

The impact of cytochrome P 450 2 C19 polymorphism on the occurrence of 1-year in-stent restenosis in patients who underwent percutaneous coronary intervention: A case-match study

In a recent manuscript, published in this issue Nozari et al. (1) entitled "The impact of cytochrome P450 2C19 polymorphism on the occurrence of one-year in-stent restenosis in patients who underwent percutaneous coronary intervention: A case-match study." evaluated the impact of cytochrome P450 2 (CYP2C19*2) polymorphism in the occurrence of in-stent restenosis among Iranian patient population.

In clinical practice, the importance of in-stent restenosis is well-known, and it is the focus of recent researches. Lower levels of the active metabolites of clopidogrel resulted in decreased platelet inhibition and a higher rate of major adverse cardiovascular events, including stent thrombosis. Metabolic pathways and isoenzymes, such as CYP2C19, play an important role in the transformation of clopidogrel into its active metabolites (2). Decreased or lost function of the CYP2C19 isoenzyme has been associated with different pharmacological outcomes, including decreased antiplatelet responsiveness, which results in a higher risk of ischemic cardiovascular events. From several gene variants, the most common is the *2 allele, which is responsible for more than 90% cases of poor metabolism. Carriers (who had at least one reduced-function allele) have a higher risk for major cardiovascular events; stent thrombosis occurs three times more often in carriers than in non-carriers (3, 4). Furthermore, the frequency of loss of function allele shows regional variance; approximately 30% of the Caucasian population has one reduced function allele (5).

However, some recently published data suggest that CYP2C19*2 carriers have a higher risk not only for stent thrombosis but also for in-stent restenosis. Several articles proved the significance of CYP2C19 polymorphism in the development of in-stent restenosis in vascular disease after endovascular treatment and stent implantation (6, 7). In contrast with these results, some other studies did not find consistent influence of CYP2C19 gene polymorphism on the clinical efficacy (8).

According to the results established by an Iranian research group, CYP2C19*2 carriers have no significant association with in-stent restenosis after 1 year of successful percutaneous coronary intervention. Although the data suggested no significant association, the prevalence of restenosis proved to be slightly higher in the CYP2C19*2/CYP2C19*1 heterozygote group. The study has some limitation: small study group does not enable the precise evaluation of the effect of the heterozygote allele. Thus, a larger patient population needs to be tested. Moreover, the absence of complete loss of function allele in the analyzed group decreases the value of the manuscript. Based on the tendency in the heterozygote group, the homozygote *2 variant is supposed to have a higher risk not only for stent thrombosis but also for in-

stent restenosis. Thus, the data provided interesting approaches regarding the association of clopidogrel metabolism and the prevalence of in-stent restenosis, although analysis of a larger patient population needs to be performed. In addition, interesting supplementary result was also established in this study; the overall frequency of heterozygote polymorphism was 11% in the study group in contrast with the previously mentioned frequency in the Caucasian population.

Finally, this study has interesting findings; however, further larger studies need to be performed to confirm the results.

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Accepted Date: 17.02.2015

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 DOI:10.5152/akd.2015.0052