

Henry Ford Health System

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Case Reports

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### **Case Report: New onset of febrile episodes on low doses of Clozapine in SICU setting**

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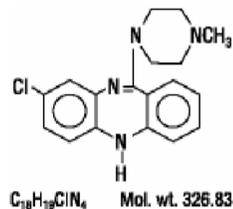


## Objectives

- Understanding the risks associated with Clozapine initiation and titration.
- Conducting a risk versus benefit analysis to start and continue treatment with Clozapine for management of severe psychosis and suicidality.
- Understanding appropriate next steps in management of clozapine-induced fever to enhance the clinical benefits of Clozapine.

## Introduction

- Clozapine, a tricyclic dibenzodiazepine derivative, is an atypical antipsychotic (3).



- Clozapine interferes with the binding of dopamine at: D1, D2, D3 and D5 receptors, it also has high affinity at D4 receptors. It is noted to be more active at the limbic than the striatal dopamine receptors which may explain the decrease in extrapyramidal side effects. (3)
- Clozapine also has antagonistic properties at: adrenergic, cholinergic, histaminergic and serotonergic receptors. (3)
- It is used in treatment resistant schizophrenia to treat positive and negative symptoms of psychosis. (3)
- It is used for reduction in risk of recurrent suicidal behavior in individuals with Schizophrenia or Schizoaffective disorders. (3)
- Side effects of Clozapine include: agranulocytosis, seizures, myocarditis, other adverse cardiovascular and respiratory effects, increased mortality in elderly patients with dementia-related psychosis, hyperglycemia and DM, neuroleptic malignant syndrome, tardive dyskinesia (less likely than other atypical antipsychotics), cardiomyopathy, pulmonary embolism, hepatitis, anticholinergic toxicity, cognitive effects and fever. (3)
- During Clozapine therapy, patients may experience temperatures above 38 degrees C (100.4F). (3)
  - The prevalence of fever varies from 0.5% to 55% depending on the study (2, 4).
  - Peak incidence of fever is within first 3 weeks of treatment.
  - Generally benign and self-limiting though may require discontinuation of treatment.
  - It may be associated with an increase or decrease in WBC or be associated with a life-threatening complication (4).
  - May be in the setting of NMS, infection or inflammation. (4)
  - May be isolated, with no other detectable etiology identified (4).

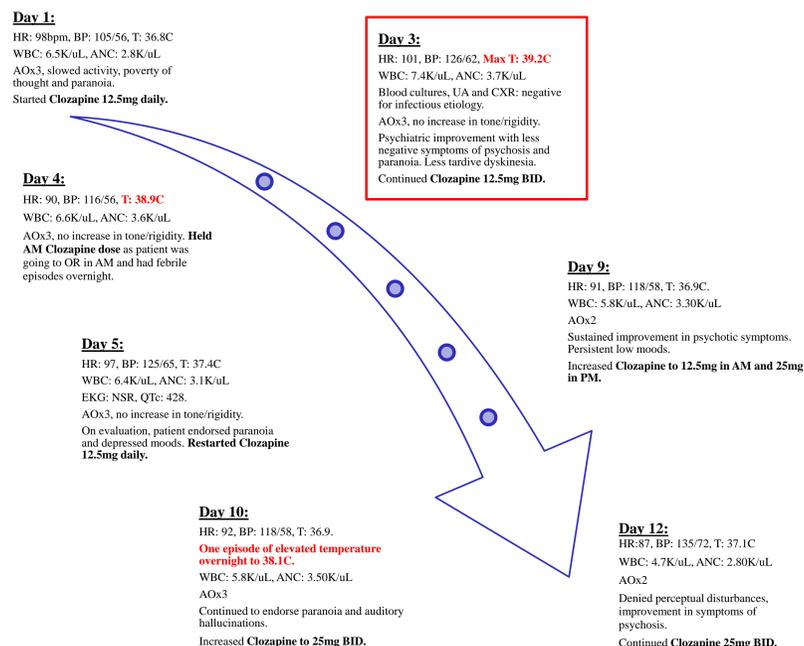
- Clinical dilemma exists to determine whether to continue Clozapine use in setting of new-onset of fever, given the short-term and long-term risks and benefits. Understanding this is important to guide and optimize clinical decision making (4).

## Patient Presentation

**60-year-old female with a past medical history of Schizoaffective disorder, seizure disorder, multiple previous suicide attempts, hypertension and diabetes.**

- Diagnosed with Schizophrenia in her 20s and had long term Psychiatric hospitalization for multiple years.
- History of catatonia, depressive symptoms, paranoia and multiple inpatient Psychiatric hospitalizations for suicide attempts (by medication overdose and cutting her neck with broken glass (hospitalized 5 months prior)).
- History of psychotropic medication trials with: Haldol and Risperdal.
- No known previous trial of Clozapine (confirmed through collateral information and the REMS program).
- Prior to this hospitalization, lived in AFC home, has a guardian and followed up with her outpatient Psychiatrist.
- Home medication regimen included: Bupropion 200mg daily, Olanzapine (sublingual) 10mg nightly, Lorazepam 0.5mg twice daily and 2mg nightly and Fluphenazine 10mg twice daily.
- Presented to HFH Hospital via EMS from AFC home after attempting suicide by jumping out the second story of the building onto the cement, in the setting of paranoid delusions.
- Sustained multiple orthopedic injuries requiring acute surgical intervention.
- Admitted to the surgical ICU for medical and surgical management.
- Psychiatry and Trauma Psychology teams were consulted.
- On evaluation, patient was a poor historian. She was noted to have flat affect, non-reactive with psychomotor retardation and slow processing speed.
- Patient continued to display paranoia post-operatively in ICU setting.
- Placed on 1:1 sitter for suicide precautions.
- After reviewing WBC/ANC, vitals and EKG: she was started on Clozaril 12.5mg daily (see sequence below).
- Restarted Lorazepam 0.5mg Bid in the setting of tachycardia, concern for withdrawal.

## Sequence of events after initiation of Clozapine



## Discussion

- This case report is of a patient who was severely ill, mentally and physically. She required multiple orthopedic surgical interventions s/p suicide attempt by jumping out of the second story of her AFC home.
- In this case study, febrile episodes (as high as 39.38C) were reported within a few low doses of Clozapine administration. This may be one of the highest documented in clozapine induction thus far. Febrile episodes were not noted consistently on additional dose increases of Clozapine.
- This case is unique as infectious work-up was done to rule-out infectious etiology and patient was closely monitored in an ICU setting. It is possible that post-operative fevers contributed to patient's presentation.
- The medication was continued through the fever with close monitoring of labs and vitals. Eventually, after tolerance was initiated and close monitoring continued, the dose was increased (even with febrile episodes) given the severity of symptoms of psychosis and suicidality.
- Coordination of care with multiple teams (including: Trauma Psychology, Surgical and ICU teams) was vital in monitoring patient's presentation and response to treatment.

## Future Directions

- New onset fevers in the setting of clozapine use should be carefully evaluated to rule-out underlying infectious etiology or medical complications (such as NMS) through close monitoring and work-up.
- Understanding risks associated with continuation of Clozapine use in comparison to benefits of treatment is vital to optimize clinical treatment.
- Further understanding of treatment options and patterns of febrile episodes, including possible etiology, is needed.



## References

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