CASE REPORT

Clozapine: Is it too Early?

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Abstract

Clozapine is an effective anti-psychotic and has long been used as an intervention for treatment-resistant schizophrenia. This case report will highlight the use of Clozapine up to 100 mg ON as a second-line medication to achieve satisfactory response after 5 weeks in an adolescent who was recently diagnosed with schizophrenia.

Keywords: Clozapine, Schizophrenia, Treatment-resistant

Introduction

Clozapine, the prototypical ‘atypical’ anti-psychotic, has been used since the 1960s. It is the most effective treatment for patients with refractory schizophrenia and improves both positive and negative symptoms. However, there is a lot of hesitancy in using it in clinical practice given its side-effects. The case presented here highlights the use of Clozapine as a second-line medication despite the commonly practice of adequate trial of two anti-psychotic.

Case Report

MFMN is a 17-year-old Malay adolescent who was brought by his family to Universiti Malaya Medical Centre due to sudden onset of abnormal behaviour for the past five days. He was talking irrationally and his family noticed that he was talking-to-himself as if he was having conversations with a real person. He was also irritable, and started to quarrel and picked fights with his siblings. MFMN was also having difficulties to sleep at night and had been spending majority of his time at the internet café. He also neglected his personal hygiene and refused to clean himself or to take his meals. He has been absent from school since the beginning of the current problems. Further history from his family revealed that a similar episode of talking-to-himself, pre-occupation with the internet and sleeping difficulties occurred about one year ago. The symptoms resolved after five days of regular benzodiazepines from a general practitioner. There was no proper psychiatric consultation after the resolution of the acute episode. However, MFMN was never back fully to his normal self as he became socially withdrawn. There was no history of psychiatric illness in his family. During the assessment, he was not co-operative, was easily distractible and he could not establish adequate eye contact. Rapport was not obtained and at the same time he was making abnormal acts as if he was performing the traditional Malay martial arts
of ‘silat’ which he was never known to have learnt before. His speech was irrelevant, incoherent and irrational with looseness of association. His affect was inappropriate to his thoughts and mood. He was hallucinating during the interview and was noted to be having conversations with invisible figures regarding his life. His cognitive functions and physical examinations were generally intact.

MFMN was subsequently investigated for any organic cause to his bizarre behaviour but the basic blood investigations and neuroimaging including CT scan of the brain produced normal results. He was subsequently diagnosed as a case of adolescent-onset schizophrenia and treated as an out-patient basis at the request of his family who was willing to monitor him and supervise his medications. He was initially started on oral Risperidone 1 mg ON with oral Clonazepam 0.5 mg ON and was subsequently seen three days after commencing treatment. His oral Risperidone was slowly increased up to 4 mg daily over the next six weeks. Although his disorganized behaviour responded to Risperidone, he was still experiencing other positive symptoms such as disorganized thoughts and delusion of thought broadcasting and also persecutory delusion. Compliance was ensured with close supervision from his parents. Also at this dose, MFMN showed clinically significant extra pyramidal symptoms (EPS) such as akathisia, parkinsonism and siallorrhoea.

After careful consideration regarding the possible history of a year with prodromal or negative symptoms before the breakthrough of current psychotic episode, a decision was taken to start MFMN on Clozapine. This was discussed with the family. This was planned to be done as an out-patient basis and the Risperidone was slowly tailed down. After his baseline blood count showed results within the normal range, MFMN was started on low dose of Clozapine at 12.5 mg ON for the first three days followed by an increase to 25 mg ON before his next appointment. The oral Risperidone was stopped completely after 3 weeks on Clozapine. At week 5 of Clozapine at the dose of 100 mg ON, MFMN showed significant improvement in his positive symptoms. The disorganized speech and behaviour was totally absent with only residual elementary auditory hallucination that occasionally comes and goes. There were no more episodes of agitation and aggression and his relationship with his family has improved. He was able to help out in doing the house chores and occasionally went out to play football with his friends. His EPS problems have improved and both he and his family was happy regarding the progress. The dose of Clozapine was further increased to achieve full remission of the symptoms.

Discussion

Schizophrenia is a chronic and debilitating disease. It is rare before the age of 13, although its symptomatology becomes quite similar to those in adults as the age increases\(^1\). Aggressive intervention is needed in adolescent-onset schizophrenia due to its poor prognosis because of early onset of illness. Clozapine is the only drug licensed for the treatment of schizophrenia in individuals as young as 16 years who are unresponsive to or intolerant of conventional medications (US Food and Drug, 1989). Usual clinical practice advocates the trial of at least two prior typical anti-psychotics at an adequate dose for an adequate amount of time or failed at least three atypical anti-psychotics before switching to Clozapine\(^2\). However, time is not a luxury when treating an adolescent who has wasted a year of his
life due to untreated psychosis. It has been suggested that Clozapine should be selected as a second-line treatment for those with a first-episode schizophrenia who have failed one trial of a second-generation antipsychotic\textsuperscript{3,4}. Although many subjects dropped-out from a study comparing Clozapine to Haloperidol due to neutropenia and seizures\textsuperscript{5}, reluctance to use Clozapine due to fear of side-effects is unjustifiable as its efficacy in children and adolescent schizophrenia has been proven\textsuperscript{6,7}. The general guidelines for the use of Clozapine in children and adolescents population are similar to those of adults. It is recommended that lower doses of anti-psychotics than adults be used in this population\textsuperscript{8}.

It is hoped that this case report will help in contributing more evidence regarding the use of Clozapine in treating schizophrenia for the children and adolescent population. This is because it is likely that more cases of children and adolescent-onset schizophrenia will be seen with the expansion of the child and adolescent psychiatry services and time is not a luxury to spare in their treatment.

References


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