Resistance to Antiplatelet Drug in Cardio-Cerebrovascular Pathology – Functional, Molecular and Clinical Aspects

Abstract

Introduction

Antiplatelet drugs are widely used in patients with acute coronary syndromes or stroke. Despite adequate antiplatelet therapy, some patients develop acute ischemic events. This is partly attributed to the fact that they have poor inhibition of platelet reactivity despite treatment.

This study aimed to assess the impact of clinical and laboratory variables on platelet response to clopidogrel and/or aspirin, evaluated using impedance aggregometry in a Romanian population.

Methods

The study included 189 patients with acute coronary syndromes and non-cardiogenic ischemic stroke. Platelet aggregation was evaluated by impedance aggregometry. CYP2C19 loss-of-function polymorphisms were detected using the Polymerase Chain Reaction - Restriction Fragment Length Polymorphism technique. Various clinical and laboratory data were also recorded.

Results

In our data set, 81% of the patients were responders and 19% non-responders to antiplatelet therapy. The distribution of CYP2C19 polymorphisms was as follows: 61.1% of patients were CYP2C19 wild-type homozygotes, 27.7% CYP2C19*2 heterozygotes, 1.1% CYP2C19*3 heterozygotes and 10% of patients CYP2C19*2 homozygotes. The highest level of association with clopidogrel response ~~status~~ was found for CYP2C19 polymorphisms, concomitant aspirin treatment, leukocyte and platelet count, history of myocardial infarction and arterial hypertension. Aspirin response ~~status~~ was associated with coadministration of beta-adrenergic blockers and with history of myocardial infarction.

Conclusion

The prevalence of antiplatelet resistance in our population was in line with that reported for Western populations. Clopidogrel response was significantly influenced by the presence of CYP2C19 polymorphisms. Interestingly, the concomitant use of aspirin had a significant impact on platelet response to clopidogrel, indicating a synergic interaction between these drugs.

Keywords: antiplatelet drugs, clopidogrel, aspirin, resistance, CYP2C19 polymorphisms