5 mg/day + amisulpride 100 mg/day; 2012/3/29, aripiprazole 15 mg/day; and 2012/4/3 aripiprazole 22.5 mg/day; D: 2012/5/3, ziprasidone 60 mg/day; and 2012/5/7 ziprasidone 120 mg/day.

Table 1. Changes in metabolic profile before and after amisulpride treatment

<table>
<thead>
<tr>
<th></th>
<th>2011-9-8</th>
<th>2012-1-12</th>
<th>2012-3-23</th>
<th>2012-4-20</th>
<th>2012-5-18</th>
<th>2012-7-5</th>
</tr>
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<tbody>
<tr>
<td>Weight, kg</td>
<td>58.5</td>
<td>62.5</td>
<td>61.5</td>
<td>61.5</td>
<td>62</td>
<td>60</td>
</tr>
<tr>
<td>BMI, kg/m2</td>
<td>25</td>
<td>26.7</td>
<td>26.3</td>
<td>26.3</td>
<td>26.5</td>
<td>25.6</td>
</tr>
<tr>
<td>GOT, U/dL</td>
<td>25</td>
<td>100</td>
<td>85</td>
<td>70</td>
<td>112</td>
<td>94</td>
</tr>
<tr>
<td>GPT, U/dL</td>
<td>35</td>
<td>154</td>
<td>134</td>
<td>125</td>
<td>170</td>
<td>174</td>
</tr>
</tbody>
</table>

Height, 153 cm; GOT, glutamic oxaloacetic transaminase; GPT, glutamic pyruvic transaminase
could monitor her lunch according to the nutritionist’s suggestion. But she still developed hyperglycemia and hyperlipidemia two months after being treated with amisulpride. She received aripiprazole for one week before her receiving amisulpride. To link the abnormal biochemical data to the use of aripiprazole was difficult.

Although Miss X had gained 4 kg in two months and the exact mechanisms of antipsychotic weight gain are unknown, changes in body weight alone might contribute to dyslipidemia [6]. However, it could not explain the dramatic elevation of triglyceride level (from 203 to 732 mg/dL). The mentally retarded patient comorbid with metabolic syndrome may lead clinician to consider genetic problems, such as Prader-Willi syndrome or Bardet-Biedl syndrome. Although Miss X had mild mental retardation but she had never had any seizure attack before, therefore, the above-mentioned syndromes are unlikely. Some may argue that the accuracy of full intelligence quotient checked in long-term schizophrenic patient, her academic performance and her working history were compatible with mild mental retardation. Cases with mental retardation have been found to have high risk for tardive dystonia after antipsychotic drug used, we cannot rule out minor structural or neuronal changes of her brain that may make her susceptible to amisulpride and in turn alters her metabolic profile.

We propose that metabolic parameters should be monitored more closely than the suggestion of the American Diabetic Association, the American Psychiatric Association and other two professional societies in psychotic patients with mental retardation [7, 8].

References
