IN THE NAME OF GOD

Article: Association of Ticagrelor vs Clopidogrel With Major Adverse Coronary Events in Patients With Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention

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Antithrombotic agents

- Anti platelets and Anti coagulants

- Anti platelets: P2Y12 receptor inhibitors
  - 1. inhibition of platelet aggregation (P2Y12 receptor inhibitor)
  - 2. prevention of thrombosis in ACS patients

  Three popular agents:
  - clopidogrel
  - Prasugrel
  - ticagrelor

Clopidogrel

- Proven clinical efficacy of clopidogrel in patients with an ACS or after PCI, either as monotherapy or in combination with aspirin
- Pharmacological limitations:
  - a prodrug, 2-step hepatic cytochrome P450 (CYP) metabolic activation
  - Inactivation before intestinal absorption
  - Several hours between ingestion and reaching therapeutic levels
  - Higher risk for acute stent thrombosis

Alternative P2Y12 inhibitors

Prasugrel

- Hepatically activated in a single-step
- Initial hydrolization into intermediate metabolite

- In comparison with clopidogrel:
  - Prasugrel has more rapid and consistent activation, with more receptor blocking active metabolite

Ticagrelor

- Directly and reversibly binds to and inhibits the P2Y12 receptor
- Orally active without the requirement of metabolic activation

- In patients with ACS, ticagrelor exhibited greater inhibition of platelet aggregation than a standard regimen of clopidogrel

Introduction

- More profound platelet inhibition with more rapid onset with ticagrelor
- Recommendation over using ticagrelor with aspirin in preference to clopidogrel for patients with acute coronary syndrome (ACS)
- PLATO trial: results and limitations
- Ticagrelor adverse effects
- Aim of the study: to assess the comparative association of ticagrelor and clopidogrel with reduced MACE using data from a population-based registry

Methods

- **Study Design and Data**: a retrospective cohort study
- The Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease registry
- **Study Population and Exposure: patients** older than 18 years, underwent PCI for ACS between April 1, 2012, and March 31, 2016, were discharged alive from index hospitalization, and filled a first prescription for clopidogrel or ticagrelor within 31 days after undergoing PCI
- **Outcomes:**
  - Primary outcome: MACE (all-cause death, hospitalization with nonfatal ACS, coronary revascularization, or stent thrombosis within 365 days after the index hospitalization)
  - Secondary outcome: a composite of all-cause death, hospitalization with ACS, or ischemic stroke, hospitalization for major bleeding, and emergency department visit for dyspnea

Results

- A total of 13897 patients
- 2760 (24.7%) were women,
- 4953 (44.3%) presented with ST-segment elevation myocardial infarction
- Ticagrelor group: younger and lower cardiovascular risk
- Clopidogrel the most frequently prescribed $P2Y_{12}$ inhibitor during the study(63.6%)
- Increased ticagrelor usage over the study (56.3% by the second half of the study)

Results

- Adverse effects (MACE and mortality, hospitalization for ACS, coronary revascularization or the composite of death, ACS, or ischemic stroke)
  - Unadjusted results
  - Adjusted results

  - Safety (major bleeding, dyspnea)
    - Unadjusted results
    - Adjusted results

Discussion

- Results differ from prior studies: differences in methodology, patient populations, and advances in interventional cardiology
  - PLATO study
  - SWEDEHEART study
- Greater antiplatelet potency of ticagrelor did not translate to reduction in MACE in this study
- Ticagrelor-related dyspnea

Conclusion

- In a large, representative population-based cohort of patients who underwent PCI for ACS primarily using second-generation drug-eluting stents, ticagrelor was not associated with a lower risk of MACE compared with clopidogrel; however, it was associated with a higher risk of major bleeding and emergency department visits for dyspnea

References

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