

Clinical response of clozapine as a treatment for delirious mania

Nabeel Wahid,¹ Garwin Chin,¹
Andia H. Turner,² Alexis Seegan²

¹School of Medicine, and ²Department of Psychiatry, University of California, Irvine, Orange, CA, USA

Abstract

Delirious mania is an understudied psychiatric disorder with a mortality rate as high as 75%. Previous case studies suggest that electroconvulsive therapy (ECT) may be an effective treatment for delirious mania, though this procedure may not always be a viable option. We describe the case of a 20-year old patient, with no previous psychiatric history, who developed delirious mania over the course of four months. ECT was not a viable option for this patient due to his religious beliefs, so alternative treatment modalities were explored. After failing trials of risperidone and olanzapine, significant improvements in symptoms were exhibited with a trial of clozapine. We propose that clozapine may be an effective option in cases of delirious mania, when ECT is not a viable option. Additional research is still necessary to understand the pathology of this condition and potential treatment modalities.

Introduction

Delirious mania is a potentially fatal yet understudied condition with no clear consensus of clinical characteristics and symptoms.^{1,2} It is not described in the most recent edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM V) and criteria used for diagnosis is mostly based on a series of case reports. Symptoms include emotional lability, delusions, insomnia, disorientation, acute onset of grandiosity, altered consciousness, incontinence/inappropriate toileting, and hyper sexuality.²⁻⁴ Given its multi-faceted symptomology, this disease may be confused with other psychiatric conditions such as bipolar disorder, psychosis, malignant catatonia, or delirium.⁵ Reports have demonstrated that trials of antipsychotics have minimal symptomatic improvement and can lead to exacerbation of the catatonia.⁶ Without prompt recognition and treat-

ment, delirious mania can progress and potentially become life-threatening,¹ with mortality rates as high as 75%.⁴ By far, the most effective described treatment for delirious mania has been electroconvulsive therapy (ECT),^{3,5-8} however, this case report describes a potential pharmaceutical alternative in cases when ECT is not a feasible option.

Case Report

A 20-year-old male, with no previous psychiatric history, was admitted for severe catatonia, mutism, and insomnia. His symptoms started four months prior with increased anxiety and depression. Although some improvement of catatonic features were seen with high doses of lorazepam, the patient appeared delirious with waxing and waning episodes of disorientation, disorganized speech and behavior, hyper-religiosity, hypersexuality, and paranoid thoughts. He had multiple episodes of enuresis and encopresis, which together with his other described symptoms appeared consistent with a diagnosis of delirious mania. Neuroleptic malignant syndrome was excluded due to lack of hyperthermia, autonomic instability and onset of symptoms prior to exposure to neuroleptic drug. Other considerations included bipolar disorder because the patient demonstrated poor sleep, distractibility, and erratic behavior. However, his presentation included multiple other symptoms and did not remain consistent enough to be attributed to bipolar disorder. Psychosis was considered, and was likely a component of what the patient was experiencing, however he had an unusual presentation that included additional symptoms unexplained by pure psychosis.

Trials of risperidone and olanzapine did not improve his symptoms. ECT was strongly recommended but was ultimately avoided due to the religious beliefs of patient's family and prolonged legal process for obtaining a court order. As such, clozapine was added to his regimen of lorazepam and valproate, and was titrated up to 450 mg per day over the course of 21 days. The daily dosing regimen for clozapine and lorazepam are included in Figure 1 (A and B respectively). The patient showed significant improvement in his orientation and thought process by day 27 of clozapine treatment (day of hospitalization 41). He was deemed safe for discharge 45 days after admission. Although he continued to show some emotional lability, the combination

Correspondence: Nabeel Wahid, 1001 Health Sciences Rd, Irvine, CA 92617, USA.
E-mail: n.wahid@uci.edu

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of clozapine, valproate, and lorazepam significantly improved his symptoms of delirium, mania, and catatonia.

Discussion

A recent systematic review of ECT found it to be an effective treatment option for all forms of catatonia, including malignant catatonia and delirious mania, even in cases that are refractory to benzodiazepines.⁷ Responsiveness to ECT in cases of delirious mania have been shown in as few as three ECT sessions.³ Additionally, given that delirious mania is difficult to diagnose and has been found in many patients with a history of bipolar disorder,² ECT could be used to treat multiple pathologies if the presentation is unclear.⁷

Nonetheless, ECT is not always accepted by patients or available by practitioners. This case demonstrates an alternative medication regimen that led to considerable improvement in symptoms. Although it could be argued that the patient may not have capacity if they are experiencing delirious mania (and an incapacitated court-ordered ECT could be pursued), it may not be in the best interest of the patient if his or her wishes are known prior to their illness.

As far as alternative treatment options for delirious mania, the literature is limited mostly to case reports. One case of delirious mania exhibited considerable improvement in symptoms with quetiapine, with the patient discharged after 29 days.⁴ Another

case described improvements with olanzapine over the course of 2 months after ECT was suspended due to technical issues.⁹ In our patient with delirious mania, olanzapine was ineffective and quetiapine was not trialed because the patient had failed two trials of other atypical antipsychotics. With limited additional treatment options shown in the literature, a trial of clozapine was started. Although a patient with delirious catatonic mania in a previous case report continued to have deterioration in mental status with clozapine treatment,⁸ our patient had considerable improvement after 27 days of treatment with clozapine. The slow titration was secondary to the patient experiencing significant side effects, and thus other patients may be able to reach a therapeutic dose in a shorter time period.

Recent studies have suggested that in patients with treatment resistant schizophrenia, clozapine has greater effectiveness than standard antipsychotics.¹⁰ Mechanistically, it is likely that the therapeutic profile of clozapine is mostly due to its antagonism to the 5-HT_{2A} and D₄ receptors along with weak D₂ antagonism.¹¹

As such, further research may consider targeting these receptors in developing new pharmaceutical treatment modalities for delirious mania.

Conclusions

Additional research is necessary to understand why clozapine is effective in some cases of delirious mania but not others. Given the nature and rarity of this disease, there are practical and ethical challenges to conducting randomized clinical trials that compare different treatment modalities. Nonetheless, clinical practice would benefit from additional literature to better understand the course of delirious mania and the optimal treatment modalities for individual patients. As case reports are the primary source for information about this illness, increasing available data is the next step in understanding the pathology underlying delirious mania and creating future treatment guidelines.

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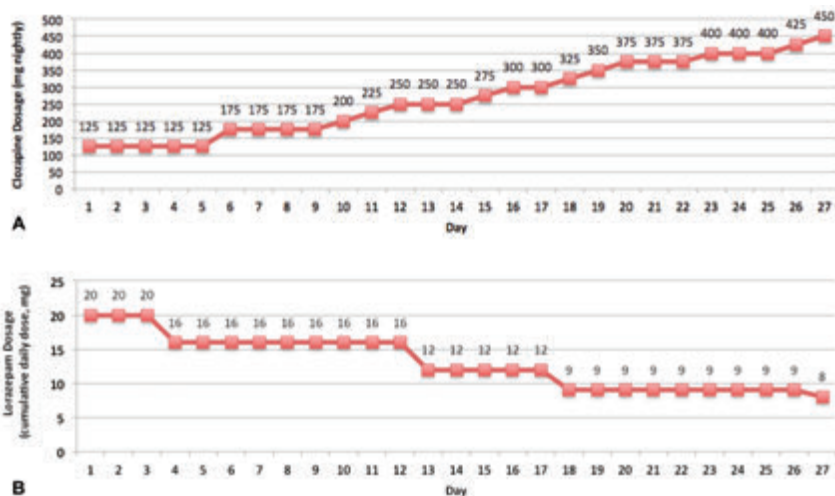


Figure 1. A) Clozapine and B) lorazepam treatment records.