IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Case Report
August 2020 Vol.:19, Issue:1

The Role of Clozapine in Treatment Resistant Depression

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An official Publication of Human Journals
ISSN 2349-7203
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Submission: 21 July 2020
Accepted: 28 July 2020
Published: 30 August 2020

HUMAN JOURNALS
www.ijppr.humanjournals.com

Keywords: Clozapine, Depression with psychotic symptoms, Treatment resistant depression, Agranulocytosis.

ABSTRACT

The purpose of this case study is to analyze the effect of clozapine in treatment resistant depression with psychotic symptoms. We thought this was an important case which will highlight the use of clozapine in such situations and that further research in this area was needed.

INTRODUCTION

Major depressive disorder with psychotic features is a distant type of depressive illness in which mood disturbance is accompanied by either delusions, hallucinations, or both[(2)]. Being affected by a mental disorder is a significant risk factor for suicide. Therefore, the identification of patients at risk for suicide among patients with mental disorder is of high clinical relevance[(3)]. Possible mechanisms of reducing suicidal thoughts and behaviours with clozapine probably involve the simultaneous modulation of dopamine, norepinephrine, and serotonin, regulation of the hormone system (pregnenolone, cortisol), and intracellular systems-dependent modulation of N-methyl-D-aspartate receptor expression, brain-derived neurotrophic factor upregulation, and regulation of the arachidonic acid cascade[(5).] We came across with such a case of a 39 year old female in the psychiatry department.

CASE PRESENTATION

Here we present a case of 39 year old female brought to psychiatry department with complaints of low mood, reluctant to take food and fluids and excessive prayer since one week. When comes to history, she had behaviour problems in past and for that, she had taken medicines from a tertiary care hospital. Also, she presented with a history of pemphigus vulgaris since 2014 and was taking medicines at the time of admission. Medicines include Prednisolone 10 mg, Calcium + Cholecalciferol and Omeprazole 20 mg. There was no family history of mental or physical illness. This information was given by her sister at the time of admission.

MENTAL STATUS EXAMINATION

- **General appearance and behavior**

Her general appearance and behavior showed that she was poorly built and malnourished, with poor grooming. She was incoperative and brought to the hospital emergency department using physical force. She had a poor rapport and was difficult to maintain an eye contact.

- **Psychomotor activity**

She has decreased level of psychomotor activity.

- **Speech**

Speech was decreased.

- **Mood and affect**

Mood appears depressed.

- **Thought**

Stream and form is normal.

- **Content**

Patient was deluded but not explained and not willing to open up about her delusion.

- **perception**

No perception abnormality elicited.

- **Cognitive function**

Patient was not cooperative for cognitive function examination.

PHYSICAL STATUS EXAMINATION

- CVS-normal
- CNS-no neurological deficit
- GIT-within normal limits
- Respiratory system-within normal limits

1 to 11 days

After the assessment of patient, doctor advised for admission. Then started with T. Olanzapine 5mg along with T. Venlafaxine, multiple vitamin injection and on next day doctor added T. Lorazepam and also recommended RT feed since the patient is reluctant to take the food and fluids. On 3rd day T, Risperidone and Trihexyphenidyl combination got added to medication chart. On 5th day doctor added T. Olanzapine and Fluoxetine

combination. After the administration of these medicines, still the patient was not ready to take food and fluids and the condition was getting worsen. On 7th day doctor advised for increasing dose of T. Olanzapine and Fluoxetine combination. These medications were continued till 10th day. In between on 9th day, patient had developed a bed sore over the dorsal region. And so on the 10th day surgery consultation had done and doctor prescribed with antibiotics for next five days. On 10th day, doctor discussed about ECT for this patient with the bystanders. But they were not willing to do the same and also doctor discussed that patients condition is not good for the anaesthesia like procedures before ECT. And the patient was getting malnourished. So, because of these reasons, doctor decided to do the therapy with Clozapine and discussed about this with the bystanders. Then on the 11th day, patient prescribed with T. Clozapine along with the previous medications and also started T. Trifluperazine and T. Trihexyphenidyl combination, multivitamins. At the time of admission, laboratory results of the patient showed that blood urea (0.9mg/dl) and Sodium level (150 mEq/L) was elevated. Blood sugar level, creatinine and potassium level was found to be normal. Packed cell volume (33.3%), HB (10.4g%), platelet count (1.6 lakhs/cumm) was found to be normal.

12th to 18th day

Above mentioned medicines were continued till 18th day (day of discharge) and on 15th day patient started to respond, agreed to take food and so RT removed. Blood counts also checked again because agranulocytosis is the serious side effect of clozapine. But the blood counts were normal. Till 18th day, doctor advised to take light food and fluids. Patient got improved well, began to speak during these days but she didn't open up about her delusion.

DISCUSSION

A randomized prospective trial examining clozapine versus treatment as usual performed in a patient population with schizoaffective disorder or bipolar disorder, the result of which suggested that clozapine had independent mood stabililzing effect.(1)

Of those who experience severe clinical depression, about 14.7% to 18.5% will develop depression with psychotic features(6). Over 20 years of research suggests that patients with psychotic features are more likely to have treatment resistant depression compared with who did not have psychotic symptoms associated with their depression.(2) In a study of 18980 people aged 15 to 100 years who where the representative of the general populations of

several European countries, the prevalence of psychotic depression was 4/1000 people. In a study of consecutively admitted patients hospitalized for major depression, Coryell and colleagues reported that 25% percentage of the patient met criteria for psychotic depression[4]. According to studies, depression is more common in women than men. The report on global burden of disease estimates the point prevalence of unipolar depressive episodes to be 1.9% for men and 3.2% for women and the 1 year prevalence has been estimated to be 5.8% for men and 9.5% for women.

CONCLUSION

Treatment resistant depression continues to a challenge for mental health care providers and in this area, further researches are needed. In this case, patient was not improving to first line therapy. As the patient became malnourished and developed infections after two weeks of therapy, she was started with clozapine. In this case, clozapine made a significant improvement in clinical state. And here the resistance to all previous treatments suggests that maybe the use of Clozapine was the reason for patient's improvement.

Author's contributions: All authors have equally contributed for making this case report to be successful.

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