Benign Ethnic Neutropenia: An Avoidable Obstacle to Clozapine Use

Neutropenia Étnica Benigna: Um Obstáculo Evitável ao Uso de Clozapina

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Dear Editor,

Benign ethnic neutropenia (BEN) is a chronic, isolated, asymptomatic hematological variant that is more common among individuals of African or Middle Eastern ancestry, with no increased risk of infection.[1] Although well described in hematology, it remains underappreciated in psychiatric practice, particularly in clozapine monitoring, where laboratory thresholds historically derived from white populations may lead to inappropriate non-initiation or premature discontinuation of this medication.[2] Treatment with clozapine is unanimously recognized by clinical guidelines as the antipsychotic therapy of choice for treatment-resistant schizophrenia.

Our review of several recent clinical cases illustrated this issue. Young patients of African ancestry with treatment-resistant schizophrenia presented with persistently low absolute neutrophil counts between 800 - 1500/μL, without recurrent infections or other signs of hematological disease. In at least one case, confirmation of the Duffy-null phenotype supported the diagnosis of BEN and allowed clozapine initiation, with a good clinical response and no hematological complications.[2] In contrast, in other cases, the lack of early recognition of BEN led to clozapine discontinuation after a single neutrophil count below 1500/μL, followed by subsequent clinical deterioration.

These observations are in line with previous reports suggesting that many historical clozapine suspensions in ethnically diverse populations may have been avoidable.[3,4]

Current evidence indicates that BEN does not increase the risk of clozapine-associated agranulocytosis, and that treatment can be safely maintained using adjusted hematological thresholds and interpretation based on the patient's individual baseline rather than fixed universal cut-offs.[1,2] Therefore, we argue that in the presence of stable, isolated neutropenia, without recurrent infections, and in patients with compatible ancestry, BEN should be taken into consideration, alongside exclusion of secondary causes. Hematology input should be considered in these cases.

The adoption of more inclusive monitoring protocols may reduce inequalities in access to clozapine and prevent inappropriate therapeutic exclusion in patients with treatment-resistant schizophrenia.

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All authors contributed equally to this manuscript and approved the final version to be published.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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