

PLASMA GLUTATHIONE IS A DETERMINANT OF NEUTROPHILS' COUNTING IN PATIENTS TAKING CLOZAPINE (CLZ)

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Background

CLZ is an atypical antipsychotic, approved for treatment-resistant Schizophrenia. CLZ is more effective than any other first- or second-generation agents to treat resistant schizophrenia. However, the use of CLZ is associated to potentially fatal agranulocytosis. The mechanism of neutrophil decline in patients treated with CLZ is still poorly understood. It has been suggested that clozapine metabolism involves an unstable reactive metabolite, nitrenium ion, which may bind covalently to endogenous glutathione (GSH).

Objective

The objective of the present study was to describe a relationship between plasma CLZ, and GSH with neutrophils counting (NC) in schizophrenic patients taking CLZ for variable time, to further characterize the mechanisms implicated in CLZ toxicity.

Methods

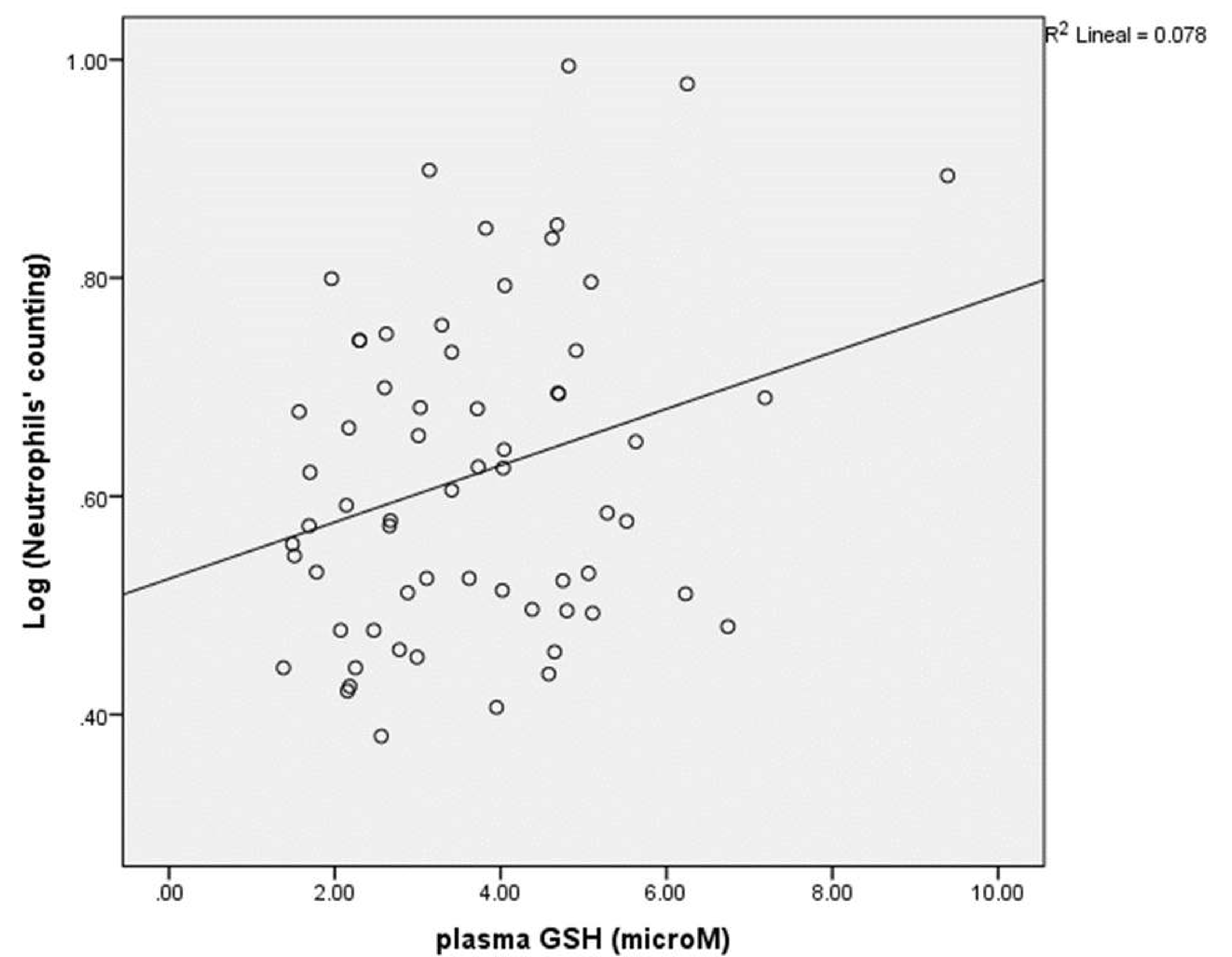
Seventy (70) patients, diagnosed with schizophrenia at the National Institute of Neurology and Neurosurgery, Mexico City, were invited to participate in the study. All of them were taking CLZ. After signed an informed consent, blood samples were obtained and centrifuged to obtain plasma samples that were stored at -20°C until analyzed. Plasma CLZ and GSH were analyzed by HPLC and fluorometry, respectively.

Conclusion

GSH was the strongest determinant of neutrophils' counting in patients taking CLZ.

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Results



Results

A multiple regression analysis was performed, taking neutrophils' counting as the dependent variable and plasma CLZ, GSH and other variables, as determinants. **Only GSH (F=6.104; p=0.017), plasma CLZ (F=4.167; p=0.047) and time taking CLZ (F=4.496; p=0.015) were determinants of NC. Concomitant drugs did not affect the relationship between NC and GSH (F=1.49, p=0.23). Figure 1 shows the relationship between NC and plasma GSH.**

Figure 1. Neutrophils' counting, as a function of plasma glutathione of Schizophrenia patients taking Clozapine at different doses.

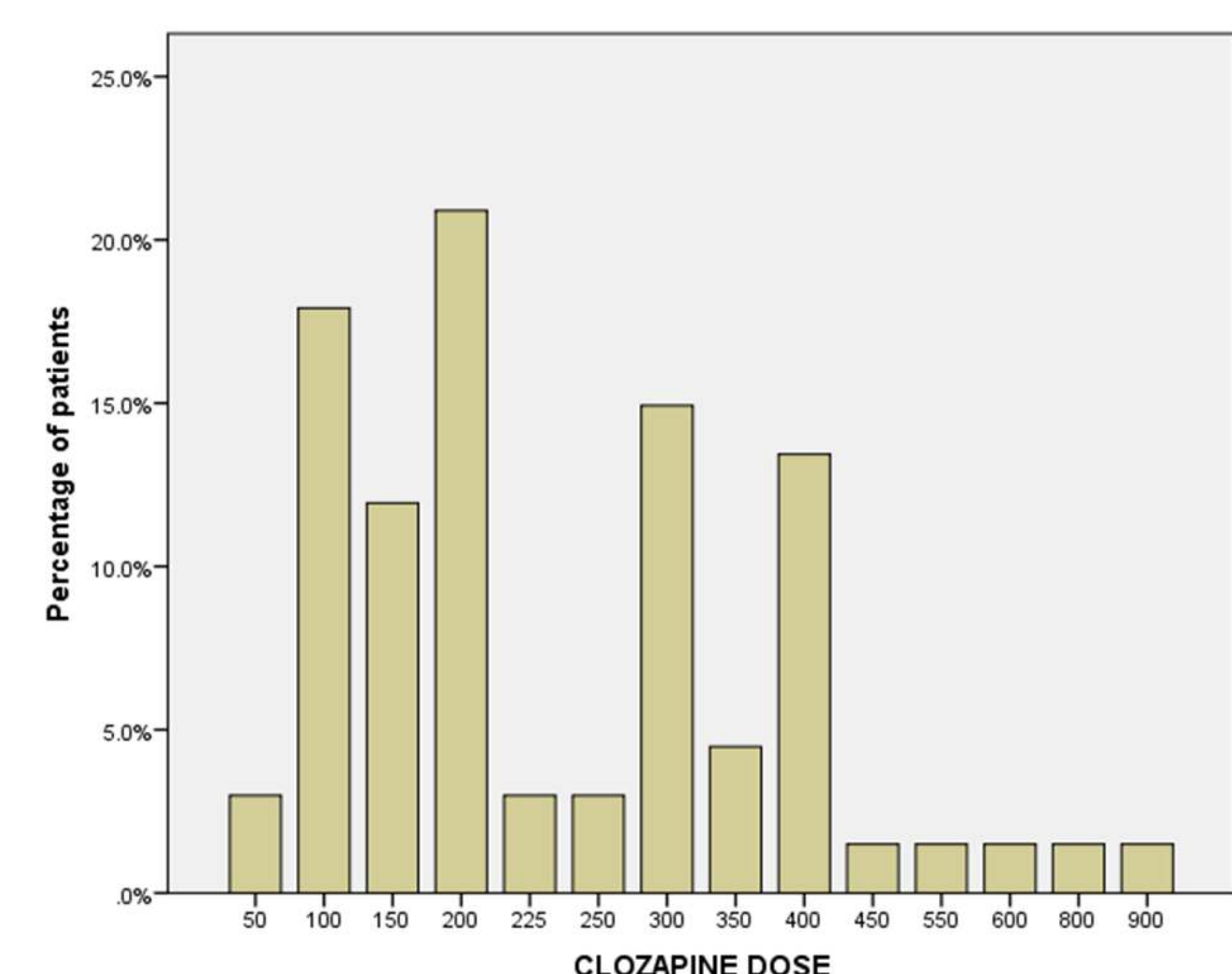


Figure 2. Doses of clozapine taken by patients