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Assessment of Safety and Efficacy of Ticagrelor with other Selected Anti-Platelet Agents in Acute Coronary Syndrome at a Tertiary Care Hospital

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A B S T R A C T

Respiratory tract infections are respiratory illnesses that refer to variety of infections of the sinuses, throat, airway or lungs. These are the most common group of infections. The respiratory infections are usually treated using antibiotics. Antibiotics are substances produced by one microorganism that selectively inhibit or kills the growth of other microorganisms. The objective of the study was to evaluate the safety and efficacy of antibiotics in respiratory tract infections and to evaluate the role of most useful and lifesaving drugs used in respiratory tract infections and to evaluate rationality of drug therapy. A Prospective observational study on evaluation of safety and efficacy of antibiotics was conducted in Narayana Medical College and Hospital in the Pulmonology department for a period of 6 months. In our study we considered 384 patients are observed. Out of that only 300 patients are willing to provide the information. Out of which age groups between 21-70 are considered with sex of 218 males and 82 females in that the maximum were smokers (75.33%) and the non-smokers (24.66%) with secondary education is high compared to primary and tertiary with average nutritional status and average hygienic conditions. Overall outcomes after using antibiotics were found to be better 66%, average 23.66% and no outcome 3.66%. Our study concluded that most of the patients who are suffering with respiratory tract infections are considered, maximum patients were using antibiotics for their beneficial and the mostly used antibiotic is Amoxicillin and Clavulanate. .

INTRODUCTION

Acute coronary syndrome is the major cause for morbidity and mortality. Effective therapy is essential to reverse ischemia. It restores normal blood flow and decreases the myocardial damage. ACS can cause mortality in patients prior to the admission into the hospital due to persistent angina symptoms and heart failure conditions [1,2].

Patients with Acute coronary syndrome had an increased risk of new ischemic events and stroke was the main cardiovascular disease burdens [3]. In patients with cardiovascular disease, platelet activation is triggered by an injured or dysfunctional vascular endothelium, which leadsto aggregation and the thrombus formation [4]. Treatment of patients with ACS includes double anti-platelet therapy with acetylsalicylic acid and a P2Y12 inhibitor to reduce the risk for thrombotic complications [5-7].

Clopidogrel, a P2Y12 receptor antagonist is a valid anti-platelet drug for ACS patients. The anti-platelet therapy is used to prevent the occurrence of ischemic events through inhibition of platelet formation and protect the distal tissues through inhibition of microembolisation [8,9]. Clopidogrel is the pro drug often requires hepatic conversion and leads to onset delay of metabolites with a wide variability of platelet inhibition between individuals [10,11] .The high bleeding risk, stent thrombosis, myocardial infarction leads to the poor response of clopidogrel, shows the limitation of its efficacy. Combining clopidogrel with aspirin may have an additive effect [12-15]. Ticagrelor is a direct acting oral antagonist; this drug has more beneficial outcomes. Ticagreloris more potent and platelet inhibition with faster onset as well offset when it is compared withthe clopidogrel [16,17]. Prasugrel is an alternative agent to clopidogrel, which has greater platelet aggregation inhibition than clopidogrel [18]. The Ticagrelor, Prasugrel and Clopidogrel has a difference in both the pharmacokinetic and pharmacodynamic profiles as well as difference in the risk conditions.

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METHODOLOGY

Place of Study

The study was carried out in the 'Department of Cardiology' at a tertiary care hospital in Nellore.

Study design

A prospective study on comparison of safety and efficacy of the anti-plateletdrugs for the treatment of ACS. The drugs included in our study are Aspirin, clopidogrel, prasugrel and ticagrelor.

Study site

The study was conducted at a tertiary care hospital, Nellore.

Study population

This study is carried out in 210 patients who are suffering with ACSand are on Anti platelet therapy.

Study duration

This study was conducted for 6 months. (December 2020 – May 2021)

Study criteria/Patient enrolment

Patients are enrolled in the study based on inclusion & exclusion criteria

a) Inclusion criteria

All patients above 18 years with Acute coronary Syndromes

- Prescribed with any of the selected anti- platelet drugs.
- Drug naïve patients
- Patients with positive ECG for ACS.

b) Exclusion criteria:

- Pregnancy and lactating women.
- Patients with conditions like CKD, stroke, CLD.
- Patients of age under 18 years.
- Patients who are unwilling.
- Patients who underwent CABG/ PCI in near past.

Study materials

- Patient informed consent form
- A specially designed questionnaire

Study method

In this study we randomly assigned patients who are diagnosed with acutecoronary syndrome and for whom invasive evaluation was planned to receive

- ✓ Aspirin (75mg - 325mg)
- ✓ Clopidogrel (75mg - 300mg)
- ✓ Ticagrelor (90mg - 180mg)
- ✓ Prasugrel (5mg - 10mg).

Statistical analysis:

The Primary end point is the composite of death, myocardial infarction, or stroke. A Major Secondary end point (the safety end point) is adverse effects of the drugs (E.g.: GI bleeding, heart burn). The endpoints have been evaluated after a 3 month follow up after the drugs initiation. Data has been expressed as percentage, mean and Kruskal Wallis statistical methodwas used to analyze the results and P – value < 0.05 was considered as statistically significant. All the analyses were carried out using Statistical Package for the Social Sciences (SPSS).

RESULTS

A total of 210 patients of age group 30-90 were randomized to Aspirin (n=50), Clopidogrel (n=50), Ticagrelor (n=30), Prasugrel (n=30), aspirin + clopidogrel as a combination therapy (n=50) were recruited under inclusion criteria and were followed for the study. The collected Acute Coronary Syndrome patient's data were analyzed based upon the following parameters of Socio-demographic data. Out of 210 patients 11 (5.2%) were in within the age group of 30-39 years, 32 (15.2%) were within 40-49 years, 64 (30.4%) were within 50-59 years, 66 (31.4%) were within 60-69 years, 29 (13.9%) were within 70-79 years and 8 (3.9%) were within 80-89 years. The mean age ofthe patients was 59.48 and these details were tabulated in Table 1.

Among 210 patients, majority of were male patients (57.2 %) than female patients (42.8%). The co morbidities having patient details were tabulated in Table 2. Among 210 patients, 110 (52.38%) patients were diagnosed with Unstable Angina, 55 (26.19%) patients were diagnosed with STEMI and 45 (21.42%) patients were diagnosed with NSTEMI. Classification based on ADR'S was tabulated in Table 3. Classification based on primary efficacy endpoint was tabulated in Table 4.

Graphical representation of classification of patients based on Efficacy outcomes was represented in Fig 1. Hypothesis test for the distribution of Efficacy outcome was represented in Fig 2 and Hypothesis test for the distribution of adverse effects was represented in Fig 3.

Age group	No. of patients	Percentage (%)
30-39	11	5.2
40-49	32	15.2
50-59	64	30.4
60-69	66	31.4
70-79	29	13.9
80-89	08	3.9

Table 1 Age wise distribution of the ACS patients.

Co-morbidities	No. of Patients	Percentage(%)
Hypertension	38	18
Diabetes	22	10.47
Asthma	10	4.76
Diabetes/ Hypertension	22	10.47
Diabetes/ Asthma	01	0.47

Table 2 Classification of patients based on co-morbidities.

Adverse effects	No. of Patients	Percentage (%)
Aspirin		
Bleeding	3	6
Heart burn	6	12
Clopidogrel		
Bleeding	5	10
Ticagrelor		
Bleeding	5	10
Prasugrel		
Bleeding	4	13.3
Heartburn	2	6.6
Aspirin +Clopidogrel		
Bleeding	9	18
Heart burn	6	12
Bleeding+ Heart burn	1	3.3

Table 3 Classification of patients based on adverse effects observed.

Primary outcome	No. of Patients	Percentage (%)
Aspirin		
Death	3	6
Re-infraction	4	8
Stroke	2	4
Clopidogrel		
Death	1	2
Re-infraction	3	4
Stroke	1	0
Ticagrelor		
Death	0	0
Re-infraction	0	0
Stroke	1	3.3
Prasugrel		
Death	2	6.66
Re-infraction	2	6.66
Stroke	1	3.33
Aspirin +Clopidogrel		
Death	1	2
Re-infraction	2	4
Stroke	0	0

Table 4 Classification of patients based on primary efficacy end point.

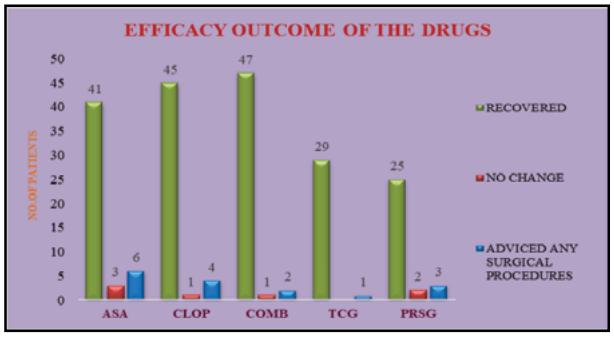
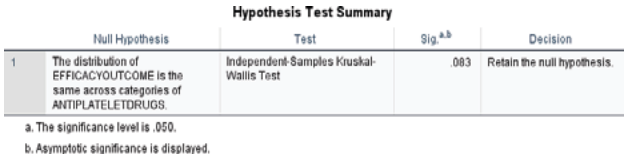


Figure 1: Graphical representation of classification of patients based on Efficacy outcome.



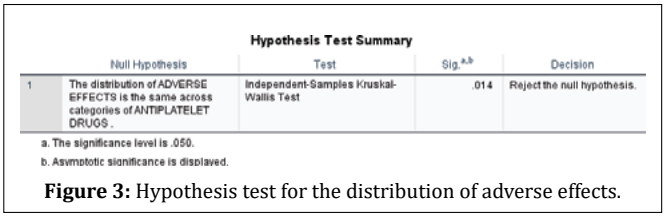
Hypothesis Test Summary

	Null Hypothesis	Test	Sig.[a,b]	Decision
1	The distribution of EFFICACYOUTCOME is the same across categories of ANTIPLATELETDRUGS.	Independent-Samples Kruskal-Wallis Test	.083	Retain the null hypothesis.

a. The significance level is .050.

b. Asymptotic significance is displayed.

Figure 2: Hypothesis test for the distribution of Efficacy outcome.



Hypothesis Test Summary

	Null Hypothesis	Test	Sig.[a,b]	Decision
1	The distribution of ADVERSE EFFECTS is the same across categories of ANTIPLATELET DRUGS .	Independent-Samples Kruskal-Wallis Test	.014	Reject the null hypothesis.

a. The significance level is .050.

b. Asymptotic significance is displayed.

Figure 3: Hypothesis test for the distribution of adverse effects.

DISCUSSION

Acute coronary syndrome is the major cause for morbidity and mortality. Acute coronary syndrome often caused by plaque rupture or clot formation in the heart arteries. This Study sought to evaluate the clinical efficacy and safety of selected anti platelet agents (i.e. aspirin, clopidogrel, prasugrel, ticagrelor) in Acute coronary syndrome at tertiary care hospital in Nellore for the duration of 6 months. The main objectives involved in the study is to identify anti platelet drugs that is more efficacious among aspirin, clopidogrel, ticagrelor, prasugrel, to analyse the safety data of anti-platelet agents include in the study and to identify adverse events that are being obstruction for the use ticagrelor and prasugrel. Among 210 patients, 120 (57.2%) were male and 90(42.8%) were female of age group 30 to 90 were randomized to aspirin (n= 50), clopidogrel (n= 50), ticagrelor (n= 30), prasugrel (n= 30), aspirin + clopidogrelas a combination therapy (n=50). Among 210 patients 110 (52.38%) patients were diagnosedwith unstable angina, 55 (26.19%) patients were diagnosed with STEMI and 45 (21.42%) patients were diagnosed with NSTEMI and Troponin – I levels is negative in maximum number of patients (71.42%) and positive in minimum number of patients (28.57%). Patients are enrolled in the study based on inclusion and exclusion criteria. Patients included in our study are all patients above 18 years with Acute coronary syndrome, prescribed with any of the study drug, drug naive patients, patients with positive ECG in Acute coronary syndrome, patients excluded in study are pregnancy and lactating women, patients below 18 years, patientswith CKD and CLD and patients who underwent CABG/ PCI near past.

Decision regarding the use of the anti-platelet agents is influenced mainly by safety andefficacy consideration, adverse effects of patients also analyzed in the study out of which bleeding has been reported in maximum number of patients in both ticagrelor 7 (23.3%) groupand combination therapy 9(21.1%) group followed by clopidogrel 5 (10%) group, prasugrel 4(6.6%) and least in aspirin (6%). A mild heart burn has also reported more in combination therapy 6 (15.3%) group and aspirin 6(12%) followed by prasugrel 2 (3.3%) group. 1 (3.3%) Patients in combination therapy were reported both heart burn and bleeding. The past medicalhistory of the patients was also examined in the study out of which the most of the patients were of Hypertension (40.86%), Diabetes mellitus (23.65%), Asthma (10.75%), Diabetes/ Hypertension (23.65%), Diabetes/ Asthma (1.075%).

Statistical analysis was performed by using Kruskal Wallis statistical method to analyse the results and p value < 0.05 was considered as statistically significant. After 3 months follow-up the efficacy end point did not differ statistically significant (p= 0.083). The primary endpoint is composite of death, myocardial infarction or stroke. The study demonstrates that ticagrelor is rapid efficacious. Death and re infarction did not occurred in ticagrelor group compared with remaining groups. The incidence of primary compositeendpoint was reduced with ticagrelor compared with aspirin, clopidogrel, prasugrel andcombination therapy.

Out of 50 patients in aspirin group 41 (82%) were recovered, 3(6%) patients had no efficacy, 6 (12%) patients were advice to undergo surgical procedure. In clopidogrel group out of 50 patients 45(90%) were recovered, 1 (2%) patient had no efficacy, 4 (8%) patients were advice to undergo surgical procedure. In case of combination therapy group out of 50patients 47(94%) were recovered, 1 (2%) patient had no efficacy, 2(4%) patients were advised to undergo surgical procedure. In ticagrelor group out of 30 patients 29 (96.6) patients were recovered, 1(3.33) patient were advice to undergo surgical procedure. In prasugrel group out of 30 patients 25 (83.3%) were recovered, 2 (6.66%) had no efficacy, 3 (10%) were advice to undergo surgical procedure. After 3 months follow-up there is a statistically significant difference (p= 0.014) in the safety endpoint of selected anti platelet agents. The secondary endpoint is adverse effects of drugs (e.g., GI bleeding, heart burn). The safety endpoint occurs maximum in 33.3% aspirin+ Clopidogrel group and 23.3% in Ticagrelor group patients.

CONCLUSION

In this study the data shown that, on Safety basis, the patients who received Aspirin + Clopidogrel drugs as combination therapy have shown excess of bleeding events and the patients who received

Ticagrelor shown minimal bleeding events compared to Prasugrel, Aspirin and Clopidogrel as monotherapy. On Efficacy basis, the selected Anti Platelet drugs did not differ statistically significant. But the patients who received Ticagrelor have shown high recovery rate compared to Aspirin, Clopidogrel, Prasugrel and Aspirin + Clopidogrel as dual therapy. Therefore, in ACS patients who received Ticagrelor therapy have shown depletion in major adverse cardiovascular events without a significant increase in bleeding events compared with other selected anti-platelet drugs. So, Ticagrelor is recommended as better therapy in acute coronary syndrome when comparedwith other selected Anti-Platelet drugs due to its efficacy rate and safety profile.

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Conflict of Interest

None

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Self

Ethical Committee Approval

We Have Memorandum of Understanding with Narayana Medical College and Hospitals to Conduct the Study.

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