Protective effect of the CYP2C19 *17 polymorphism with increased activation of clopidogrel on cardiovascular events.

Abstract:
The prodrug clopidogrel requires activation by cytochrome P-450 (CYP) enzymes for its antiplatelet effect. The genes encoding enzymes for clopidogrel activation are polymorphic, leading to reduced or increased function, depending on the respective genotype. Reduced-function alleles have been associated with an increase in cardiovascular events. We tested the association of the presence of the ABCB1 (C/T) T-allele, CYP2C19*2 (G/A) A-allele, or CYP2C19*17 (C/T) T-allele with the primary end point of the need of clinically-driven target lesion revascularization (TLR) and the secondary end points of major adverse cardiovascular events (MACE; including death, myocardial infarction [MI], and TLR) at 1 year in a high-risk population of 928 patients with acute MI. Carriers of the CYP2C19*17 T-allele, with increased clopidogrel activation, had a 37% relative reduction in the TLR incidence, the primary end point (14.0% vs 22.3%, P = .002), and a 22% relative reduction of the secondary end point MACE (22.0% vs 28.1%, P = .04) compared with noncarriers, respectively. The association of the T-allele with TLR remained significant in the multivariate analysis (P = .001). The ABCB1 (C/T) and the CYP2C19*2 (G/A) polymorphisms were not associated with the incidence of TLR or MACE. Based on the genetic analysis
in a high-risk population of acute MI patients with interventional treatment and continuous clopidogrel therapy, our study found a protective effect for carriers of an increased-function CYP2C19*17 T-allele with significantly lower rates of TLR and MACE. T-allele carriers with acute MI and increased clopidogrel activation had significantly reduced clinical event rates.

Zeitschriftentitel / Abkürzung:
Am Heart J

Jahr: 2010
Band: 160
Heft / Issue: 3
Seiten: 506-12
Sprache: eng
Print-ISSN: 0002-8703
TUM Einrichtung: I. Medizinische Klinik und Poliklinik

Occurences:
- Einrichtungen > Fakultäten > Fakultät für Medizin > Kliniken und Institute > I. Medizinische Klinik und Poliklinik (Kardiologie) > 2010

Entries: