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*J Thromb Thrombolysis*. 2011 Feb 3. [Epub ahead of print]

### Relationship between peripheral arterial reactive hyperemia and residual platelet reactivity after 600 mg clopidogrel.

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#### Abstract

Clopidogrel reduces long-term ischemic events in patients with acute coronary syndrome or stable angina (SA) undergoing percutaneous coronary intervention (PCI). Endothelial function improvement has been proposed, among other factors, for this beneficial effect of clopidogrel, but whether this might be associated to its anti-platelet action remains unclear. We tested the hypothesis that clopidogrel improvement of peripheral vascular endothelial function might be associated with inhibition of platelet aggregation. Endothelial function was evaluated before and at least 12 h after 600 mg clopidogrel in 43 SA pts undergoing elective PCI by: (a) reactive hyperemia peripheral arterial tonometry (measuring the Endoscore); (b) circulating endothelial microparticles (EMPs). Response to clopidogrel was measured with point-of-care VerifyNow P2Y12 assay and expressed as platelet reaction unit (PRU) and percent platelet inhibition (%PI). High platelet reactivity after clopidogrel was defined as PRU  $\geq$  240. Endothelial function improved after clopidogrel in 20 pts. Changes in Endoscore ( $\Delta$  Endoscore) were significantly correlated with both PRU ( $r = -0.61$ ,  $P < 0.001$ ) and %PI ( $r = 0.57$ ,  $P < 0.001$ ). Endoscore significantly increased after clopidogrel in pts with PRU  $< 240$  ( $0.38 \pm 0.26$  to  $0.57 \pm 0.33$ ,  $P < 0.001$ ), but did not in pts with PRU  $\geq 240$  ( $0.53 \pm 0.31$  to  $0.40 \pm 0.37$ ,  $P = 0.12$ ). EMPs were also significantly reduced in pts with PRU  $< 240$  ( $222 [140-593]$  to  $142 [83-371]/\mu\text{l}$ ,  $P = 0.001$ ), while no changes were observed in pts with PRU  $\geq 240$  ( $256 [178-531]$  to  $388 [238-499]/\mu\text{l}$ ,  $P = 0.55$ ). In patients with stable coronary artery disease, a single 600 mg clopidogrel loading dose improves vascular endothelial function. This improvement is associated with optimal platelet inhibition and it is not observed in patients with post-clopidogrel high platelet reactivity.

PMID: 21290254 [PubMed - as supplied by publisher]

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