Dose-Dependent Clozapine-Induced Skin Picking and Self-Injurious Behaviour in Treatment-Resistant Schizophrenia

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Abstract

Clozapine is a second-generation antipsychotic used for treatment-resistant schizophrenia. Obsessive-compulsive symptoms induced by clozapine is a known entity. Skin-picking is closely related to obsessions and excoriation disorder is now categorised under obsessive-compulsive and related disorders. Skin-picking associated with clozapine dose increments has been reported in a young male from India. Apart from this, skin-picking and self-injurious behaviour associated with clozapine use are not well described in the literature. Here we report a young Sri Lankan male with treatment-resistant schizophrenia presenting with self-injurious behaviour that is related to clozapine-induced compulsive skin-picking. Due to the partial response, clozapine dose of the described patient was increased above 550 mg/day. Skin-picking was seen only above this dose and the addition of risperidone helped to resolve the psychotic symptoms and keep the clozapine dose at the previous level. The current report is unique in the sense that the self-injurious behaviour was associated with clozapine dose increments.

Keywords: Obsessive-Compulsive Disorder, Self-injurious Behaviour, Skin-picking, Clozapine, Sri Lanka

INTRODUCTION

Clozapine is a second-generation antipsychotic used for treatment-resistant schizophrenia. It is well established that clozapine induces obsessive-compulsive symptoms in patients with schizophrenia. Among patients on clozapine, one fifth were noted to have obsessive-compulsive symptoms and a majority has had symptoms prior to the commencement of the antipsychotic. Furthermore, clozapine is known to be effective for self-injurious behaviour in individuals with intellectual disability and borderline personality disorder. Skin-picking is a form of self-injury that is closely associated with obsessive-compulsive symptoms. Excoriation (skin-picking) disorder is now categorised under obsessive-compulsive and related disorders in the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM 5). Sri Lanka is a South Asian nation with a population of 22 million. The mental health services are mostly hospital-based and subspecialties in psychiatry are at an initial stage of development. Here we report a young Sri Lankan male with treatment-resistant schizophrenia presenting with skin-picking and self-injurious behaviour related to increment in dose of clozapine. An independent psychiatrist assessed the capacity to give consent and written informed consent was obtained for publication. We could not access any reports of clozapine-induced self-injurious behaviour from Sri Lanka.
CASE REPORT

Mr G is a 32-year-old male treated with clozapine for treatment-resistant schizophrenia. As an inpatient, he had partial improvement of psychotic symptoms at a dose of 550 mg/day after gradual increments. When the dose was increased further to 600 mg/day, he started to show self-injurious behaviour. He inflicted wounds on the dorsal left foot requiring acute surgical interventions for bleeding. After a few days, he developed features of cellulitis of the affected limb. This needed surgical opinion and intravenous antibiotics. The self-injurious behaviour continued, and surgical examination revealed that the injury had reached the periosteum of the third metatarsal bone. Mr G reported severe pain on the left foot but continued to inflict more harm on himself.

Considering this new behaviour and the potential impact on physical health, the clozapine dose was reduced to 550 mg/day. With this dose reduction, the self-injurious behaviour reduced and ceased within a week. Due to the persistence of psychotic symptoms of the patient, the dose was increased to 575 mg/day four weeks later. This led to a return of self-injurious behaviour and the dose was brought down to 550 mg/day again, which resulted in a cessation of injurious behaviour. On assessment, the patient had developed compulsive skin-picking. Sequential observations revealed that the intensity and frequency of skin-picking were associated with clozapine dose changes. A limitation was the unavailability of facilities to check serum clozapine levels.

On mental state assessment, the patient had developed an obsession, a recurrent, unpleasurable, resisted thought that there is a foreign body embedded in his left foot. To relieve the distress associated with this thought he repetitively attempted to check the presence of this object by picking on the skin. In between episodes of self-injurious behaviour, he frequently felt his behaviour is unreasonable and irrational, which was a stark difference to his strong delusional beliefs. The Yale-Brown Obsessive-Compulsive Scale assessment indicated symptoms in the extreme range while the clozapine dose was at 600 mg/day and the severity dropped to the mild range after the dose was reduced.

The skin-picking was not related to his psychotic symptoms and were not present before the dose increments above 550 mg/day. Risperidone was added as an augmenting agent with reduction of psychotic symptoms clinically and according to the Brief Psychiatric Rating Scale. A radiograph taken of the left foot after a month revealed features suggestive of osteomyelitis and orthopaedic opinion was taken.

DISCUSSION

This report describes a young Sri Lankan male with treatment-resistant schizophrenia treated with clozapine. Due to the partial response, increasing clozapine above 550 mg/day induced new-onset skin-picking and self-injurious behaviour. We could not access any prior publications on clozapine-induced self-injurious behaviour from Sri Lanka.

According to the DSM 5, the skin-picking disorder’s diagnostic criteria include, recurrent skin picking resulting in skin lesions, repeated attempts to stop, clinically significant distress or impairment of functioning, skin picking not attributable to the physiological effects of a substance/medical condition and not better explained by symptoms of another mental disorder. Due to the skin-picking being associated with clozapine dose increments in the described patient, it could not be classified as the skin-picking disorder. It is thought that defects in fronto-striatal pathways that implement top-down inhibitory control might contribute to the repetitive skin-picking behavior. Clozapine induced skin picking has been reported previously in a 26-year-old man in India with intellectual disability and treatment-resistant schizophrenia. This patient from the neighbouring nation developed skin-picking above the clozapine dose of 350 mg/day and improved with the addition of a selective serotonin reuptake inhibitor escitalopram.

It is argued that non-suicidal self-injury is closely related to obsessive-compulsive disorder. Non-suicidal self-injury involves deliberate harm to the body without suicidal intent and includes cutting, scratching, skin picking, and burning. Diagnostic criteria for psychogenic excoriation have been proposed and published earlier. These criteria include three subtypes, which were impulsive, compulsive, and mixed types. Impulsive skin picking occurs in response to feelings of tension in the individual. It is performed with minimal awareness of such and with little resistance. On the other hand, the other subtype compulsive skin picking is identified to be performed in response to an obsession/anxiety. Even though performed deliberately, the person retains the insight into the irrationality of the excoriation related behaviour. The described patient probably had
compulsive skin-picking as he had an obsession and felt the irrationality of his behaviour at times.

Obsessive-compulsive symptoms are a recognised complication of clozapine therapy for treatment-resistant schizophrenia. The mechanism of clozapine-induced obsessions is postulated to be due to anti-serotonergic properties at 5HT1C, 5HT2A and 5HT2C receptors. Suicidal obsessions as a dose-dependent adverse effect of clozapine have been reported from Croatia. Here the increase of clozapine dose from 150 to 300 mg/day was associated with the occurrence of ego-dystonic suicidal obsessions in a 54-year-old male. As in the current case, reduction of clozapine dose and the addition of another antipsychotic led to the cessation of suicidal symptoms. Obsessions with clozapine are mainly linked with the 5HT2 affinity and it would be rational to add an antipsychotic which has less 5HT2A/5HT2C affinity than clozapine such as quetiapine. However, in the current report, we found that the addition of risperidone helped to resolve the psychotic symptoms and keep the clozapine dose at the previous level.

In relevance to self-injurious behaviour associated with obsessions, there is a report of an older Indian male who presented with genital self-mutilation and an 11-year-old Sri Lankan boy pulling out his own teeth. Clozapine is known to be effective in reducing self-injurious behaviour in offenders and prisoners where more personality disorders are seen compared to the general population. However, the current report is unique in the sense that the self-injurious behaviour was induced by the clozapine dose increments.

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