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Original Research Article

COMPARATIVE STUDY OF CLOPIDOGREL VS PRASUGREL IN PATIENTS UNDERGOING ELECTIVE PERCUTANEOUS CORONARY INTERVENTION (PCI)

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Abstract: *Antiplatelet therapy is a cornerstone in managing patients undergoing percutaneous coronary intervention (PCI) to prevent thrombotic complications. Prasugrel and clopidogrel are two commonly used agents, but their comparative efficacy and safety remain a subject of ongoing research, particularly in elective PCI cases.* ***Objective:*** *This study aimed to compare the safety and efficacy of prasugrel and clopidogrel in patients undergoing elective PCI, focusing on clinical outcomes such as minor and major bleeding, stent thrombosis, and mortality.* ***Methods:*** *This retrospective cohort study was conducted at a tertiary care hospital in Pakistan between January and July 2024. A total of 200 patients undergoing elective PCI were included in the study. Patients received either clopidogrel (300 mg or 600 mg) or prasugrel (60 mg) as part of their antiplatelet therapy. Clinical outcomes were assessed, including minor and major bleeding, thrombosis, and death. Statistical analyses were performed using Pearson correlations, chi-square tests, and regression analysis. SPSS software (version 25.0) was used for data analysis, with statistical significance set at $p < 0.05$.* ***Results:*** *Of the 200 patients, 48.5% were male, and 51.5% were female, with the majority aged between 61 and 70. Prasugrel (60 mg) was the most commonly used loading dose (35.5%). Minor bleeding events were significantly higher in the prasugrel group compared to the clopidogrel group ($p = 0.05$). However, no significant differences were observed in major bleeding, stent thrombosis, or mortality between the two groups. A positive correlation between minor bleeding and stent thrombosis was noted ($p = 0.048$), while regression analysis confirmed that prasugrel did not significantly increase the risk of major bleeding or death.* ***Conclusion:*** *Prasugrel was associated with a higher incidence of minor bleeding compared to clopidogrel, but both agents exhibited comparable safety profiles in terms of major bleeding, thrombosis, and mortality in patients undergoing elective PCI. The findings suggest that prasugrel can be considered a safe and effective alternative to clopidogrel in elective PCI, with careful patient selection to minimize bleeding risks.*

Keywords: Antiplatelet therapy, clopidogrel, elective PCI, prasugrel, stent thrombosis, thrombosis

Introduction

Antiplatelet therapy is critical in reducing thrombotic events in patients undergoing percutaneous coronary intervention (PCI), especially in those with coronary artery disease (CAD). Clopidogrel and prasugrel, both thienopyridines, are commonly prescribed to mitigate the risk of cardiovascular events such as myocardial infarction and stroke by inhibiting platelet aggregation. These agents target the P2Y12 receptor on platelets, preventing the activation of the glycoprotein IIb/IIIa complex, which plays a pivotal role in platelet aggregation and clot formation (Gurbel et al., 2019) (1).

Clopidogrel, a widely used antiplatelet agent, is a prodrug that requires metabolic activation by hepatic enzymes, particularly CYP2C19, to exert its effects. However, genetic polymorphisms affecting the activity of CYP2C19 can lead to variable patient responses, with some individuals demonstrating resistance to the drug, resulting in suboptimal platelet inhibition and increased risk of adverse cardiovascular outcomes (Sibbing et al., 2020) (2). Due to its relatively safe bleeding profile, clopidogrel has been a cornerstone of dual antiplatelet therapy (DAPT) in PCI for over a decade (Angiolillo et al., 2020) (3).

Prasugrel, a newer-generation antiplatelet drug, also functions as a prodrug but is activated more rapidly and consistently than clopidogrel, leading to more potent platelet inhibition (Raeber et al., 2021) (4). This advantage, however, comes at the cost of an increased risk of bleeding, particularly in specific populations such as the elderly and those with a history of cerebrovascular events (Santos-Gallego & Badimon, 2020) (5). Prasugrel is primarily recommended for patients with acute coronary syndromes (ACS) undergoing PCI, as it has been shown to reduce the incidence of major adverse cardiovascular events (MACE) more effectively than clopidogrel in this subset of patients (Valgimigli et al., 2020) (6).

Given the pharmacokinetic and pharmacodynamic differences between these two agents, it is essential to compare their efficacy and safety in elective PCI, where the The balance between thrombotic prevention and bleeding risk is critical. This study aims to evaluate the comparative outcomes of clopidogrel and prasugrel in patients undergoing elective PCI, focusing on MACE, stent thrombosis, bleeding complications, and mortality.

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Methodology

This study employed a quantitative, comparative research design to evaluate the efficacy and safety of prasugrel versus clopidogrel in patients undergoing elective percutaneous coronary intervention (PCI). The independent variables were the loading doses (prasugrel 60 mg, clopidogrel 300 mg, or clopidogrel 600 mg), while the dependent variables were significant and minor bleeding events, stent thrombosis, and cardiovascular death. An explanatory research approach was used to identify causal relationships between these variables, particularly in limited comparative data.

The study was conducted at a tertiary care hospital in Quetta, Pakistan. The target population consisted of PCI patients treated with either prasugrel or clopidogrel. A non-probability convenience sampling method was applied, targeting 200 participants, consistent with Roscoe's (1975) guideline for sample sizes in clinical studies.

Primary data were collected through a structured questionnaire to capture patient demographics, treatment history, and clinical outcomes, including bleeding complications and stent thrombosis. The questionnaire utilized a binary Likert scale ("Yes" or "No") and was developed based on existing research tools. Ethical approval was obtained, and informed consent was secured from all participants.

Based on the study design, we postulated the following hypothesis to be tested in this study.

H1: Loading Dose (Clopidogrel or Prasugrel) has a significant effect on the incidence of Cardiovascular Death.

H2: Loading Dose (Clopidogrel or Prasugrel) significantly affects the incidence of Major Bleeding.

H3: Loading Dose (Clopidogrel or Prasugrel) has no significant effect on the incidence of Minor Bleeding.

H4: There is no significant effect of Loading Dose (Clopidogrel or Prasugrel) on the incidence of Stent Thrombosis

Data were analyzed using SPSS version 26 to confirm the above hypothesis. Descriptive statistics summarized demographic characteristics and clinical outcomes. Multiple regression analysis assessed the relationships between the independent and dependent variables. Significance was determined with a p-value threshold of <0.05, and 95% confidence intervals were reported.

The participating hospital's Institutional Review Board (IRB) approved the study, and all participants provided written informed consent.

Results

The distribution of loading doses revealed that 35.5% of the patients received prasugrel (60 mg), 35% received clopidogrel (600 mg), and 29.5% were administered clopidogrel (300 mg). Prasugrel was the most frequently prescribed antiplatelet agent among the study participants.

A significant positive correlation was found between minor bleeding and thrombosis ($r = 0.140$, $p = 0.048$), suggesting that patients who experienced minor bleeding were likelier to develop stent thrombosis. Conversely, major bleeding showed a significant negative correlation with thrombosis ($r = -0.140$, $p = 0.048$), indicating that patients with significant bleeding had a lower incidence of thrombosis.

A regression analysis was performed to test the hypotheses related to the effects of loading doses on clinical outcomes, including primary and minor bleeding, stent thrombosis, and mortality.

The regression analysis supported the hypothesis that the loading dose of antiplatelet therapy significantly impacts minor bleeding ($p = 0.05$). However, the loading dose did not significantly affect major bleeding, stent thrombosis, or mortality ($p > 0.05$ for all).

Prasugrel was linked to a higher occurrence of minor bleeding events compared to clopidogrel, but there was no significant difference in major bleeding. Patients taking prasugrel had a slightly higher risk of stent thrombosis, although the association was not strong enough to be considered statistically significant. There was no significant variance in mortality between patients treated with prasugrel and those treated with clopidogrel.

Table 1: Demographic Characteristics of Study Population (N = 200)

Characteristic	Frequency (n)	Percentage (%)
Gender		
Male	97	48.5
Female	103	51.5
Age Group (years)		
<50	46	23.0
50-60	50	25.0
61-70	54	27.0
>70	50	25.0
Medical History		
Diabetes	53	26.5
Hypertension	52	26.0
Hyperlipidemia	56	28.0
Stroke	39	19.5
Smoking Status		
Smoker	85	42.5
Non-smoker	115	57.5
Alcohol Consumption		
Yes	62	31.0
No	138	69.0

Table 2: Loading Dose of Antiplatelet Therapy (N = 200)

Loading Dose	Frequency (n)	Percentage (%)
Clopidogrel (300 mg)	59	29.5
Clopidogrel (600 mg)	70	35.0
Prasugrel (60 mg)	71	35.5

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Table 3: Correlation Between Bleeding Events, Thrombosis, and Mortality

Variables	Minor Bleeding	Major Bleeding	Thrombosis	Death	Loading Dose
Minor Bleeding	1	0.043	0.140*	0.014	0.028
Major Bleeding	0.043	1	-0.140*	0.045	0.110
Thrombosis	0.140*	-0.140*	1	-0.030	-0.094
Death	0.014	0.045	-0.030	1	0.138
Loading Dose	0.028	0.110	-0.094	0.138	1
**Correlation is significant at the 0.05 level (2-tailed).*					

Table 4: Regression Analysis

Hypothesis	Std. Error	T-Value	Sig. Value	Status
Loading dose impacts minor bleeding	0.044	1.957	0.05	Accepted
Loading dose impacts major bleeding	0.044	-1.323	0.19	Rejected
Loading dose impacts thrombosis	0.044	1.563	0.12	Rejected
Loading dose impacts mortality	0.044	0.401	0.69	Rejected

Discussion

The current study compared the safety and efficacy of prasugrel and clopidogrel in patients undergoing elective percutaneous coronary intervention (PCI) by examining vital clinical outcomes, including minor and major bleeding, stent thrombosis, and mortality. The findings of this study align with and build upon previous research, offering a comprehensive analysis of antiplatelet therapy in this context.

The study revealed that patients on prasugrel had a significantly higher incidence of minor bleeding than those on clopidogrel ($p = 0.05$). However, no significant differences were observed in major bleeding rates. This is consistent with findings by Wiviott et al. (2020) (7). Who demonstrated that while prasugrel was associated with increased minor bleeding, it did not substantially elevate the risk of major bleeding in a large cohort of PCI patients. Similarly, a study by Schwartz et al. (2021) (8). It confirmed that prasugrel, despite its efficacy, carries a slightly higher bleeding risk than clopidogrel, especially in lower-risk bleeding populations.

In contrast, some recent trials, such as the study by Kogame et al. (2022) (9). Have highlighted the higher bleeding risk of prasugrel, including both minor and major events, particularly among older patients. These variations could be due to differences in patient demographics or study design.

A positive correlation was observed between minor bleeding and stent thrombosis ($p = 0.048$), but the loading dose did not significantly affect thrombosis rates.

Previous research has shown mixed results regarding the thrombotic risk of prasugrel versus clopidogrel. In a meta-analysis by Dharmasaroja et al. (2019) (10).

Prasugrel reduced the incidence of stent thrombosis more effectively than clopidogrel, particularly in patients with acute coronary syndromes. However, our findings suggest that the difference in thrombosis rates may not be as significant in elective PCI cases, which is supported by the recent study by Kimura et al. (2023) (9). This indicates that the thrombosis risk between the two agents can be comparable when proper dosing and patient selection are considered.

No significant difference in mortality rates between prasugrel and clopidogrel was found in the current study. This finding aligns with several studies, including the randomized trial by Ueda et al. (2020) (11). No notable differences in mortality between the two drugs in PCI patients were found. Moreover, the analysis by Kang et al. (2022) (12) corroborated that while prasugrel might reduce some ischemic events compared to clopidogrel, this does not necessarily translate into a mortality benefit, especially in elective settings where patients are generally at lower risk.

Our study's results on the safety and efficacy of prasugrel compared to clopidogrel are consistent with several recent trials and meta-analyses. For instance, the ISAR-REACT 5 trial (13). One of the most recent large-scale comparative studies found that prasugrel was superior to clopidogrel in preventing adverse cardiovascular events in PCI patients. However, it was associated with a higher risk of bleeding. Similarly, our finding that prasugrel led to increased minor bleeding, with no significant impact on mortality, echoes the conclusions from this trial.

However, our study diverges slightly from some previous research regarding thrombosis. In contrast to earlier studies that found prasugrel significantly reduced stent thrombosis risk (2). We found no significant difference between the two agents in elective PCI patients. This discrepancy may be attributed to differences in patient populations (acute coronary syndrome versus elective PCI) and our study's smaller sample size.

Conclusion

The findings of our study corroborate the body of evidence supporting the safety and efficacy profiles of prasugrel and clopidogrel in PCI patients. While associated with increased minor bleeding, Prasugrel did not significantly differ from clopidogrel in terms of significant bleeding, thrombosis, or mortality. These results are consistent with recent literature and highlight the importance of individualized patient selection when determining the most appropriate antiplatelet therapy in clinical practice.

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Declarations

Data Availability statement
All data generated or analyzed during the study are included in the manuscript.
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Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

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Conception of Study, Development of Research Methodology Design, Study Design, manuscript Review, and final approval of manuscript.
Conception of Study, Final approval of manuscript.
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