

THE ASSOCIATION BETWEEN SERUM CLOZAPINE AND NORCLOZAPINE LEVELS AND METABOLIC PARAMETERS IN PATIENTS WITH SCHIZOPHRENIA

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BACKGROUND AND AIM: Monitoring clozapine blood levels is important as it may help minimize side effects and ensure optimal therapeutic response. There are few studies on this subject in our country. This study aimed to measure serum clozapine and norclozapine levels in schizophrenia patients undergoing treatment with clozapine and investigate their association with metabolic parameters.

METHODS: This study involved 80 patients (27 females, 53 males) with schizophrenia. Clinical assessments included interviews, the Positive and Negative Syndrome Scale (PANSS) to evaluate the severity of schizophrenia symptoms, and the UKU Side Effect Rating Scale to identify drug-related side effects. Measurements of waist circumference, body weight, height, and blood pressure were taken, and routine complete blood count and biochemical analyses were performed. Blood samples were collected for therapeutic drug monitoring, and serum levels of clozapine and norclozapine were determined using liquid chromatography-mass spectrometry (LC/MS-MS). The study was approved by Erciyes University Ethics Committee (2021/835) and funded by the Scientific Research Projects Unit (TTU-2022-11600).

RESULTS: Only 10% of patients had clozapine blood levels within the normal therapeutic range (350-600 ng/mL). Clozapine level in 71.25% of patients were higher than the recommended therapeutic range, despite administered standard doses. This patient group had also higher clozapine dose, norclozapine level, clozapine/norclozapine ratio and clozapine concentration/dose ratio as well as higher body weight, BMI and waist circumference. Patients with clozapine blood levels in the therapeutic range had better metabolic values than the other groups. Clozapine levels were positively correlated with BMI ($r=0.249$, $p=0.026$) and total cholesterol levels ($r=0.247$, $p=0.027$), but no association with other side effects.

CONCLUSIONS: The study revealed that therapeutic blood levels of clozapine can be effectively achieved with lower dosages in our country population. Additionally, maintaining clozapine blood levels within the therapeutic range through personalized dosing may help minimize metabolic side effects.

Keywords: Schizophrenia, clozapine, therapeutic drug monitoring, metabolic side effects