Amisulpride implicated in the onset of tardive dyskinesia in a man who previously took sulpiride

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Both amisulpride and sulpiride are less associated with acute extrapyramidal symptoms. However, we report the case of a 52 year-old man with schizophrenia who received amisulpride due to the recurrence of acute psychotic symptoms. Despite improvement over positive symptoms, tardive dyskinesia developed soon after using amisulpride. The involuntary movements were slightly improved after amisulpride was cross-tapered to risperidone. Although lower risk of extrapyramidal symptoms is associated with amisulpride, there is still some risk of developing tardive dyskinesia.

Key words: Amisulpride, tardive dyskinesia, schizophrenia

Introduction

Tardive dyskinesia is characterized by involuntary and irregular choreoathetoid movements. Traditionally, tardive dyskinesia was more often seen after typical antipsychotic treatment. Atypical antipsychotics are less commonly associated with inducing tardive dyskinesia. It has been reported that tardive dyskinesia disappears after atypical antipsychotics treatment (Peritogiannis, Tsouli, Zafiris, Pappas, & Mavreas, 2006). However, some patients developed tardive dyskinesia after receiving atypical antipsychotics. Amisulpride is a highly selective dopamine D$_2$/D$_3$ receptor antagonist. A meta-analysis of randomized controlled trials showed that amisulpride was significantly superior to typical antipsychotics in acute extrapyramidal effects (Leucht, Pitschel-Walz, Engel, & Kissling, 2002). Nevertheless, cases of developing tardive dyskinesia after receiving amisulpride as well as other atypical antipsychotics have been reported (Fountoulakis et al., 2006, Masdrakis et al., 2007). Here, we present a case that developed tardive dyskinesia soon after receiving amisulpride.
Case report

This is the case of a 52 year-old unmarried man suffering from schizophrenia, and paranoia. He was raised in a working-class family. He had a head injury with concussion at the age of five. Besides being isolated and introverted, he had frequent conflicts with his family in his teenage years. He graduated from a junior high school in Taiwan. He began to drink about 2 beers per day at the age of 20. He never married and lived on part-time jobs and family support.

At the age of 48 (in 2004), he started to have delusions of persecution. At that time, someone attempted to assassinate President Chen (also the presidential candidate) in Taiwan. It was the first time that he began to have the sense that someone wanted to kill him. He heard voices telling that killers were chasing him. He thought those men who had the opposite political position would hurt him. With symptoms of poor sleep, wandering around, self-talking and poor appetite for several weeks, his mother brought him to the hospital, his first psychiatric admission. Paranoid schizophrenia was diagnosed according to the text revision of the 4th edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR). After treatment for a month, he was free from the delusion of being hunted. Then, he seldom had auditory hallucinations and less feeling of being persecuted by others. He was discharged with sulpiride 400mg daily.

In the following three years, he had fairly regular follow up at our hospital and found a part-time job as a security guard in a parking lot. No obvious acute extrapyramidal symptoms were noted when receiving sulpiride.

Nevertheless, despite regular medication, he began to experience delusions of persecution again with the approaching presidential election in March 2008. He could sense that someone would assassinate him again. Hearing voices shouting at him, he could no longer do his job and felt horrible. He skipped the medicine for several days and was brought to our hospital by his family. This was his second admission. The psychiatric symptoms were almost the same as diagnosed during his first admission. Derogatory auditory hallucinations and persecution delusions were noted. He said everybody thought he was insane, but he insisted that all these things were real. He denied using any alcohol or illicit drugs in the past 3 years. Meanwhile, he agreed to join our amisulpride research and began to take amisulpride 400mg daily three days later. In the admission routine, the white count and electrolyte were within normal range. His aspartate aminotransferase and alanine aminotransferase were 36 and 41 U/L, respectively. At first, the auditory hallucination rapidly improved. His positive symptoms responded well to amisulpride. He did not feel any kind of threat from the environment just a few days after receiving...
Amisulpride implicated previously took sulpiride. He stopped saying someone would kill him and felt much ease at the ward. 

Nevertheless, when his psychiatric symptoms were improving, we noticed the development of a slight involuntary movements over his jaw. Three days later, the involuntary chewing movement was more obvious. Moreover, we found him standing with mild tilting backwards. No other localized tremors were found. Tardive dyskinesia was impressed first and the amisulpride dosage was tapered to 200mg daily but there was little impact. Oral involuntary movement was still obvious. Therefore, we had no choice but to discontinue amisulpride and began risperidone treatment 2mg daily. With the beginning of risperidone 2mg daily, the involuntary movements were not progressing. He was discharged as a result of his improvement in positive psychiatric symptoms and tardive dyskinesia. One week after discharge, he came back to our service. His oral involuntary movements, though, still persisted but did improve gradually. Presently, he is keeping risperidone 2mg daily for his psychiatric symptoms, although the improvement in tardive dyskinesia is limited.

Discussion

Atypical antipsychotics were considered to be less involved in tardive dyskinesia (Correll, Leucht, & Kane, 2004). Moreover, secondary antipsychotics have been implicated in treating tardive dyskinesia (Truol, Von Hippel, Raape, & Konig, 2002). Improvement of tardive dyskinesia following amisulpride treatment was also reported (Peritogiannis et al., 2006). A 48-week prospective study showed risperidone might be beneficial for pre-existing tardive dyskinesia (Bai et al., 2005). Nevertheless, atypical antipsychotics may develop tardive dyskinesia in some cases. Although the real mechanism is still unknown, it is believed that individual atypical antipsychotic may vary in their propensity to cause tardive dyskinesia, which may be partly due to differences in dopamine D2 receptor affinity (Bressan, Jones, & Pilowsky, 2004).

Amisulpride, an atypical antipsychotic, has selective actions at dopamine D2/D3 receptors. Recently, a meta-analysis of randomized controlled trials showed that amisulpride was significantly superior to typical antipsychotics in extrapyramidal side effects when amisulpride was given in low doses, 50-300 mg daily (Leucht et al., 2002). The annualized amisulpride-induced tardive dyskinesia rate was 1.5% in a long-term treatment of schizophrenia study (Rein & L'Heritier, 1999). However, despite the reduced extrapyramidal symptoms with amisulpride, two cases of amisulpride-induced tardive dyskinesia were reported in 2006 (Fountoulakis et al., 2006) and 2007 (Masdrakis et al., 2007), respectively. Here, we reported the case of a 52 year-old male who developed tardive dyskinesia, oral involuntary movement,
after receiving amisulpride for several days. The most notable event is the development of tardive dyskinesia soon after receiving amisulpride in our case. Usually, it takes a long time to develop tardive dyskinesia after receiving antipsychotics. Therefore, we wondered what triggered the tardive dyskinesia in our case. Was it simply due to using amisulpride? Was there a possibility of sulpiride-induced tardive dyskinesia after discontinuing sulpiride? There may be a third possibility that the fast onset of amisulpride-induced tardive dyskinesia after long-term sulpiride treatment could be due to the similar pharmacologic structure.

Both sulpiride and amisulpride belong to the benzamide series. Sulpiride is a selective antagonist of dopamine D2 receptors. It does not block the dopamine D1 receptors, except in high concentrations. Therefore, the selective action may do well for tardive dyskinesia. Moreover, some cases even showed the disappearance of tardive dyskinesia after three months and, in some cases, the movements did not reappear after discontinuing sulpiride (Gerlach & Casey, 1984).

In our case, the patient took sulpiride for three and half years without developing any obvious extrapyramidal symptoms. However, he had intermitted drugs 2 weeks before this admission. (Unclear) After admission, we tried amisulpride to better control his positive symptoms. Indeed, the delusion of persecution and auditory hallucination improved several days after amisulpride 400mg treatment (daily).

However, tardive dyskinesia and involuntary oral chewing movements occurred one week after amisulpride treatment. Since sulpiride and amisulpride are both pharmacologically less related to the development of tardive dyskinesia, even in some cases showing benefits over tardive dyskinesia, it is still likely to, in some way, induce tardive dyskinesia in our case. It is not easy to distinguish which medication contributed to tardive dyskinesia in this patient. Although the patient took sulpiride for much longer and tardive dyskinesia usually occurred long after antipsychotics treatment, the patient developed tardive dyskinesia during amisulpride treatment. However, whether the same benzamide series antipsychotics affect the development of tardive dyskinesia remains unclear. Few cases show fast onset of tardive dyskinesia after antipsychotics treatment. It occurs to us that amisulpride which contributes to tardive dyskinesia soon after several days using may be related to the previous medication, sulpiride, also a benzamide derivative. There may be some complex mechanisms contributing to tardive dyskinesia. We need more evidence and better technology to determine the underlying pathology.

**Conclusion**

With the prevalence of atypical antipsychotics treatment, we should still bear in mind the risk of tardive dyskinesia,
though some studies show improvements of tardive dyskinesia by atypical antipsychotics treatment. Amisulpride is not an exception. The earlier we notice the involuntary movements due to tardive dyskinesia, the better we can switch to other atypical antipsychotic therapy. Moreover, studies on the risk of tardive dyskinesia with secondary generation antipsychotics are limited. Long-term study is needed to determine the risk of tardive dyskinesia in patients treated with secondary generation antipsychotics.

References

Amisulpride 导至一位之前服用 sulpiride 的男性产生遲發性運動不能

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Amisulpride 及 sulpiride 是比較不會引起急性錐體外症狀的藥物，然而我們報告一個 52 歲的男性妄想型精神分裂病人，他因反覆的急性精神症狀發作而接受 amisulpride，雖然急性症狀的改善，但遲發性運動不能在接受該藥後不久就發生。不自主運動在改成 risperdone 後有些微改善，因此，雖然 amisulpride 是比較不會產生錐體外症狀，它依然有可能產生遲發性運動不能的危險性存在。

關鍵詞：Amisulpride、遲發性運動不能、精神分裂病

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