Case report

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Tardive Orofacial Dyskinesia due to Aripiprazole in the Treatment of Schizophrenia

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Keywords

Aripiprazole; brexpiprazole; drug induced dyskinesia; orofacial dyskinesia; tardive dyskinesia

Abstract

Aim: To highlight tardive dyskinesia (TD) as a notable side effect of aripiprazole in the treatment of schizophrenia and discuss the potential therapeutic benefit of brexpiprazole as an alternative. **Case Report:** A 45-year-old male, diagnosed with schizophrenia, exhibited significant remission of psychotic symptoms after being treated with aripiprazole (10mg/day). However, after one year of consistent treatment, he developed tardive orofacial dyskinesia, characterized by lip-smacking and chewing motions. An extensive neurological evaluation with the aid of non-contrasted brain CT confirmed the TD diagnosis. Transitioning the patient from aripiprazole to brexpiprazole resulted in a cessation of TD symptoms within four months, with a continued stable remission of his psychotic symptoms. **Conclusions:** Despite its dopamine receptor partial agonism, which theoretically reduces the risk, aripiprazole can induce TD. It is crucial for clinicians to remain vigilant and monitor for TD even when prescribing second-generation antipsychotics like aripiprazole. In cases of aripiprazole-induced TD, brexpiprazole may offer an effective therapeutic alternative, warranting further research and attention.

Introduction

Tardive dyskinesia (TD) is a potentially debilitating movement disorder linked to antipsychotic use, often posing therapeutic challenges [1-3]. Although second-generation antipsychotics (SGA) are reportedly safer than first-generation counterparts regarding movement disorders, aripiprazole still presents some risk [4]. The aim of this report is to illustrate the risk of TD associated with aripiprazole, and to discuss brexpiprazole as a potential remedial approach.

Case Presentation

Mr. A, a 45-year-old man, arrived at our clinic in November 2019, challenged with symptoms indicative of schizophrenia since the prior year. His complaints spanned auditory and tactile hallucinations, paranoid delusions, and feelings of passivity. He also showed reduced social interaction, limited speech, diminished motivation, and a marked inability to derive pleasure from activities. His family and friends painted a worrying picture as well, whereby Mr. A often appeared to be speaking to someone unseen and, on many occasions, his speech was difficult to understand. By late 2019, a significant decline in his work per-

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formance, punctuated by a two-month absence from work, and the strain on personal relationships compelled his wife to seek our expertise. Mr. A reported no family history of psychiatric conditions. He has an extensive 68 pack-year smoking history, having started smoking at age ten. Yet, he had always steered clear of alcohol and illicit drugs.

Using the DSM-5 criteria, we diagnosed Mr. A with schizophrenia. By January 2020, he agreed to begin treatment with aripiprazole and stabilized at 10mg/day. Just two months into the treatment, he reported a significant reduction of his psychotic symptoms.

However, by the end of the following year, logistical challenges compelled him to transition his care to a nearby primary care doctor. Though he was maintained on the same dose of aripiprazole, he noted a 13 kg weight gain since starting aripiprazole and felt sleepier during the day. More alarmingly, in 2022, he began exhibiting involuntary lip movements and chewing actions that persisted for half a year, which was also noticeable to the people around him. Therefore, Mr. A came back to our clinic for a re-evaluation. A subsequent neurological evaluation confirmed the diagnosis of TD, and also found no signs of rigidity or tremors. A brain CT scan was normal. We then decided to taper off aripiprazole and start him on brexpiprazole, which was gradually increased to 3mg/day. Following this change, his TD symptoms receded over four months, and brexpiprazole continued to keep his psychotic symptoms at bay for the next eight months.

Discussion and Conclusion

The exact cause of TD remains elusive. One leading theory is the dopamine hypersensitivity hypothesis, suggesting that chronic blocking of dopamine D2 receptors leads to an increase in dopamine receptor sensitivity in certain brain areas, potentially causing TD [3]. Interestingly, studies suggest that aripiprazole does not usually block more than 80% of these receptors due to its partial agonist nature, making TD less expected [4]. But some cases, including Mr. A's, challenge this notion. For him, the 10mg/day dose was at the lower threshold of effectiveness, hinting at other potential risk factors, like his severe schizophrenia symptoms and long-term smoking [5].

Local guidelines recognize TD as a possible side effect of antipsychotics but provide no explicit management protocol. We contemplated the use of vesicular monoamine transporter - 2 inhibitors, but their unavailability directed our decision. Hence, the switch from aripiprazole to brexpiprazole was made, largely because of its distinct receptor activity profile, presenting it as a safer option [6,7]. It is noteworthy that the patient had previously manifested tardive dyskinesia symptoms while on a partial agonist; this made the choice of another dopamine agonist less appealing. Quetiapine was also considered as an alternative. However, given the patient's weight gain on aripiprazole, introducing quetiapine, which has a potential for weight gain, seemed less optimal [8]. Even though clozapine stood as another potential therapeutic alternative, its selection at that point would not have been the most judicious. clozapine is typically considered once other antipsychotic avenues have been fully explored, and in this scenario, we still had other viable therapeutic strategies to consider.

Brexpiprazole and aripiprazole, while structurally similar, exhibit distinct binding properties to both dopamine and serotonin receptors. Specifically, aripiprazole functions as a dopamine system stabilizer due to its higher affinity for D2 receptors compared to the 5 - HT1A and 5 - HT2A receptors. In contrast, brexpiprazole acts as a serotonin-dopamine activity modulator (SDAM). This modulation results from its balanced affinities for D2, 5 - HT1A, and 5 -HT2A receptors [7].

The clinical relevance of these differences is also highlighted by Otsuka's hypothesis. Otsuka posited that potent antagonism to 5-HT2A receptors can mitigate aripiprazole-induced akathisia. Moreover, even though both drugs function as D2 partial agonists, brexpiprazole demonstrates a slightly lower affinity for D2 receptors (0.30 nmol/L) compared to aripiprazole (0.34 nmol/L). This nuanced difference could lead to reduced incidences of akathisia and other extrapyramidal side effects with brexpiprazole [7].

In conclusion, TD, while less common with newer antipsychotics, remains a genuine concern, whereas aripiprazole is not an exception. Mr. A's case serves as a reminder that TD can be a side effect of aripiprazole. His improvement after shifting to brexpiprazole suggests its potential utility for patients experiencing TD with aripiprazole [9].

Acknowledgments

None.

Conflict of Interest

None to declare.

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