

Clopidogrel Inhibitory Effect with Omeprazole, Pantoprazole, or Famotidine- A Crossover Study

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Background: Concerns have been raised about the potential for Proton-pump inhibitors (PPIs) to blunt the efficacy of clopidogrel. Since clopidogrel's effect is influenced by the genetic activity of the CYP450 system, there is a need to examine the effect of PPI on clopidogrel resistance after cancelling genetic differences. We assessed the effects of 2 different PPI and one H2 blocker on platelet reactivity in patients treated with aspirin and clopidogrel in a crossover trial where each patient was treated with all 3 anti-acid regimens.

Methods: Patients treated with aspirin and clopidogrel were assigned to receive 3 consecutive treatment periods of one month each, in which they were treated with one of the 3 study medications. The medications tested were: Omeprazole (20mg*2/d), Famotidine (40mg*2/d) and Pantoprazole (20mg*2/d). At the end of each phase, platelet function was evaluated using the Verify Now system.

Results: Regardless of the cutoff used to define resistance, patients on Omeprazole were significantly more resistant to clopidogrel compared to famotidine or pantoprazole, respectively (48%, 33% and 31% when using the 208 PRU cutoff, p=0.04) and (37%, 17% and 23% when using the 230 PRU cutoff, p=0.003). These changes represent up to 100% increase in the number of resistant patients to clopidogrel when comparing Omeprazole to other anti acid regimens.

Conclusions: We show, for the first time, that after cancelling genetic bias that might have existed in other trials, Omeprazole is significantly associated with more clopidogrel resistance compared to other anti-acid regimens.