

## **ABSTRACT**

### **Objective**

To determine the incidence, characteristics, complications and predictors of clozapine-induced fever, and to measure any association between clozapine-induced fever and clinical response.

### **Method**

A retrospective chart review of 227 inpatients newly started on clozapine from March 2003 to December 2006 was conducted. Demographic characteristics, presence of fever, investigations carried out, fever characteristics and complications of fever were recorded and analyzed. Fever was defined as temperature at or above 38°C in tympanic route. Clozapine-induced fever was diagnosed by negative physical examination and investigation findings. Patients with clozapine-induced fever were compared with their fever-free counterparts on demographic and clinical factors. Multivariate conditional logistic regression was performed to identify predictors of clozapine-induced fever. Clinical Global Impression Scale (CGI) based on case notes was used to measure clinical response and its association with clozapine-induced fever was examined.

## **Results**

Thirty-one out of 227 patients (13.7%) developed clozapine-induced fever. The means for day of onset of clozapine-induced fever after clozapine initiation and duration of fever were 13.7 and 4.7 days respectively. The mean highest body temperature was 38.8°C. Two patients (6.5%) with clozapine-induced fever developed complications, one with hypotension and oxygen desaturation, and the other suffered from dehydration with increase in serum creatinine level. Fever resolved within 48 hours after clozapine discontinuation in 79% of the patients. One out of seven patients (14.3%) had fever upon re-challenge. Clozapine-induced fever was associated with rate of titration more than 50mg/week (OR=18.9, 95% CI=5.3-66.7,  $p<0.001$ ), concomitant use of valproate (OR=3.6, 95% CI=1.5-8.9,  $p=0.006$ ), and presence of physical illness (OR=3.2, 95% CI=1.2-8.3,  $p=0.019$ ). No association was found between clozapine-induced fever and clinical response.

## **Conclusion**

Clozapine-induced fever is common. Careful monitoring of vital signs and hydration status is necessary. Slower rate of clozapine titration may be helpful, especially in patients with underlying physical illness and concomitant valproate treatment. Clozapine-induced fever was not shown to be associated with short-term clinical

improvement in this study.

**Keywords:** clozapine, fever, adverse effects