

Aripiprazole and Delirium

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Background. Delirium is a common condition frequently seen in consultation-liaison psychiatry. It is especially common among medically compromised patients and is an indicator of the severity of the medical illness. In addition, it is associated with a higher morbidity, mortality or longer hospitalization. Traditionally, haloperidol has been used to treat delirium-associated agitation. However, atypical antipsychotics are being increasingly used to treat delirium.

Methods. Two case studies of delirium that were treated with 30 mg and 15 mg aripiprazole were described. The improvement of delirium was monitored using the Mini-Mental Status Exam (MMSE) and Delirium Rating Scale (DRS).

Results. In both cases, the patients' confusion, disorientation, and agitation improved within 7 days of treatment. In the first case, the patient's MMSE score improved from 5 to 28, while his DRS score decreased from 28 to 6. In the second case, her MMSE score improved from 7 to 27, while her DRS score went down from 18 to 6.

Conclusions. To the best of our knowledge, this is the first report on the utilization of aripiprazole in the successful treatment of delirium. Although these cases showed positive results, future studies should be performed in order to further substantiate its use in delirium treatment.

Keywords Aripiprazole, delirium, atypical, antipsychotics, neuroleptics

INTRODUCTION

Delirium is a common condition that occurs in the presence of a major medical illness. It is an acute fluctuating condition that affects the patient's attention and cognitive function. It is important to recognize and treat delirium because it may be associated with increased morbidity and mortality, as well as longer hospitalizations. The symptoms of delirium consist of delusions, hallucinations, confusion, and disorientation. Traditionally, haloperidol, a typical antipsychotic, has been the drug of choice in the treatment of delirium, despite the fact that it has not been approved by the Food and Drug Administration (FDA) (1). While it has been noted to help improve delirium, haloperidol has been associated with serious adverse effects, including extra-pyramidal side effects, tardive dyskinesia, and neuroleptic malignant syndrome (2). Thus, it was thought that aripiprazole, a new atypical antipsychotic, might be helpful in treating delirium because it has a low adverse effects profile. In this paper, we will report on the use of aripiprazole in the treat-

ment of two cases of patients with delirium. To the best of our knowledge, this is the first published report of such an intervention.

CASE ONE

The patient, M.I., is a 62-year-old African-American male with no previous psychiatric history. However, the patient does have a medical history of hypertension, diabetes mellitus, and diabetic nephropathy, with resulting chronic renal failure that was being treated with dialysis three times per week. In addition, he has a history of non-compliance with his dialysis. The patient was admitted to the emergency room of a teaching hospital after complaining of lethargy, disorientation, and confusion. He had missed his dialysis two times in a row and came in with electrolyte abnormalities. He was admitted to the intensive care unit for correction of these abnormalities. While in the ICU, he was found to be disoriented in relation to time and place. He also had visual and tactile hallucinations, as well as physical aggression towards the nursing staff. A psychiatric consultation was called to help manage the patient and evaluate

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his change in mental status. A capacity evaluation was also desired, as the patient was still refusing dialysis.

On the mental status examination, the patient was found to be disoriented with respect to time, place, and person. He had significant cognitive deficits, including lack of attention and concentration. On MMSE, he scored a 5 out of a total of 30. In particular, he had difficulties with attention, memory, and concentration. He scored 28 on the DRS (8). The patient was deemed to lack capacity and was diagnosed with delirium secondary to electrolyte imbalances resulting from chronic renal failure.

Methods

Consent for dialysis was obtained from his next of kin and the decision was made to start him on aripiprazole 30 mg po qhs. This drug was chosen to be used because it has a more favorable adverse effects profile. The patient's progress was followed on a daily basis. Aripiprazole was continued for 10 days and then discontinued.

Results for Case One

It was noted that M.I.'s degree of confusion, disorientation, and agitation improved, as compared to the baseline. By the seventh day, the patient was alert and oriented. His MMSE score increased dramatically from 5 to 28, and his DRS score was reduced from 28 to 6. It is thought that aripiprazole specifically contributed to the improvement in his delirium, while the dialysis also helped M.I. in the recovery process. After the patient fully recovered, he was subsequently discharged to the outpatient clinic.

CASE TWO

The patient, B.F., is a 37-year-old Native American female with a history of alcohol dependency. The patient was admitted to the emergency room of a teaching hospital after experiencing a grand mal seizure, presumably related to alcohol withdrawal. Psychiatry consultation was called after the patient was found to have confusion and agitation. She was experiencing visual hallucinations, consisting of bugs crawling all over the wall, and she had autonomic instability. A diagnosis of delirium tremens was made based on the clinical findings.

The patient was unable to give a coherent medical history because of her significant confusion. However, collateral information from her husband revealed a significant history of alcohol consumption. She drank about a quart of vodka every day, and had been drinking for several years. She had been in alcohol rehabilitation programs three times in the past but would always relapse after discharge. She had no other previous psychiatric history. Her last drink was two days prior to presentation.

Her mental status exam revealed a disheveled woman who looked significantly older than her age. She was disoriented with respect to time, place, and person and was responding to internal stimuli. She had marked disturbances in her concentration and attention. She scored a 7 out of a total score of 30 on the MMSE, in particular having difficulties in areas of concentration, memory, and attention. She scored 18 on the DRS. A diagnosis of delirium secondary to alcohol withdrawal was made.

Methods

The patient was started on IV lorazepam 2 mg q 4 hours. Aripiprazole 15 mg po qhs was added at the same time to control her agitation and confusion. In addition, she was given parenteral thiamine and oral folic acid. The dose of lorazepam was gradually titrated down over the next two weeks. Improvement was measured by tracking her MMSE and DRS scores throughout the course of her hospital stay. Aripiprazole was discontinued on the seventh day because of a rapid resolution of her delirium.

Results for Case Two

The patient continued to improve and was less confused and agitated by 48 hrs later. Improvement was also measured by an increase in her MMSE score from 7 to 27 and a decrease in her DRS score from 18 to 6 on the seventh day. The patient was subsequently transferred to an inpatient alcohol rehabilitation unit.

DISCUSSION

Delirium is an acute condition that causes disturbances of consciousness with the reduced ability to focus, sustain, or shift attention. Delirium can be associated with changes in cognition, such as waxing and waning of the level of consciousness. A delirious state can also include memory deficits, as well as disorientation and language disturbances. In addition, the patient can develop perceptual abnormalities, such as auditory and, more commonly, visual, and tactile hallucinations.

Delirium is essentially a manifestation of an underlying medical or surgical illness; thus, the treatment of delirium should primarily involve treating the underlying pathology. However, since the symptoms of delirium include agitation, disturbances of consciousness, and perceptual abnormalities, high-potency antipsychotics are an invaluable adjunct treatment. In particular, antipsychotics are useful in the treatment of the psychosis and insomnia that are often associated with delirium. Traditionally, haloperidol, a typical antipsychotic which selectively antagonizes dopamine D2 receptors, has been the gold standard in the treatment of delirium. However, in the early 1990s, the new generation of atypical antipsychotics were introduced into the market. In addition to the selective

dopamine D2 blockade, the mechanism of action of these antipsychotics involves preferential serotonergic (5HT_{2a}) blockade, which has resulted in a significantly lower rate of extra-pyramidal adverse effects. These atypical antipsychotics have been found to be effective and better tolerated than typical antipsychotics in the treatment of schizophrenia and bipolar II disorder. However, their use in delirium has not been systematically studied, and no atypical antipsychotics have been approved by the FDA for the treatment of delirium. While atypical antipsychotics are not FDA approved for the treatment of delirium, they nevertheless may prove to be helpful in light of the fact that typical antipsychotics, which are not FDA approved either, have been found to be effective.

The atypical antipsychotics that have been described as efficacious in delirium include risperidone (3), olanzapine (4), quetiapine (5), and ziprasidone (6). To date, there are no published studies utilizing aripiprazole to treat manifestations of delirium. Aripiprazole is the sixth second-generation antipsychotic recently approved by the FDA for the treatment of schizophrenia. Aripiprazole is not a dopamine antagonist, but rather it is considered a partial dopaminergic agonist, acting on both post-synaptic dopamine D₂ receptors and pre-synaptic autoreceptors. In addition, it displays partial agonism at serotonin 1_a receptors and antagonism at serotonin 2_a receptors (7). It is thus hypothesized to improve both the positive and negative symptoms of schizophrenia, and it is well tolerated among these patients (7). It is, therefore, thought that aripiprazole would be helpful in treating the delusions (positive symptoms) and poor cognitive function (negative symptoms) often seen in delirious patients.

Atypical antipsychotics, such as aripiprazole, come in a variety of formulations including disposable sublingual and injectable forms. This may be helpful for acutely ill individuals who are not able to swallow and absorb oral tablets.

In this report, we described the successful treatment of two patients with delirium using aripiprazole. Among other factors, antipsychotics should be prescribed based on their efficacy and adverse effects profile. In the first case, a dose of 30 mg of aripiprazole was chosen because of the severity of the patient's delirium (as evidenced by a DRS score of 28), while a dose of 15 mg was used in the second case because the symptoms were less severe (DRS score of 18). While choosing the appropriate dose of an atypical antipsychotic to treat delirium, one should consider factors such as previous response, severity of symptoms, tolerability, and drug-drug interactions. For patients with liver disease, as well as for elderly patients, the dose should be adjusted downward. In patients with kidney disease, there is no

evidence to date that suggests a dose reduction is necessary, but as with any other medical conditions, one should administer drugs with caution, starting at a minimum dose, monitoring carefully for tolerability. Both patients described in this paper tolerated aripiprazole well and experienced an improvement in MMSE and DRS scores within 7 days. Based on the findings in these case studies, a dose range of 15 mg to 30 mg of aripiprazole may be effective in treating delirium.

CONCLUSION

Aripiprazole, a second-generation atypical antipsychotic, appears to be effective in the treatment of agitation and confusion in patients suffering from delirium. It should be noted that in both cases, the underlying medical condition was treated, as is expected in all cases of delirium. While aripiprazole may have a promising future in the treatment of delirium, it must be realized that this is only a report of two cases. Therefore, further case reports and controlled studies will be necessary to understand the precise role of aripiprazole in the treatment of delirium.

*It should be noted that the authors had no conflicts of interest in conducting these case studies and writing this manuscript. No grants were received for conducting this study.

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