

Safety and efficacy of Clopidogrel versus Ticagrelor in treating non-STEMI elderly patients

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Abstract:

Background: Acute coronary syndrome describes a wide range of clinical conditions that are caused by acute myocardial ischemia. A mismatch between myocardial oxygen demand and supply constitutes the fundamental pathology of ACS. An independent risk factor for major adverse events following acute coronary events, age is furthermore, being a significant risk factor for atherosclerotic cardiovascular disease. In order to prevent recurrent thrombotic events in patients with dual antiplatelet therapy non-ST-elevation acute coronary syndrome, comprising a P2Y12 inhibitor and aspirin is critically important. For their demonstrated anti-inflammatory effects in addition to their antithrombotic properties, antiplatelet medications have been utilised to improve clinical outcomes in patients with atherosclerotic cardiovascular diseases. Methodology: The study. The study included 200 elderly patients presenting with NSTEMI. They were categorized into two groups: group 1: 100 NSTEMI patients received clopidogrel, and group 2: 100 NSTEMI patients received ticagrelor. Results: Patients who received clopidogrel demonstrated significantly lower minor bleeding ($P = 0.011$) and overall bleeding ($P < 0.001$). Additionally, major bleeding was reduced in participants who received clopidogrel than in patients who received ticagrelor but without statistical significance ($P = 0.123$). Insignificant differences were reported regarding stent thrombosis, stroke, myocardial infarction, CV death, urgent revascularization and transient ischemic attacks. Conclusion: As an alternative to ticagrelor, clopidogrel is beneficial for elderly patients. Without increasing ischemic risk, clopidogrel is associated with a significantly reduced risk of major and minor bleeding.

Keywords: Acute coronary syndrome, clopidogrel, elderly, ticagrelor.

1. Introduction

There is an observed upward trend in the non-ST-elevation acute coronary syndrome (NSTEMI-ACS) ratio to ST-elevation acute coronary syndrome (STEMI-ACS). This trend can likely be attributed to demographic factors such as an ageing population and elevated prevalence of diabetes. ACS patients constitute a heterogeneous population whose morbidity and mortality risks vary [1]. The prevention of recurrent thrombotic events in patients with NSTEMI-ACS requires dual antiplatelet therapy (DAPT), which consists of a P2Y12 inhibitor and aspirin. In ACS patients, it is advised that the more potent P2Y12 inhibitors, prasugrel or ticagrelor, be used in lieu of clopidogrel, unless an excessive risk of bleeding exists [2].

At this time, clopidogrel is frequently prescribed as an antagonist of the platelet P2Y12 receptor. Patients undergoing percutaneous coronary interventions or who have an ACS are concurrently administered this medication with aspirin in order to reduce the likelihood of subsequent major adverse cardiovascular events (MACE), including stent thrombosis and ACS recurrence. Notwithstanding this, the principal MACE aetiology, which may transpire notwithstanding the advised DAPT, has been attributed to the variable pharmacodynamic efficacy of these medications, specifically clopidogrel [3].

Ticagrelor is the first P2Y12 antagonist capable of reversibly binding that is permitted for the ACS treatment in cases. Ticagrelor was found to be more effective than clopidogrel in avoiding myocardial infarction, stroke, and cardiovascular death in multiple clinical trials. As patients advance in age, their susceptibility to bleeding and thrombotic events escalates, thereby presenting a challenge in determining the most effective antithrombotic therapy [4].

While age did not appear to be a determining factor in the superiority of ticagrelor, older patients experienced a higher incidence of ticagrelor-related bleeding (including fatal bleeding) compared to clopidogrel-related bleeding [5].

2-Patients and Methods:

This was a prospective randomized clinical study that was performed at the cardiovascular medicine department of Benha University Hospital and Madinat Nasr Health Insurance Hospital during the period from January 2022 to January 2023

Patients

The study included 200 elderly patients presenting with NSTEMI, they were categorized into two groups

Group 1: 100 NSTEMI participants received clopidogrel.

Group 2: 100 NSTEMI participants received ticagrelor.

Inclusion criteria:

The research population comprised patients who aged 70 years or older and presented with NSTEMI, which is defined as a symptoms spectrum consistent with acute myocardial ischemia or infarction and characterised by sudden decrease in coronary blood flow without ST segment elevation or new onset LBBB on the patient's ECG.

Patients already on DAPT before admission, contraindication to one of the P2Y12 inhibitors, who receiving oral anticoagulants, major surgery within 90 days before randomization, clinically significant out of range values for haemoglobin or platelet count, and cardiogenic shock, or having a life expectancy < 1 year at the time of screening were excluded from the study.

Methodology:**A) Complete history taking including the following data:**

Age, gender, presence or absence of hypertension, diabetes, smoking, dyslipidemia, history of IHD, prior PCI or CABG, history of stroke, onset, offset, character and duration of chest pain.

B) Complete clinical examination including:

including diastolic and systolic blood pressure heart rate, and killip class.

C) Standard ECG including the following data:

It was done for every patient to detect the presence of any ischemic changes, brady or tachyarrhythmias and chamber enlargement.

D) Routine laboratory investigations including:

- Serum creatinine.
- High sensitive troponin (hs-TnI).Lipid profile including TC, LDL, HDL and TG.

- Creatine kinase-myocardial band

E) Transthoracic echocardiography :

It was done for all patients, using an echocardiograph equipped with a broad band transducer to assess ejection fraction (by modified Simpson method),segmental regional wall motion abnormality, diastolic dysfunction and valvular heart disease.

F) Coronary angiography:

Coronary angiography was performed for all patients according to their clinical condition by the percutaneous femoral or radial approach by an interventional cardiologist.

Primary outcome:

*The outcome of the bleeding is either major or minor PLATO bleeding. Major bleeding is characterised by a haemoglobin drop of three grammes or more, severe hypotension, or substantial disability that necessitates medical intervention. Conversely, minor bleeding is defined as any bleeding that does not require medical intervention.

* MACE defined as myocardial infarction, all-cause mortality, and stroke.

Secondary outcome:

Including urgent revascularisation, definite stent thrombosis, cardiovascular death, unstable angina, and transient ischaemic attack.

3- Results:

Insignificant differences were found between the studied groups regarding age (75 ± 5 vs. 77 ± 5 years, $P = 0.9$), gender ($P = 0.853$), diabetes (48 patients vs 54 patients, $P = 0.34$), hypertension (53 patients vs 51 patients, $P = 0.85$), smoking (46 patients vs 49 patients, $P = 0.8$), ejection fraction ($p = 0.63$), and triglycerides ($P = 0.33$) (Table 1)

Table (1) General and clinical characteristics of the studied patients

		Clopidogrel (n = 100)	Ticagrelor (n = 100)	P-value
Age (years)	Mean \pm SD	75 \pm 5	77 \pm 5	0.9
Gender	Males	60 (60)	61 (61)	0.853
	Females	40 (40)	39 (39)	
Diabetes mellitus	n (%)	48 (48)	54 (54)	0.34
Hypertension	n (%)	53 (53)	51 (51)	0.85
Smoking	n (%)	46 (46)	49 (49)	0.8
Ejection fraction (%)	Mean \pm SD	51 \pm 13	50 \pm 11	0.63
Triglycerides	Mean \pm SD	129 \pm 38	146 \pm 41	0.33

Patients who received clopidogrel demonstrated significantly lower minor bleeding (15 patients vs. 37 patients, $P = 0.02$) and overall bleeding (28% vs. 51%, $P = 0.01$). Additionally, major bleeding was decreased in participants who received clopidogrel than in participants who received ticagrelor but without statistical significance ($P = 0.133$) (Table 2).

No significant differences were reported regarding myocardial infarction ($P = 0.731$), stroke ($P = 0.8$), CV death ($P = 0.582$), stent thrombosis ($P = 0.9$), urgent revascularization ($P = 0.9$), and transient ischemic attacks ($P = 0.9$) (Table 2).

Table (2) Different outcomes in the studied groups

		Clopidogrel (n = 100)	Ticagrelor (n = 100)	P-value
Major bleeding	n (%)	13 (13)	24 (24)	0.133
Minor bleeding	n (%)	15 (15)	37 (37)	0.02*
All bleeding	n (%)	28 (28)	51 (51)	0.01*
Myocardial infarction	n (%)	6 (6)	4 (4)	0.731
Stroke	n (%)	4(4)	2 (2)	0.8
CV death	n (%)	6 (6)	4 (4)	0.582
Stent thrombosis	n (%)	5 (5)	2 (2)	0.9
Urgent revascularization	n (%)	3 (3)	3 (3)	0.9
Transient ischemic attacks	n (%)	2 (2)	1 (1)	0.9

4. Discussion

The fundamental pathology of ACS is a mismatch between the oxygen demand and supply in the myocardium. UA, NSTEMI, and STEMI each denote different forms of thrombotic vessel occlusion, with degrees of this incongruity varying [6].

Consistent with our findings, [7] a meta-analysis conducted in 2015 compared alternative oral P2Y12 inhibitors (Ticagrelor or Prasugrel) to clopidogrel in NSTEMI patients. The results of this analysis demonstrated that the risk of major and minor bleeding was significantly elevated with newer oral P2Y12 inhibitors.

Furthermore, [8] in 2020, the Popular AGE study was conducted on NSTEMI participants who aged 70 years or older. The findings of this trial demonstrated that clopidogrel treatment led to a considerably reduced incidence of bleeding in comparison to ticagrelor treatment, not only for the composite minor and major bleeding outcome, but also for fatal bleeding and major unrelated to PLATO-CABG. Thrombotic events did not offset the advantageous effects of clopidogrel, resulting in a net clinical benefit outcome that was not inferior in nature.

This finding is consistent with the comparable thrombotic event rates between the two treatment groups reported in 2017 [9]. The TOPIC trial demonstrated that a one-month transition from DAPT involving aspirin and a more recent P2Y12 blocker to DAPT (aspirin and clopidogrel) following ACS is more effective than maintaining the same DAPT strategy in avoiding bleeding complications without an elevation in ischaemic events.

Although, this finding contradicted the PLATO trial results conducted in 2009, (10) which detected that ticagrelor was more effective than clopidogrel in reducing the combined cardiovascular death, myocardial infarction risk, and stroke.

5. Conclusion

As an alternative to ticagrelor, clopidogrel is beneficial for elderly patients. Without increasing ischemic risk, clopidogrel is associated with a significantly reduced minor and major bleeding risk.

Finding: Nil

Conflict of interest: Nil

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