

Case Report

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

Layani C Rathnayake¹, Miyuru Chandradasa^{2,3} and Jayan Mendis⁴

¹District Base Hospital, Dickoya, Sri Lanka

²Department of Psychiatry, Faculty of Medicine, University of Kelaniya, Ragama, Sri Lanka

³Colombo North Teaching Hospital, Ragama, Sri Lanka

⁴General Sir John Kotelawala Defence University, Colombo, Sri Lanka

Correspondence: Miyuru Chandradasa, Senior Lecturer, Department of Psychiatry, Faculty of Medicine, University of Kelaniya, PO Box 6, Thalagolla Road, Ragama, Sri Lanka 11010

Email: miyuruc@kln.ac.lk

 ORCID ID: <https://orcid.org/0000-0002-1873-8228>

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 schizophrenia¹. 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 antipsychotic². Furthermore, clozapine is known to be effective for self-injurious behaviour in individuals with intellectual disability and borderline personality disorder^{3,4}. 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)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^{6,7}. The mental health gap is wide and even major psychiatric disorders such as schizophrenia are known to have a long duration of untreated psychosis⁸. 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 reduced⁹.

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 Scale¹⁰. 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 disorder¹⁰. 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 behavior¹¹. Clozapine induced skin picking has been reported previously in a 26-year-old man in India with intellectual disability and treatment-resistant schizophrenia¹². 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 escitalopram¹².

It is argued that non-suicidal self-injury is closely related to obsessive-compulsive disorder¹³. Non-suicidal self-injury involves deliberate harm to the body without suicidal intent and includes cutting, scratching, skin picking, and burning¹³. Diagnostic criteria for psychogenic excoriation have been proposed and published earlier. These criteria include three subtypes, which were impulsive, compulsive, and mixed types¹⁴. 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/anxiety¹⁴. 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 schizophrenia¹. The mechanism of clozapine-induced obsessions is postulated to be due to anti-serotonergic properties at 5HT_{1C}, 5HT_{2A} and 5HT_{2C} receptors¹. Suicidal obsessions as a dose-dependent adverse effect of clozapine have been reported from Croatia¹⁵. 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 5HT_{2A}/5HT_{2C} affinity than clozapine such as quetiapine¹⁵. 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-mutilation¹⁶ and an 11-year-old Sri Lankan boy pulling out his own teeth¹⁷. 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 population¹⁸⁻²⁰. However, the current report is unique in the sense that the self-injurious behaviour was induced by the clozapine dose increments.

REFERENCES

- Schirmbeck F, Zink M. Clozapine-induced obsessive-compulsive symptoms in schizophrenia: a critical review. *Current Neuropharmacology* 2012;10(1):88–95. <https://doi.org/10.2174/157015912799362724>
- Grover S, Hazari N, Chakrabarti S, Avasthi A. Relationship of obsessive compulsive symptoms/disorder with clozapine: A retrospective study from a multispeciality tertiary care centre. *Asian Journal of Psychiatry* 2015;15:56–61. <https://doi.org/10.1016/j.ajp.2015.05.002>
- Hammock R, Levine WR, Schroeder SR. Brief report: effects of clozapine on self-injurious behaviour of two risperidone non-responders with mental retardation. *Journal of Autism and Developmental Disorders* 2001;31(1):109-13. <https://doi.org/10.1023/a:1005626100084>
- Zarzar T, McEvoy J. Clozapine for self-injurious behaviour in individuals with borderline personality disorder. *Therapeutic Advances in Psychopharmacology* 2013;3(5):272-4. <https://doi.org/10.1177/2045125313484323>
- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. American Psychiatric Publishing, 2013. <https://psycnet.apa.org/doi/10.1176/appi.books.9780890425596>
- Chandradasa M, Kurupparachchi KA. Child and youth mental health in post-war Sri Lanka. *BJPsych International* 2017;14(2):36-37. <https://doi.org/10.1192/s2056474000001756>
- Chandradasa M, Champika L. Subspecialisation in postgraduate psychiatry and implications for a resource-limited specialised child and adolescent mental health service. *Academic Psychiatry* 2019;43(1):135-139. <https://doi.org/10.1007/s40596-018-0920-8>
- Chandradasa M, Champika L, Gunathillaka K, Mendis J. Association of duration of untreated psychosis and functional level, in first episode of schizophrenia attending an outpatient clinic in Sri Lanka. *Journal of the Postgraduate Institute of Medicine* 2016;3(E33):1–6. <https://doi.org/10.4038/jpgim.8112>
- Goodman WK, Price LH, Rasmussen SA, Mazure C, Fleischmann RL, Hill CL, et al. The Yale-Brown Obsessive-Compulsive Scale. I. Development, use, and reliability. *Archives of General Psychiatry* 1989;46(11):1006–1011. <https://doi.org/10.1001/archpsyc.1989.01810110048007>
- Overall JE, Gorham DR. The brief psychiatric rating scale. *Psychological Reports* 1962;10(3):799-812. <https://doi.org/10.2466/pr0.1962.10.3.799>
- Blum AW, Chamberlain SR, Harries MD, Odlaug BL, Redden SA, Grant JE. Neuroanatomical Correlates of Impulsive Action in Excoriation (Skin-Picking) Disorder. *Journal of Neuropsychiatry and Clinical Neurosciences* 2018;30(3):236–241. <https://doi.org/10.1176/appi.neuropsych.17050090>
- Reddy B, Das S, Guruprasad S. A case of clozapine-induced skin picking behaviour. *General Psychiatry* 2018;31(2). <https://doi.org/10.1136/gpsych-2018-000012>
- McKay D, Andover M. Should non-suicidal self-injury be a putative obsessive-compulsive-related condition? A critical appraisal. *Behavior Modification* 2012;36(1):3-17. <https://doi.org/10.1177/0145445511417707>
- Arnold LM, Auchenbach MB, McElroy SL. Psychogenic excoriation. Clinical features proposed diagnostic criteria, epidemiology and approaches to treatment. *Molecular Diagnosis and Therapy* 2001;15(5):351–359. <https://doi.org/10.2165/00023210-200115050-00002>
- Aukst-Margetić B, Margetić B, Maršanić VB. Suicidal obsessions as dose-dependent side-effect of clozapine. *Psychopharmacology Bulletin* 2011;44(1):65.
- Pandit L, Vardhan V. Late-onset obsessive-compulsive disorder presenting as genital self-mutilation. *Australian & New Zealand Journal of Psychiatry* 2013;47(10):969-70. <https://doi.org/10.1177/0004867413486843>
- Chandradasa M, Champika L, Hettiarachchi D, Wijetunge S, Mendis J. Serious bodily harm related to Obsessions from Sri Lanka. *Psychiatria Danubina* 2017;29(1):81-83. <https://doi.org/10.24869/psyd.2017.81>
- Zarzar TR, Catlett TL, O'Connell MG, Harrelson BH, Wilson VP, Rashad GN, et al. Clozapine Reduces Self-Injurious Behaviour in a State Prison Population. *Journal of the American Academy of Psychiatry and the Law* 2019;47(1):61–67. <https://doi.org/10.29158/JAAPL.003818-19>

19. Verdolini N, Murru A, Attademo L, Garinella R, Pacchiarotti I, del Mar Bonnin C, et al. The aggressor at the mirror: Psychiatric correlates of deliberate self-harm in male prison inmates. *European Psychiatry* 2017;44:153–160. <https://doi.org/10.1016/j.eurpsy.2017.04.002>
20. Chandradasa M, Champika L, Mendis S, Fernando F. Female offenders with Psychiatric disorders. *Sri Lanka Journal of Psychiatry* 2015;6(1):32–34. <https://doi.org/10.4038/sljpsyc.v6i1.8060>