ORIGINAL RESEARCH PAPER

Psychiatry

SAFETY AND EFFICACY OF OLANZAPINE IN MDR-TB MEDICATION INDUCED PSYCHOSIS: A CASE SERIES

KEY WORDS:

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ABSTRACT

Anti-tubercular drugs are known to cause psychiatric manifestations such as delusions, hallucinations, psychomotor agitation and sleep disturbances. Cycloserine has been associated with psychiatric symptoms in approximately 12% of cases. Most studies have demonstrated the use of haloperidol and risperidone in management of psychiatric manifestations of anti-tubercular drugs. This study aims to evaluate the effectiveness of olanzapine as a monotherapy in the treatment of MDR-TB medication induced psychosis.

INTRODUCTION

Mycobacterium tuberculosis is transmitted via air-borne droplets and has a person-to person transmission. The disease almost always primarily affects the respiratory system although it may later affect various other body systems.[1]

The clinical features of tuberculosis have a gradual onset and include low-grade fever that typically rises in the evening with night sweats, loss of weight, persistent cough with sputum production and haemoptysis.[1,2]

A tuberculosis specimen that is resistant to both Rifampicin and Isoniazid with or without resistance to other first line anti-tuberculosis drugs, based on rapid molecular testing.[3]

As per Indian Central Tuberculosis division guidelines, a patient with a tuberculosis specimen that is resistant to only Rifampicin (RR) is also treated as a case of MDR Tb.

Psychiatric manifestations have been implicated as the second most common cause of treatment drop out of anti-tuberculosis drugs. Studies have reported that as high as 21.3% drop out of treatment. Out of which 10%(ten percent) develop psychosis.[4,5]

Psychosis associated with anti-tuberculosis treatment has been observed with isoniazid, cycloserine, fluoroquinolones and ethambutol.[6,7]

The incidence of cycloserine-induced psychosis is approximately 12%.[8]

There exist multiple hypotheses regarding the mechanism of isoniazid-induced psychosis. One theory suggests that isoniazid weakly inhibits monoamine oxidase (MAO), which may elevate monoamine levels and contribute to psychiatric symptoms. Patients carrying certain NAT2 genetic variants are particularly vulnerable to developing isoniazid-related psychosis due to reduced drug metabolism and subsequent elevated plasma levels.[9]

Cycloserine's activity as an NMDA receptor antagonist is a mechanism closely linked with central nervous system (CNS) disturbances.[10]

Psychiatric side effects can include delusions, hallucinations, abnormal behavior, disorganized thinking, euphoria and anxiety. There have been reports of memory loss and even death linked to isoniazid.[9,11]

MATERIALS AND METHODS

Study Design: Observational, cross sectional study

Study Period: 6 Months

Study Size: 76 patients referred to department of psychiatry in a tertiary care hospital

Inclusion Criteria

- Age: Above 18 yrs
- Signed consent from the patient or a primary caregiver in a language best understood by them
- Patients referred to department of psychiatry for pre-MDR Evaluation.

Exclusion Criteria

- Age <18 yrs
- Patients or caregivers who did not give their consent to be a part of the study.
- Patients with known psychiatric illness such as depression or anxiety

Tools Used

Brief Psychiatric Rating Scale[12]

- Assessment tool for determining the severity of psychosis.
- Consists of 18 items, yielding a total score between 18 to126

Study Procedures

This case series study was carried out in patients of a Tertiary Care Centre over 6 months. Prior approval by Institutional ethics committee was obtained. 76 patients who met the criteria for inclusion were enrolled in the study after obtaining a written informed consent by a responsible caregiver. Brief psychiatric rating scale was administered at baseline on first of pre-MDR evaluation, after emergence of symptoms and 15 days after initiating the treatment. The study involves 12 patients who developed psychosis after initiation of treatment.

RESULTS

During the period of assessment, 76 patients were referred to Department of Psychiatry in view of Pre-MDR evaluation. A mental status examination was conducted to evaluate symptoms of psychosis prior, after emergence of symptoms and after initiating treatment for psychosis. BPRS data were collected in all three conditions, and findings were generated accordingly.

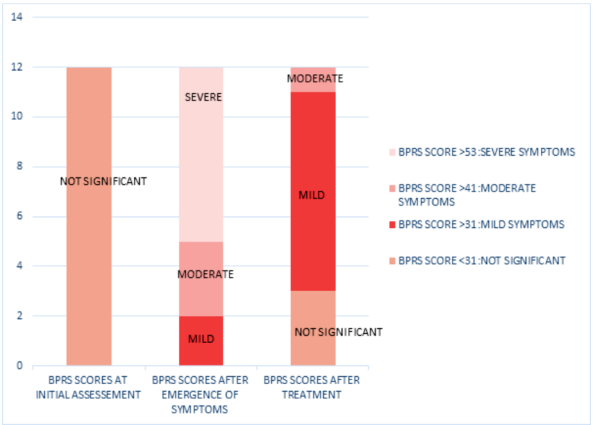
A p- value of 0.0092 is less than the significance level of 0.05, which means that the difference between the initial and after treatment scores is statistically significant. This suggests that the treatment likely had a meaningful and positive effect on the scores.

BPRS Scores on Initial Assessment, After Emergence of Symptoms and After Treatment

AGE/ SEX	BPRS SCORES AT INITIAL ASSESSMENT	BPRS SCORES AFTER EMERGENCE OF SYMPTOMS	BPRS SCORES AFTER TREATMENT WITH OLANZAPINE

48/M	24	46	32
22/F	30	56	36
27/F	28	74	43
23/F	22	78	38
27/M	24	64	32
21/M	27	48	18
19/F	22	78	40
24/F	23	88	34
50/M	25	50	32
28/F	18	67	33
26/M	20	35	18
41/M	22	38	20

BPRS Scores on Initial Assessment, After Emergence of Symptoms and After Treatment



12 patients were evaluated before starting treatment for MDR-Tuberculosis, and none showed any significant psychiatric symptoms.

However, after beginning the MDR-TB treatment, all 12 patients developed psychiatric symptoms, which were assessed using the BPRS (Brief Psychiatric Rating Scale). The results showed that 2 patients had mild symptoms with BPRS Score >31, 3 had moderate symptoms with BPRS Score >41, and 7 had severe symptoms with BPRS Score >53.

Following this, all patients were treated with OLANZAPINE, and their condition was reassessed after 15 days. The follow-up BPRS scores showed significant improvement: 3 patients had no significant symptoms with BPRS Score <31, 8 had only mild symptoms, and 1 patient had moderate symptoms.

CONCLUSION

OLANZAPINE was found to be a safe and effective monotherapy for managing MDR-TB-induced psychosis without compromising antituberculosis regimen, with improvements in BPRS scores and minimising the risk of side effects, that are commonly associated with other antipsychotics.

OLANZAPINE was observed to enhance the overall general health of the patients by increasing their appetite and contributing to weight gain.

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