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SCIENTIFIC LETTER

Genotyping single-nucleotide polymorphism CYP2C19*2, pharmacodynamic evaluation of high on-clopidogrel treatment platelet reactivity and the cardiologist

*Genotipificación del polimorfismo de nucleótido simple CYP2C19*2, evaluación farmacodinámica de la alta reactividad plaquetaria en tratamiento con clopidogrel y el cardiólogo*

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Sir, we have read with interest Cedillo-Salazar et al. report[1] and we believe pertinent make some comments.

Effectiveness of clopidogrel depends on its conversion to an active metabolite by CYP2C19 enzymes through two different metabolic set-ps. Individuals who carry one or two loss-of-function alleles (LOF) of the CYP2C19*2 – heterozygous or homozygous single-nucleotide polymorphism (SNP) – are associated with an intermediate or poor metabolism for clopidogrel, respectively[2].

The prevalence of SNP CYP2C19 has an ethnic expression, ~2% of Caucasians, 4% of African-Americans, and 14% of Chinese are CYP2C19*2/*2 carriers[2], in Mexicans, the prevalence of CYP2C19 in not well established. In Mexico, there are two main populations: native groups (Amerindians) and mestizos the result of post-Columbian admixture[3]. Mexican Amerindians are geographically located mainly in the center and southeast of the country[3]. Salazar-Flores et al.[3] reported CYP2C19*2/*2 frequency of 10% in Tarahumaras, 1.4% in mestizos and 0% in Purepechas, Tojolabales, Tzotziles y Tzetzales. CYP2C19*1/*2 is absent in Tzetzales and ranging from 6.6% to 40.5% in the other groups. León-Moreno et al.[4] reported *2/*2 genotype present only in North Lacandons in 2-2.7% and *1/*2 ranging from 12% to 33%.

We previously reported[5] 109 patients with acute coronary syndrome (ACS) treated with percutaneous coronary intervention (PCI), from Saltillo and Puebla genotype frequency CYP2C19*2/*2 of 0.92%, and CYP2C19 *1/*2 of 17.4%[5]. In contrast, Viveros et al.[6] in Morelia in 90 PCI patients reported CYP2C19*2/*2 frequency of 3.9% and CYP2C19 *1/*2 of 17%[6]. Cedillo-Salazar informed CYP2C19*2/*2 frequency of 3.9% and 21.6% for CYP2C19 *1/*2[1]. These findings reinforce the concept of intrapopulation variation found in Mexico and the possible real and practical non-theoretical clinical impact.

Respect to the pharmacodynamic evaluation of the clopidogrel response, the authors divided patients arbitrarily into three groups and use the term "clopidogrel resistance"[1]. This term should be used if we employ a laboratory technique that detects the activity of the target receptor before and after the administration of the specific

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antiplatelet agent. Therefore, the absolute level of platelet reactivity during treatment, that is, "high on-treatment platelet reactivity" (HTPR) has been proposed as a better measure of thrombotic risk than responsiveness to clopidogrel[7]. The link between HTPR and ischemic or bleed events is well established[7,8] and is accepted a therapeutic window using VerifyNow, with cutoff point for ischemic events >208 PRU[7] and <85 PRU for hemorrhages[7].

The potential benefits of genotyping are remarkable in ACS/PCI patients because LOF allele carriers can be identified, and alternative antiplatelet strategy can be instituted[9,10].

Currently, there is conflicting evidence in regard to the use both, platelet function tests and CYP2C19 genotyping, but it is generally accepted that its use should be individualized in those patients at high risk and not routinely.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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