Clozapine in Borderline Personality Disorder and Intellectual Disability: A Case Report of Four-Year Outcome

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Evidence on the usefulness of clozapine in people with borderline personality disorder is becoming more readily available. While most of the research points to the significant initial improvement, there is a paucity of information on the long-term outcome. Evidence on the use of clozapine in people with the dual diagnoses of intellectual disability and borderline personality disorder is also lacking. This case report highlights the sustained global improvement in a person with mild intellectual disability and borderline personality disorder with a low dose of clozapine. Follow up over a four-year period indicates the potential for developing long-term side effects, the need for monitoring and regular risk-benefit analysis with the active involvement of the individual receiving treatment in decision making.

Keywords: aggression, antipsychotic, borderline personality disorder, clozapine, depression, developmental disability, impulsivity, intellectual disability, mental retardation, mood, pharmacotherapy, psychiatric disorder, self-injury

The use of clozapine in the treatment of resistant schizophrenia is now well established. Clozapine is also increasingly recognized as an effective treatment in several other conditions such as rapid cycling bipolar disorder, schizoaffective disorder, psychosis in Parkinson’s disease and in those with brain injury. The effect of clozapine on aggression and self-injurious behavior, in patients with and without schizophrenia, has also been a focus of research.

There is increasing interest in the use of clozapine in the treatment of borderline personality disorder. Whilst it is generally recognized that the treatment of personality disorder is predominantly psychological, targeted drug treatment of individual symptoms may be helpful in some patients. In a recent review of the treatment of personality disorder, Tyrer and Bateman noted, “If recommendations are based on evidence alone, there is no reason why drug treatment should be regarded as secondary and psychological treatment primary.” They concluded that medications would continue to be used in the treatment of personality disorder and had the potential to be an important intervention.

There is a growing evidence base in support of the use of clozapine in people with borderline personality disorder. In comparison, the drug treatment of borderline personality disorder in people with intellectual disability is limited to isolated case reports. Mavromatis described a significant clinical improvement with the use of olanzapine, as part of a comprehensive treatment package, for two people with borderline personality disorder and intellectual disability. This study also suggested that people with intellectual disability and borderline personality disorder might respond differently to psychotropic medications than the general population. To our knowledge there have been no reports of the use of clozapine in people with both intellectual disability and borderline personality disorder.

This is a case report of a person with mild intellectual disability and severe borderline personality disorder who achieved a marked improvement in all areas of functioning with clozapine treatment. An initial improvement in her impulsivity led to a significant reduction in aggression and self-injury, which was sustained over a four-year follow-up period.

CASE REPORT

Ms. A is a 29-year-old female with Mild Intellectual Disability and Borderline Personality Disorder. She did not have a family history of mental illness or intellectual disability. She was born at full term without any reported perinatal complications. Developmental delays in learning
education was mainly in the special school system. She had a series of traumatic childhood experiences including childhood sexual abuse, parental violence and parental divorce. Throughout childhood she displayed a number of behavioral problems, which escalated to such a level that by the age of 11 years she had been admitted to a residential school for children with learning difficulties and behavioral problems. She was referred to a child psychiatrist around this time and was prescribed an anti-depressant. Although she had a short period of counseling it was abruptly terminated following a severe escalation in her disturbed behavior.

Starting from early adulthood her contact with the adult psychiatric service for people with intellectual disability was mainly in crises with self-harm or disturbed behavior. During a typical six-month period she had 20 episodes of risk-taking/dangerous behavior including absconding from home, threatening to jump off buildings, property damage, superficial cutting, making false emergency telephone calls and assaulting police officers. She reported feelings of abandonment, emptiness and hopelessness. There were no sustained periods of low mood or any persistent psychotic symptoms. At times she would report flashbacks of the childhood sexual abuse and hearing a male voice (which she recognized as one of her abusers) asking her to harm herself; however, this voice was transient and disappeared once the crisis was resolved.

Due to frequent crises and high impulsivity, the psychiatric team found it difficult to engage her in therapeutic work. She was tried on a number of psychototropic medications. These medications included two mood stabilizers (carbamazepine and lithium), five antidepressants (fluoxetine, trazodone, sertraline, paroxetine, and fluvoxamine) three anxiolytics (diazepam, propranolol, and lorazepam) and eight antipsychotics (zuclopenthixol dihydrochloride, flupentixol decanoate, thioridazine, risperidone, olanzapine, sulpiride, amisulpride, droperidol, and haloperidol). Typically a newly started medication would produce a small benefit that would not last beyond an initial 2-3 week “honeymoon” period. She, however, stayed on these medications at standard doses for prolonged periods without any evidence of benefit.

Despite a high level of support in the community, she required frequent admissions to the acute inpatient unit. A typical acute admission would be precipitated by self-harm or aggressive behavior accompanied by significant distress and marked agitation. Immediately after admission, her behavior on the ward would be extremely disturbed with self-harming attempts, assaults on staff, breaking windows, and attempts to light fires. She also absconded from the ward on many occasions. Her last admission, more than four years ago, occurred following a series of aggressive behaviors which included an assault on a police officer and damage to a police car.

On her last admission, a thorough review of her past history and current presentation confirmed her diagnoses as Borderline Personality Disorder and Mild Mental Retardation using DSM IV criteria. The features of Borderline personality disorder she displayed, that began by early adulthood and was evident in a variety of contexts, included a pervasive pattern of instability of interpersonal relationships, self-image and marked impulsive behavior. She also had an affective instability and displayed severe behavioral outbursts of intense anger. She experienced chronic feelings of emptiness, fear of abandonment and repeated emotional crises. A further assessment of her adaptive living skills was made using the Vineland Adaptive Behavior Scale and her level of functioning was confirmed as being in the Mild Intellectual Disability range.

A trial of clozapine treatment was considered in view of her high levels of impulsivity and arousal, lack of response to numerous previous antipsychotic medications and some evidence of effectiveness of clozapine in similar situations. The multi-professional team responsible for her care were in agreement after carrying out a risk-benefit analysis, that a trial of treatment with clozapine was justified. A second opinion from an independent psychiatrist was sought, who was in agreement that a trial of the off-license use of clozapine would be reasonable. Ms. A also gave her informed consent for clozapine treatment.

Clozapine was started at a dose of 12.5 mg twice daily and was increased in two steps to 50 mg twice daily. Slight drowsiness in the morning was the only initial side effect noted. A marked reduction in her level of disturbed behavior was noted within two weeks of starting clozapine with further improvement over the next few weeks. By the end of the sixth week of treatment, she was well enough to be discharged having had a settled period of over a month with several home leaves. The two main areas of improvement were significant reductions in her impulsivity and emotional lability. At the time of discharge both Ms. A and her mother reported that it was the most remarkable change that she had ever had. Subsequent to discharge she was
able to build a trusting relationship with her treating team, discussing her feelings more openly. She was able to describe a pattern where she would experience a slow build up of emotions such as the fear of rejection, anxiety, memories of sexual abuse and anger leading to crises, which would manifest as highly disturbed behavior. With the support from her community team, she was able to avoid the emotional problems escalating to crises and use alternative coping strategies.

She has remained on clozapine 50 mg twice daily for the past three and a half years. Over this time not only has her improvement been sustained, but it has also led to significant improvement in her living skills and confidence level. Her mood has remained euthymic and there is no evidence of any psychotic symptoms. Although she continues to have occasional thoughts of self-harm, in response to stressful situations, she is able to resist these thoughts and discuss them with her community team. She currently feels much more in control of herself and is able to think about the possible consequences before acting.

Table 1 compares the number of behavioral incidents in the three years prior to and the three years following clozapine treatment.

Table 1. Comparison in Number of Behavioral Incidents Three Years Prior and Three Years Following Clozapine Treatment

<table>
<thead>
<tr>
<th>Behavior rated</th>
<th>Three year period before clozapine Number of Incidents</th>
<th>Three year period after clozapine Number of Incidents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deliberate self-harm</td>
<td>35</td>
<td>1</td>
</tr>
<tr>
<td>Physical aggression</td>
<td>23</td>
<td>0</td>
</tr>
<tr>
<td>Damage to property</td>
<td>34</td>
<td>0</td>
</tr>
<tr>
<td>Hospital admission</td>
<td>15</td>
<td>0</td>
</tr>
</tbody>
</table>

**Adverse Effects**

Unfortunately, several months after starting clozapine, she was diagnosed with type II diabetes mellitus. There is no family history of diabetes. She was obese prior to clozapine treatment and has gained further weight since. In view of these side-effects the risk and benefits of clozapine were discussed in detail with Ms. A and, at her request, her mother. Ms. A was provided adequate time to contemplation and clarification as was necessary. She took an active part in decision making with support from her mother and gave her consent to continue clozapine, whilst addressing diabetes with oral hypoglycemic medication, diet control and other weight management measures including fitness sessions at a gymnasium. A specialist diabetes nurse is regularly monitoring her glycemic control which is normal. She has at no stage withdrawn her consent to treatment with clozapine and is aware that she is able to do so at any point in time.

**Discussion**

This report outlines the case of a young woman with Borderline Personality Disorder and Mild Intellectual Disability. She has shown a dramatic and sustained improvement following the introduction of a low dose of clozapine treatment.

There are several possible explanations for this improvement. Natural, spontaneous remission of symptoms of a borderline personality disorder is unlikely to occur so dramatically and with such a clear time correlation with the introduction of clozapine. Whilst many argue that individuals with borderline personality disorder may “mature” over time, such changes are more likely to occur at a later stage of life and at a slower pace. It should also be noted that prior to clozapine treatment Ms. A’s level of disturbed behavior was escalating rather than diminishing.
There were no changes in social circumstances or life-changes that could account for her recovery. No other changes were made to her multidisciplinary treatment program at the time of introduction of clozapine or over the next few months. It is thus unlikely that some other unknown treatment or environmental change was responsible for her improvement. Although it is not possible to rule out a “delayed response” to previous psychological, pharmacological or social treatment, we feel that this is highly unlikely given the long time interval involved and the fact there was no sign of improvement until clozapine was started. We also considered the possibility of a placebo effect but think this unlikely given the clear temporal relationship of sustained improvement, which occurred in the second week of treatment and increased over the next few weeks and had not occurred with any other medications. Over a period of many years the patient had several independent psychiatric assessments, including assessments in the inpatient unit. There is no evidence from any of these assessments to suggest the possibility of schizophrenia or related disorders. It is unlikely that she had an undiagnosed schizophrenic or other psychotic illness that has responded to clozapine. The dose of clozapine used here was 100 mg daily, which is well below the range at which it is used in the treatment of schizophrenia, generally 400-800 mg daily.

This case report shows the dramatic and sustained improvement of a person with borderline personality disorder and intellectual disability. Our clinical impression is that much of this improvement can be attributed to a marked decrease in the patient’s impulsivity leading to significant and persistent reduction in her self-harm and aggression. It has been postulated that excessive impulsivity reflects central serotonergic system dysfunction and that clozapine may improve this due to its potent 5-HT2 antagonistic activity.1

We feel that the reduction in impulsivity gave her an increased ability to engage with her therapeutic program. Clozapine in other words appears to have given her “thinking time” allowing her to be more receptive to the psychological support provided and successfully use alternative coping strategies. The sustained period of improvement has given her the time to change the maladaptive coping strategies and establish a more positive and healthy outlook about herself and life in general. During the course of clozapine treatment the patient developed diabetes mellitus and gained a substantial amount of weight. As with any other treatment the potential adverse effects must be carefully weighed up in balance against its possible therapeutic benefits.

REFERENCES


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