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**TCT-206**

Effect of the \(\alpha_{2A}\)-Adrenergic Receptor Genetic Variants on Platelet Reactivity and Adverse Clinical Events in Chinese Patients with Dual Antiplatelet Therapy after Percutaneous Coronary Intervention

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**BACKGROUND**

Platelet \(\alpha_{2A}\)-Adrenergic Receptor (\(\alpha_{2A}\)-ARs) potentiates epinephrine-induced platelet aggregation in response to sympathetic stimulation. Genetic variants of the \(\alpha_{2A}\)-AR are associated with different antiplatelet reactivity. The effect of genetic variants of the \(\alpha_{2A}\)-ARs on platelet reactivity and clinical outcomes has not yet been reported in Chinese patients with dual antiplatelet therapy after percutaneous coronary intervention. The aim of this study was to investigate the effect of the \(\alpha_{2A}\)-AR variants on platelet reactivity and clinical outcomes in these patients.

**METHODS**

1056 patients with dual antiplatelet therapy after percutaneous coronary intervention were enrolled in a single-center registry. All known \(\alpha_{2A}\)-AR genetic variants including rs11195419, rs3750625, rs13306146, rs553668 were detected by the ligase detection reaction and the antiplatelet effect was assessed by thromboelastography. Primary clinical endpoints included cardiovascular death, nonfatal myocardial infarction, target vessel revascularization, and stent thrombosis. The secondary clinical endpoints were angina recurrence, re-admission, and in-stent restenosis. The follow-up periods were 6 months and 12 months.

**RESULTS**

The frequencies of the \(\alpha_{2A}\)-AR variants were respectively 18.09%, 17.17%, 25.43%, 43.71%. Genotypic distributions of all the variants were in conformity with Hardy-Weinberg equilibrium except rs13306146. Platelet ADP inhibition was significantly different among wild type, heterozygote and homozygote mutated groups carrying rs11195419 genetic variant (53.86% vs 50.20%, 27.80% vs 39.81% vs 39.28% vs 53.02% vs 19.53% vs 0.12% or 37.55% vs 15.80%, 10.50% vs 0.00% and the homozygote mutated groups have the lowest ADP inhibition of the three groups variants. However, there were no significant differences in ADP inhibition among the rs553668 genotype types (50.20% vs 27.83% vs 4.09% vs 29.41% vs 52.11% vs 0.00%, P = 0.158). At the multivariable analysis, the presence of the rs11195419 (95%CI: -0.006 -0.039, P = 0.039) or rs553668 (95%CI: -0.001 -0.023, P = 0.023) genetic variants was an independent predictor of the ADP inhibition. However, there were no significant differences in the composite clinical outcome across the rs11195419, rs3750625, rs553668 genotype groups at both 6 and 12 months follow-up period (P > 0.05).

**CONCLUSIONS**

The presence of mutated alleies of \(\alpha_{2A}\)-AR genetic variants (rs11195419, rs3750625) except rs553668 is associated with decreased ADP-induced platelet reactivity in Chinese patients with DAPT after percutaneous coronary intervention. However, none of the \(\alpha_{2A}\)-AR genetic variants significantly influenced the clinical outcomes of DAPT in these patients.

**CATEGORIES OTHER**

Genomics / Proteomics

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**TCT-207**

Comparative efficacy & safety of Prasugrel, Ticagrelor, standard & high dose Clopidogrel in patients undergoing percutaneous coronary intervention (PCI): A network meta-analysis

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**BACKGROUND**

Higher loading and maintenance dose Clopidogrel overcomes delayed and often variable effect of standard dose Clopi-
dogrel in majority of the patients. However, data comparing this strategy with potent alternatives such as Ticagrelor & Prasugrel are scarce.

**METHODS**

Comparative safety, efficacy and resource utilization of prasugrel, ticagrelor and standard dose clopidogrel as antiplatelet therapy were compared with pooled data from the CLARITY-TIMI 65 study (prasugrel vs clopidogrel) and PLATO study (ticagrelor vs clopidogrel). Whether higher dose of clopidogrel overcomes delayed and variable effect of standard dose was explored in a network meta-analysis with adjusted random-effects model, using relative risk (RR) as effect measure. Meta-analysis techniques in STATA 13 were used to assess whether higher loading dose of clopidogrel could achieve similar results as prasugrel and ticagrelor.

**METHODS**

Comparative safety, efficacy and resource utilization of prasugrel, ticagrelor and standard dose clopidogrel as antiplatelet therapy were compared with pooled data from the CLARITY-TIMI 65 study (prasugrel vs clopidogrel) and PLATO study (ticagrelor vs clopidogrel). Whether higher loading dose of clopidogrel overcomes delayed and variable effect of standard dose was explored in a network meta-analysis with adjusted random-effects model, using relative risk (RR) as effect measure. Meta-analysis techniques in STATA 13 were used to assess whether higher loading dose of clopidogrel could achieve similar results as prasugrel and ticagrelor.
**RESULTS** Thirty trials, with 34,563 person years of follow up data after PCI, were included in the analysis. Prasugrel (86%) emerged as best drug to prevent definite or probable stent thrombosis, followed by Clopidogrel HD (66%) and Ticagrelor (44%), with Clopidogrel SD being the worst. Myocardial infarction was least likely to be prevented by Clopidogrel SD (0%) after PCI, and rest three were superior to it (Prasugrel 74%; Clopidogrel 70%; Ticagrelor 56%). Clopidogrel SD (18%) was least effective in preventing cardiovascular deaths after PCI. Prasugrel (73%) was likely most effective in preventing cardiovascular deaths followed by Ticagrelor (62%) and Clopidogrel HD (47%). Ticagrelor (68%) reduced all-cause mortality by a small margin compared to rest of treatments (Prasugrel 50%; Clopidogrel 48%; Ticagrelor 34%). Clopidogrel SD (79%), followed by Clopidogrel HD (53%) and Ticagrelor (48%), resulted in significantly lower TIMI major bleeding complications compared to Prasugrel. Analysis of any bleeding revealed similar trend. Clopidogrel HD performed better than Prasugrel in terms of bleeding complications. Results of direct pairwise comparison and network meta-analysis were consistent in the direct of overall effect (Figure).

**CONCLUSIONS** Prasugrel is most effective drug to prevent post PCI ischemic events but at the expense of higher bleeding. Ticagrelor followed by Clopidogrel HD appears to strike the right balance between efficacy & safety.

**CATEGORIES CORONARY:** Pharmacology/Pharmacotherapy

**KEYWORDS** Antiplatelet therapy, Percutaneous coronary intervention