

Blonanserin treatment in patients with methamphetamine-induced psychosis comorbid with intellectual disabilities

Kosuke Okazaki
Manabu Makinodan
Kazuhiko Yamamuro
Tomoyo Takata
Toshifumi Kishimoto

Department of Psychiatry, Nara
Medical University School of
Medicine, Kashihara, Japan

Objective: Methamphetamine (MA) use has recently been associated with high levels of psychiatric hospitalization and serious social dysfunction. MA use causes frequent psychotic symptoms, which can be treated with antipsychotics. However, people with intellectual disabilities (ID) are vulnerable to adverse effects resulting from treatment with antipsychotic medications.

Method: We report two cases of MA-induced psychosis (MAP) in patients with ID who were treated with the antipsychotic blonanserin.

Results: In both the cases presented, symptoms of psychosis were improved by switching medications from other antipsychotic drugs to blonanserin. Despite the presence of ID in these patients, no significant adverse effects, such as sedation, were detected after treatment with blonanserin.

Conclusion: Blonanserin may be an effective and well-tolerated pharmacotherapeutical treatment for patients with MAP comorbid with ID. However, further work is necessary to validate this claim.

Keywords: methamphetamine, methamphetamine-induced psychosis, intellectual disabilities, blonanserin

Introduction

Approximately 5% of the adult population in the United States has used methamphetamine (MA) at least once, and there are approximately 35 million MA users worldwide, including in Japan.^{1,2} MA intake causes psychotic symptoms, such as paranoid delusions and hallucinations, in individuals without pre-existing psychotic manifestations.^{3,4} MA-induced psychosis (MAP) occurs in 10% to 60% of MA abusers.⁵ MAP is likely due to repeated administration or the use of high doses⁶ in MA abusers who are especially vulnerable. It can have deleterious physical effects, including changes in brain volume,^{7,8} pulmonary hypertension,⁹ and kidney damage.¹⁰ MAP is associated with the long-term enhancement of dopamine release in the striatum and nucleus accumbens. Therefore, dopamine antagonists, including atypical antipsychotics, have potential for the treatment of patients with MAP.¹¹

People with intellectual disabilities (ID) suffer disproportionately from substance abuse problems, including use of MA.¹² The prevalence of use and misuse of several illicit drugs is relatively higher among people with ID than among people without ID.¹³ However, treatment of individuals with MAP comorbid with ID can be challenging since patients with ID are more likely to experience adverse effects, such as tardive dyskinesia, akathisia, weight gain, and sedation with antipsychotics treatment,¹⁴ which

Correspondence: Manabu Makinodan
Department of Psychiatry, Nara Medical
University School of Medicine, 840
Shijo-cho Kashihara, Nara 634-8521,
Japan
Tel +81 744 22 3051
Fax +81 744 22 3854
Email mmm@naramed-u.ac.jp

might be due to minute structural brain abnormalities.¹⁵ Blonanserin is an atypical antipsychotic drug that exhibits a high affinity for the dopamine D₂/D₃ and the serotonin 5-HT_{2A} receptors.¹⁶ Thus, blonanserin is efficacious in the treatment of positive and negative symptoms as well as cognitive impairments.¹⁷ Moreover, blonanserin is generally well tolerated and is less likely to elicit adverse effects such as body weight gain, hyperprolactinemia, and extrapyramidal symptoms.^{18,19} Antipsychotics with few adverse effects, such as blonanserin,²⁰ are required for the treatment of patients with MAP comorbid with ID.

To the best of our knowledge, this is the first report to assess the use of blonanserin in the treatment of patients with MAP comorbid with ID. These two cases support the effectiveness of blonanserin as a viable alternative to antipsychotics for treating patients with MAP comorbid with ID.

Case presentation

Case A

Patient A was a 25-year-old woman with mild ID (Full Intelligence Quotient [FIQ] =53). She had performed poorly in school from junior high school onwards and occasionally taken organic solvent. She started intermittently using MA at 15 years of age after graduating from junior high school. She began experiencing visual and auditory hallucinations at 19 years of age; at the age of 21 years, treatment began for her at a local clinic with atypical antipsychotics including aripiprazole (30 mg/day), olanzapine (10 mg/day), and paliperidone (6 mg/day) (drugs were administered non-concurrently). Although she continued to take the medicines, adverse effects such as drowsiness, weight gain, and amenorrhea led her to keep complaining about the prescriptions. Eventually, every treatment failed to improve her symptoms despite good compliance to the treatment. The auditory hallucinations had a significant negative impact on her activities of daily living and social relationships, contributing to self-mutilation (cutting herself repeatedly) and an incident in which she ran away from home. She was referred to our hospital at 24 years of age.

Examinations including magnetic resonance imaging (MRI) indicated no brain abnormalities in Patient A. She was diagnosed with MAP in accordance with the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5). Symptoms of MAP were assessed using the Japanese version of the Positive and Negative Symptom Scale (PANSS),²¹ in which higher scores indicate greater severity according to a 7-point Likert scale. Subscale scores were calculated using small sets of variables based on the

three domains of the PANSS: positive, negative, and general psychopathological symptoms.²² Patient A obtained a PANSS score of 156. She did not have schizophrenia or any other psychiatric disorders, and was thus prescribed 8 mg of blonanserin, with the expectation that it would elicit the fewest adverse effects. Every 3 days, the dose was increased by 4 mg until it reached 20 mg/day. Over the course of 2 weeks, the patient showed improvements with respect to her positive symptoms, and she obtained a PANSS score of 87. However, when the blonanserin dose was increased to 20 mg/day, patient A developed akathisia and was thus prescribed clonazepam. Within several days, the symptoms of akathisia had nearly disappeared. Therefore, the dosage of blonanserin was increased to 24 mg/day. After 1 month with a daily blonanserin dosage of 24 mg/day with clonazepam, Patient A reported that her auditory hallucinations had nearly disappeared, with few adverse effects (PANSS score of 62). Patient A was able to continue taking blonanserin and clonazepam for at least 18 months (PANSS score of 39).

Case B

Patient B was a 24-year-old woman with mild ID (FIQ=63). She had repeated a year in high school because of poor academic performance and occasionally taken organic solvent. She started using MA around the age of 19 years. At the age of 22 years, she began to experience Capgras delusions and delusions of persecution. She visited the local clinic and was prescribed aripiprazole (12 mg/day). Owing to drowsiness, she discontinued therapy. At the age of 24 years, the Capgras delusions and delusions of persecution resulted in patient B dispersing burning oil and brandishing a kitchen knife and golf club with the intention of harming her family, after which she was admitted to our hospital. MRI revealed no signs of brain abnormality in Patient B. She was diagnosed with MAP in accordance with the DSM-5 and her PANSS score, which was 144. Patient B did not have schizophrenia or any other psychiatric disorders. Blonanserin was prescribed with the expectation that it would lead to a few adverse effects; dosing was progressively increased to 12 mg/day. After 2 weeks at 12 mg/day, psychomotor excitation had improved and Capgras delusions had subsided (PANSS score of 88). Subsequently, the dosage of blonanserin was increased to 16 mg/day; however, this led to extrapyramidal symptoms. Therefore, patient B was concomitantly prescribed biperiden. Patient B was discharged from the hospital 2 weeks after treatment because her symptoms improved substantially, with a few adverse effects (PANSS score of 74) as a result of concomitant blonanserin and biperiden therapy.

Patient B was able to continue taking blonanserin and biperiden for at least 12 months (PANSS score of 43).

Discussion

To the best of our knowledge, the cases presented here represent the original evidence of prolonged and well-tolerated blonanserin therapy, leading to a reduction in positive symptoms in patients with MAP comorbid with ID.

In many studies, atypical antipsychotics such as risperidone,²³ olanzapine,²⁴ quetiapine,²⁵ and aripiprazole²⁶ have been prescribed to treat patients with MAP. However, a few studies have shown reliable effects of antipsychotics in treating MAP, and no significant differences in clinical efficacy among antipsychotics have been reported in MAP patients.²⁷ Treatment of patients with MAP comorbid with ID can be particularly challenging because of increased vulnerability to adverse effects from any antipsychotic drugs.¹⁴ Although the detailed mechanisms contributing to the vulnerability in people with ID are unknown, these patients are unable to discontinue neuroleptic treatment.²⁸ Whereas brain abnormalities that might induce drug vulnerability were not detected by MRI in the two cases, both patients somehow experienced several adverse effects with antipsychotics treatment as expected. Consequently, it is necessary to select appropriate antipsychotics for patients with MAP and comorbid ID, considering the benefits of pharmaceutical treatment in this population. Blonanserin was prescribed to the patients with the expectation that it would be well tolerated and elicit fewer adverse effects, resulting in the rapid amelioration of symptoms.

Previous research suggests that people with ID suffer disproportionately from substance abuse problems. This may be due to a lack of empirical evidence to inform prevention and treatment efforts.¹² As mentioned, people with ID are particularly susceptible to the adverse effects of antipsychotics because their brain structure differs from that of the general population. Therefore, it is important to choose antipsychotics with fewer adverse effects and high efficacy. Blonanserin is considered to be an effective and generally well-tolerated option for the treatment of schizophrenia.²⁰

Blonanserin is a second-generation antipsychotic that possesses unique features compared with other antipsychotics. It has dopamine D₂ receptor, dopamine D₃ receptor, and serotonin 5-HT_{2A} receptor blocking activity. While it blocks dopamine D₂ receptors, thus improving positive symptoms,²⁹ blonanserin has weak dopamine D₁ receptor and adrenergic alpha₁ receptor blocking

activity and is almost completely devoid of histamine H₁ and muscarinic M₁ antagonist activity.¹⁷ Thus, it elicits a few adverse effects when used to treat psychosis, even in patients with ID. Previous studies have suggested that dopamine D₃ receptor activity can influence cognitive function by modulating the medial prefrontal cortex, despite the relatively small number of dopamine D₃ receptors in this region.^{18,30} Together with our results, these data suggest that blonanserin is an effective and well-tolerated treatment, even in patients with MAP comorbid with ID. Indeed, blonanserin might represent a better option compared with other traditional antipsychotic agents, as it appears to lead to fewer adverse effects.

As this report involves only two cases, a major limitation of our study is the small sample size. Another limitation is that the use of organic solvent might affect their intelligence. Future studies should continue to assess the effectiveness of blonanserin in treating patients with MAP comorbid with ID.

Conclusion

These two cases indicate that blonanserin might function as an efficacious and well-tolerated therapy in the treatment of patients with MAP and comorbid ID. Further studies with larger sample sizes are needed to validate the efficacy, safety, and tolerability of blonanserin in the treatment of patients with MAP comorbid with ID.

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Author contributions

KO and TT were involved in the collection of the data and wrote the first draft of the manuscript. KY, MM, and TK supervised the entire project, were critically involved in the design, and contributed to the editing of the final manuscript. All authors contributed toward data analysis, drafting and revising the paper and agree to be accountable for all aspects of the work.

Disclosure

The authors have no competing interests to declare that are relevant to the content of this submission.

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