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Blonanserin Therapy Improves Irritability in an Autistic Patient

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ABSTRACT

Patients with autistic disorders (AD) exhibit irritability, aggression, deliberate self-injury, and tantrums, which often exacerbate social and communication problems and impair family life and/or school adjustments. Risperidone and aripiprazole have been approved by the U.S. Food and Drug Administration for treating irritability in children and adolescents with AD. The efficacy of other second-generation antipsychotics (SGA), such as quetiapine and olanzapine, for AD-associated irritability have been demonstrated in open-label trials. However, no study has yet evaluated the effectiveness and safety of blonanserin (BNS) for treating irritability in patients with AD in Japan. In this case report, we describe an AD patient who exhibited irritability while on standard antipsychotics that was improved by BNS. BNS may be effective and safe for treating AD-associated irritability. Further large-scale controlled studies will be needed to confirm our findings.

Keywords: blonanserin, autistic disorder, irritability, treatment, antipsychotics

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INTRODUCTION

Patients with autistic disorder (AD) often exhibit irritability, aggression, deliberate self-injury, and tantrums. These behaviors impair sociability, communication, and adjustments with family life and/or school, and may worsen the social and behavioral deficits characteristic of the patients' age levels.

Risperidone (RIS) and aripiprazole (APZ) have been approved by the U.S. Food and Drug Administration for the treatment of irritability (including aggressive behavior, deliberate self-injury, and temper tantrums) in children and adolescents with AD. In addition, other second-generation antipsychotics (SGA), such as quetiapine and olanzapine, have been reported based on the results of open-label trials to be effective for treating irritability in AD patients [1, 2]. However, to date, there have been no studies evaluating the effectiveness and safety of SGA for the treatment of irritability in Japanese AD patients.

Blonanserin (BNS) is a novel atypical antipsychotic agent that was developed in Japan. BNS strongly disrupts the functions of dopamine D2 and serotonin 5-HT2A receptors.

Below, we report on a patient with AD who exhibited irritability despite being treated with standard antipsychotics that was improved by BNS.

CASE PRESENTATION

The patient was male, 17 years and 11 months old, and had been diagnosed as AD. He was referred to us by another hospital and was already taking 15 mg APZ at the time of consultation. Psychiatric diagnoses were made according to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR) criteria [3]. We used the Aberrant Behavior Checklistcommunity

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irritability subscale (ABC-I) scores [4], a subscale of the ABC that provides an informant-rated measure of the severity of irritability commonly observed in AD patients. The degrees of irritability are not defined in accordance with ABC-I scores (e.g., ABC-I score ranges for mild, moderate, and severe irritability are not provided). In a double-blind comparison study of APZ administration, patients were required to have an ABC-I score of ≥18 at the time of screening and baseline. Mean ABC-I sores were reduced from 29.6 at baseline to 16.7 post-dose in the APZ group [5].

The patient exhibited irritability, deliberate selfinjury, and tantrums. We determined that APZ was not effective, and therefore discontinued APZ administration and initiated RIS treatment. The patient's ABC-I score was 30. Administration of RIS (2 mg/day) was initiated when the patient's symptoms worsened. An increase in the dose to 4 mg RIS per day resulted in somnolence in a few days and severe dry mouth in 4 weeks. The patient's ABC-I score at week 4 was 18. Because RIS decreased the patient's excitability, treatment was continued; however, there was a marked reduction in the patient's daily activities due to the sedative effect of RIS. In addition, severe polydipsia emerged, and urination frequency increased. We tapered the dose of RIS to reduce the adverse effects associated with the treatment. When the dose was reduced to 2.5 mg/day, self-injury and tantrums recurred after 3 weeks. The patient's ABC-I score at week 7 was 25. RIS treatment was discontinued and BNS treatment (4 mg/day) was initiated, and the dose of BNS was increased to 16 mg/day after 5 weeks. Hyperactivity and irritability improved 3 weeks after BNS treatment (16 mg/day) initiation, no clinical laboratory abnormalities, such as body weight gain or changes in blood pressure or pulse rate, were observed, and no adverse reactions emerged during treatment. Psychiatric symptoms improved to a remarkable extent after 8 weeks, at which point the patient's ABC-I score was 19. No psychotropic medications other than antipsychotics were used.

DISCUSSION

BNS is an atypical antipsychotic drug that is indicated for schizophrenia in Japan and Korea. BNS has a high affinity for dopamine D2 and serotonin 5-HT2A receptors. Furthermore, unlike other secondgeneration atypical antipsychotic drugs, BNS has a higher affinity for D2 than for 5-HT2A. BNS also exhibits low affinity for muscarine M1, histamine H1, adrenaline alpha 1, and serotonin 5-HT2C receptors [6, 7]. Therefore, compared to other antipsychotics, BNS is advantageous in that it results in fewer adverse reactions, less body weight gain, a lower risk of excessive sedation, less digestive system disturbance, and a lower likelihood of orthostatic hypotension. Compared to RIS, BNS has the same risk of adverse reactions, such as extrapyramidal symptoms, coma due to diabetes mellitus, and QT prolongation, as well as a higher risk of akathisia, but there is less risk of hyperprolactinemia, weight gain, and orthostatic hypotension [6]. Oversedation or dry mouth did not occur after switching from RIS to BNS. Excessive sedation is thought to be minimal with BNS because it has less affinity for histamine H1, muscarine M1, adrenaline alpha 1, and serotonin 5-HT2C receptors than other SGAs. Because oversedation may reduce the activity of AD patients, BNS, which results in less sedation, may be advisable.

This patient was started on 16 mg/day BNS to treat irritability resulting from an autism disorder, and this treatment improved the patient's ABC-I score from 25 to 19. Hyperactivity and irritability improved 3 weeks after BNS treatment initiation. In a placebo-controlled, double-blind comparison in schizophrenia patients, BNS (10 mg/day) groups experienced significantly greater reductions in Positive and Negative Syndrome Scale (PANSS) total scores compared to placebo from week 1 onward [8]. The results of this patient suggest that the onset of efficacy against irritability and excitement in AD patients may be slower than that of its antipsychotic effects in schizophrenic patients. A dose of 16 mg/day BNS, the recommended dose for the treatment of schizophrenia, was used in this study. The established APZ doses are an initial dose of 2 mg/day, a recommended dose of 5–10 mg/day, and a maximum dose of 15 mg/day for the treatment of irritability in children and adolescents with AD [5, 9]. The RIS initial dose is 0.25 mg/day (<20 kg) or 0.5 mg/day (≥20 kg), with titration of 0.25–0.5 mg at ≥2 weeks to the target dose of 0.5 mg/day (<20 kg) or 1 mg/day (≥20 kg), and the effective dose range is 0.5–3 mg/day for the irritability associated with AD [10,11]. These results suggest that the appropriate antipsychotic doses for AD with irritability and excitement may be lower than those for schizophrenia. Lower doses than those used in schizophrenia may be sufficiently effective for AD patients.

Although other antipsychotics improve irritability due to AD, there have been no previous reports on this aspect of BNS. We therefore decided to present

this case report to propose the usefulness of BNS administration for irritability due to AD. Many aspects of the pathology of AD and the efficacy of BNS remain to be elucidated, and further experience and information collection are necessary.

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