The Selection of $P2Y_{12}$ Receptor Inhibitor for Patients with CYP2C19 Intermediate metabolizers After Percutaneous Coronary Intervention. Wu Y[1], Yu D[2], Zhang L[2], Sun Q[2], Yu H[2], Shi T[1] ([1]*Department of Pharmacy,* [2]*Department of Cardiology, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, Anhui, 230001,P.R. China*)

ABSTRACT

Background: Dual antiplatelet therapy (DAPT) with aspirin plus one kind of $P2Y_{12}$ receptor inhibitor is the key to reducing cardiovascular events after percutaneous coronary intervention (PCI). The newer 2017 ESC focused update on DAPT in coronary artery disease favor the more ticagrelor over clopidogrel. But yet, ticagrelor has been proven to increase the non-CABG related bleeding in PLATO trial. Clinical studies have confirmed that the incidence of ticagrelor related bleeding is higher in Asians. Hence, clopidogrel remains the most commonly prescribed $P2Y_{12}$ receptor inhibitor, particularly for those patients with CYP2C19 wild-type in China. The FDA has issued a black-box warning about the reduced effectiveness of clopidogrel in patients carrying two CYP2C19 loss-of-function (LOF) alleles and suggested that these patients receive a higher dose of clopidogrel or an alternative antiplatelet agent. So what should we do for individual carriers of one LOF allele(defined as intermediate metabolizers, IMs)? Against this background, the purpose of this study is to determine whether ticagrelor is superior to clopidogrel for patients with CYP2C19 IMs after PCI.

METHODS: A retrospective study was conducted in 414 patients who underwent PCI and identified as IMs by CYP2C19 testing from September 2017 to January 2019. Patients were prescribed aspirin plus either ticagrelor with 90mg twice daily (defined as ticagrelor group, n=162) or clopidogrel with 75mg daily (defined asclopidogrel group, n=252). Risk of major adverse cardiovascular event(MACE) and bleeding events over one year was evaluated.

RESULTS: Kaplan-Meier curve showed that the cumulative bleeding rate was higher in the ticagrelor group than in the clopidogrel group(Log-rank *P=0.047*). This phenomenon was driven by trivial bleeding incidence (Log-rank *P=0.039*). However, after adjusting for baseline characteristics, it were BMI (HR=0.028, 95%CI:1.000-1.209, *P=0.028*) and smoking history(HR=0.362, 95%CI:0.153-0.853, *P=0.020*), but not $P2Y_{12}$ receptor inhibitor, that were determined as independent factors of bleeding event. No difference was observed in the incidence of MACE.

CONCLUSIONS: The selection of P2Y12 receptor inhibitor may have no influence on the outcomes of PCI patients with CYP2C19 IMs. Effect of clinical features on the outcome should be considered.

KEY WORDS

Dual antiplatelet therapy; $P2Y_{12}$ receptor inhibitor; CYP2C19; Intermediate metabolizers; Percutaneous coronary intervention