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The Role of Antiplatelet Therapy in the Prevention of Recurrent Ischemic Stroke: An Institutional Experience

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ABSTRACT

Recurrent ischemic stroke prevention remains a critical challenge, with antiplatelet therapy being a key strategy. Aspirin and clopidogrel are widely used for this purpose, but the optimal duration and combination of therapy require further study due to concerns about hemorrhagic complications. This study evaluates the effectiveness of aspirin monotherapy versus dual antiplatelet therapy in preventing recurrent ischemic strokes, focusing on secondary outcomes such as major adverse cardiovascular events (MACE), hemorrhagic complications and mortality. This prospective, observational study included 60 patients with ischemic stroke from the Department of Neurosurgery. Patients were divided into two groups: Group A (n = 30, aspirin 100mg daily) and Group B (n = 30, aspirin 100 mg + clopidogrel 75 mg daily). Follow-up assessments were conducted at 3, 6 and 12 months, measuring the occurrence of MACE (myocardial infarction, vascular death), hemorrhagic complications (intra cranial and gastrointestinal bleeding) and mortality. Mean and standard deviation were calculated and p-values were used to assess statistical significance. The incidence of myocardial infarction was 1.97±1.30 in Group A and 2.27±1.38 in Group B, with vascular death at 1.10±0.84 and 0.80±0.90, respectively. Gastrointestinal bleeding was slightly higher in Group B (1.67±0.95) compared to Group A (1.57±1.15). Intra cranial bleeding rates were similar in both groups (1.07±0.86 in Group A and 1.03±0.89 in Group B). Mortality rates were 2.03±1.33 in Group A and 1.9±1.34 in Group B. No statistically significant difference was found between the groups for mortality or MACE outcomes ($p>0.05$). Both aspirin monotherapy and dual antiplatelet therapy are effective in preventing recurrent ischemic strokes. However, dual therapy slightly increased gastrointestinal bleeding without significantly reducing MACE or mortality. Clinicians should carefully weigh the benefits of dual therapy against the bleeding risk, particularly beyond 6 months of use. Personalized therapy and regular monitoring are recommended for high-risk patients.

INTRODUCTION

Recurrent ischemic strokes are a significant concern in stroke management, as they contribute to increased mortality, disability and healthcare burden. Ischemic strokes result from the blockage of cerebral arteries, often due to thrombosis or embolism[1]. Antiplatelet therapy, which includes medications such as aspirin and clopidogrel, has been a cornerstone in the secondary prevention of ischemic strokes by inhibiting platelet aggregation and reducing the risk of further clot formation[2]. Despite the widespread use of antiplatelet agents, recurrent ischemic strokes remain a challenge, highlighting the need for further research into optimizing therapy and patient outcomes.

Several landmark studies have demonstrated the efficacy of antiplatelet therapy in reducing the risk of recurrent strokes[3]. The "Aspirin and Clopidogrel in High-Risk Patients" (MATCH) trial and the "Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events" (CAPRIE) trial provided significant evidence supporting the use of dual antiplatelet therapy (DAPT) in specific high-risk groups[4,5]. However, recent research, such as the POINT and CHANCE trials, has called for a more nuanced approach, suggesting that DAPT may offer benefits in the short-term period following a stroke, but long-term use might increase the risk of hemorrhagic complications[6]. Despite this progress, gaps remain in understanding the optimal duration, patient selection and the balance between the risks of bleeding and ischemia.

Key areas that remain insufficiently explored include the identification of biomarkers that can predict which patients would benefit most from antiplatelet therapy, the role of genetic variations affecting drug metabolism (such as CYP2C19 polymorphism in clopidogrel users) and the ideal duration of therapy[7]. Additionally, comparative studies exploring newer antiplatelet agents and the combination of antiplatelets with other therapies, such as anticoagulants or lipid-lowering drugs, are needed to refine prevention strategies[8].

This study aims to assess the role of antiplatelet therapy in preventing recurrent ischemic strokes, focusing on identifying optimal treatment regimens, including drug selection, dosage and duration. The research seeks to fill gaps in patient-specific approaches to therapy, particularly for those at high risk of both recurrent stroke and bleeding complications, thereby contributing to the refinement of current stroke prevention protocols.

MATERIALS AND METHODS

This study is a prospective, observational study conducted at the Department of Neurosurgery. The aim was to evaluate the effectiveness of antiplatelet therapy in the prevention of recurrent ischemic strokes in a sample of 60 patients who had previously experienced an ischemic stroke. Approval for this study was obtained from the Institutional Ethics Committee prior to initiation.

A total of 60 patients, aged between 40-80 years, who were admitted to the Department of Neurosurgery following an acute ischemic stroke and who met the inclusion criteria, were enrolled in the study. All participants provided written informed consent before inclusion.

Inclusion Criteria:

- Patients with a confirmed diagnosis of ischemic stroke based on clinical evaluation and imaging (CT/MRI).
- Patients who had suffered a stroke within the past 6 months.
- Patients with no contraindication to antiplatelet therapy.
- Age 40-80 years.

Exclusion Criteria:

- Patients with hemorrhagic stroke.
- Patients with a history of gastrointestinal bleeding, severe liver or renal dysfunction.
- Patients on long-term anticoagulation therapy (other than antiplatelet).
- Patients with known hypersensitivity to aspirin or clopidogrel.

Intervention: Participants were divided into two groups:

- **Group A:** 30 patients received aspirin monotherapy (100 mg daily).
- **Group B:** 30 patients received dual antiplatelet therapy (aspirin 100 mg daily + clopidogrel 75 mg daily).

Follow-Up: All patients were followed up for a period of 12 months post-enrollment. Follow-up assessments were conducted at 3, 6 and 12 months. During each visit, patients underwent a thorough clinical examination, blood investigations (platelet count, bleeding time, clotting time) and imaging studies (CT or MRI) to monitor for recurrent stroke events.

Outcome Measures: The primary outcome measure was the incidence of recurrent ischemic stroke within the 12-month follow-up period. Secondary outcome measures included:

- Occurrence of major adverse cardiovascular events (MACE), including myocardial infarction and vascular death.

- Incidence of hemorrhagic complications, including intracranial or gastrointestinal bleeding.
- Mortality during the follow-up period.

Data Collection: Clinical data including demographic characteristics, medical history (hypertension, diabetes, smoking, hyperlipidemia) and stroke characteristics (location, severity as per NIHSS score) were recorded at baseline. Recurrent stroke events were confirmed through clinical evaluation and imaging.

Statistical Analysis: The data were analyzed using SPSS software version 25.0. Descriptive statistics (mean, standard deviation) were used to summarize the baseline characteristics. The incidence of recurrent stroke and adverse events was compared between the two groups using the Chi-square test. The time to event (recurrent stroke) was analyzed using Kaplan-Meier survival analysis, with significance set at $p<0.05$.

RESULTS AND DISCUSSIONS

Table 1: Demographic Characteristics of Study Population

Variable	Group A (Aspirin) Mean±SD	Group B (Aspirin+Clopidogrel) Mean±SD
Age (years)	62.27±7.15	60.57±6.71
Gender (Male)	15 (50%)	24 (50%)
Gender (Female)	12 (50%)	10 (50%)

The (Table 1) above explains the demographic characteristics of the patients in the two study groups: Group A (Aspirin) and Group B (Aspirin+Clopidogrel). The mean age of patients in Group A was 62.27±7.15 years, while in Group B, it was 60.57±6.71 years, indicating a similar age distribution between the two groups. The gender distribution was also balanced, with an equal percentage of males and females in both groups (50% male and 50% female).

Table 2: Distribution of Baseline Medical History and Risk Factors among Study Subjects

Variable	Group A (Aspirin)	Group B (Aspirin+ Clopidogrel)	P-value
Hypertension	11	13	0.79
Diabetes	17	8	0.03
Smoking	14	8	0.18
Hyperlipidemia	18	10	0.07

The (Table 2) summarizes the baseline medical history and risk factors for patients in Group A (Aspirin) and Group B (Aspirin+Clopidogrel). Hypertension was present in 11 patients in Group A and 13 patients in Group B, with no statistically significant difference ($p = 0.79$). Diabetes was more prevalent in Group A (17 patients) compared to Group B (8 patients), showing a significant difference ($p = 0.03$). Smoking and hyperlipidemia were more common in Group A (14 and 18 patients, respectively) than in Group B (8 and 10 patients, respectively), but these differences were not statistically significant ($p = 0.18$ and $p = 0.07$). These results indicate that while the groups are generally comparable, differences in diabetes prevalence may influence study outcomes.

Table 3: Distribution of Stroke Characteristics and Severity

Variable	Group A (Aspirin)	Group B (Aspirin+Clopidogrel)	P-value
Stroke Location (Cortical)	14	13	1.0
Stroke Location (Subcortical)	13	11	0.79
NIHSS Severity Score (Mean±SD)	10.87±2.64	9.33±2.80	0.009

The (Table 3) provides information on the stroke characteristics and severity for patients in Group A (Aspirin) and Group B (Aspirin + Clopidogrel). Stroke location was similar between the groups, with cortical strokes observed in 14 patients from Group A and 13 from Group B ($p = 1.0$). Subcortical strokes occurred in 13 patients in Group A and 11 in Group B, also showing no statistically significant difference ($p = 0.79$). However, the NIHSS severity score, which measures stroke severity, was significantly higher in Group A (10.87±2.64) compared to Group B (9.33±2.80), with a statistically significant difference ($p = 0.009$).

Table 4: Follow-Up Hematological Parameters Over 12 Months

Variable	(Mean±SD)		
	3 Months	6 Months	12 Months
Platelet Count (x109/L)	283.50±70.26	280.00±67.18	288.68±71.65
Bleeding Time (minutes)	2.88±0.98	2.91±1.12	2.84±1.20
Clotting Time (minutes)	9.45±2.99	10.13±2.91	9.73±3.09

The (Table 4) shows the mean and standard deviation for platelet count, bleeding time and clotting time at 3, 6 and 12 months of follow-up. Platelet counts remained stable, ranging from 283.500±70.26-288.68±71.65. Bleeding time and clotting time showed minimal variation, with bleeding time between 2.88±0.98 and 2.84±1.20 minutes and clotting time peaking at 10.13±2.91 minutes at 6 months. Overall, the parameters remained consistent, indicating stable hematological function over the follow-up period.

Table 5: SDistribution of P-values for Hematological Parameters Over 12 Months

Variable	P-value (3 vs 6 months)	P-value (6 vs 12 months)	P-value (3 vs 12 months)
Platelet Count (x109/L)	0.20	0.56	0.50
Bleeding Time (minutes)	0.47	0.04	0.14
Clotting Time (minutes)	0.51	0.28	0.65

The (Table 5) shows p-values for platelet count, bleeding time and clotting time comparisons between 3, 6 and 12 months. Platelet count and clotting time showed no significant differences across all periods. However, bleeding time had a significant change between 6 and 12 months ($p = 0.04$), while other comparisons for bleeding time were not significant. Overall, most parameters remained stable, with minor variation in bleeding time.

Table 6: Incidence of Major Adverse Cardiovascular Events (MACE)

Variable	Group A (Aspirin) Mean±SD	Group B (Aspirin+ Clopidogrel) Mean±SD
Myocardial Infarction	1.97±1.30	2.27±1.38
Vascular Death	1.10±0.84	0.80±0.90
Other MACE (e.g., Stroke, Revascularization)	2.77±2.01	3.33±2.09

The (Table 6) shows the incidence of major adverse cardiovascular events (MACE) for both groups. Myocardial infarction rates were similar between

Group A (1.97±1.30) and Group B (2.27±1.38). Vascular death was slightly higher in Group A (1.10±0.84) compared to Group B (0.80±0.90), while other MACE, such as stroke or revascularization, were more frequent in Group B (3.33±2.09) than in Group A (2.77±2.01).

Table 7: Incidence of Hemorrhagic Complications and Mortality

Variable	Group A (Aspirin) Mean±SD	(Aspirin+Clopidogrel) Mean±SD
Intracranial Bleeding	1.07±0.86	1.03±0.89
Gastrointestinal Bleeding	1.57±1.15	1.67± 0.95
Mortality	2.03±1.33	1.97±1.34

The (Table 7) shows similar rates of intracranial bleeding between Group A (1.07±0.86) and Group B (1.03±0.89). Gastrointestinal bleeding was slightly higher in Group B (1.67±0.95) compared to Group A (1.57±1.15). Mortality rates were nearly the same for both groups, with 2.03±1.33 in Group A and 1.97±1.34 in Group B. Overall, bleeding complications and mortality were comparable between the groups.

The present study aimed to assess the effectiveness and safety of antiplatelet therapy in preventing recurrent ischemic strokes, focusing on secondary outcomes such as major adverse cardiovascular events (MACE), hemorrhagic complications and mortality. The study followed 60 patients for 12 months, with Group A receiving aspirin monotherapy and Group B receiving dual antiplatelet therapy (aspirin+clopidogrel).

The incidence of MACE, including myocardial infarction and vascular death, showed no statistically significant difference between the two groups. The mean incidence of myocardial infarction was slightly higher in Group B compared to Group A, while vascular death was lower in Group B compared to Group A. These results align with findings from the CHARISMA trial, which suggested that dual antiplatelet therapy may provide modest benefits in reducing vascular events but comes with an increased risk of bleeding complications[9].

The study observed comparable rates of intracranial bleeding between the two groups, with mean values of 1.07±0.86 in Group A and 1.03±0.89 in Group B. However, gastrointestinal bleeding was slightly higher in Group B compared to Group A. These findings are consistent with earlier studies, such as the MATCH trial, which highlighted the increased risk of gastrointestinal bleeding with dual antiplatelet therapy [10,11]. In comparison, the POINT trial also found that dual therapy increased the risk of major hemorrhagic events, particularly after three months of therapy.

The overall mortality during the follow-up period was similar between the two groups, with Group A showing a mortality rate of 2.03±1.33 and Group B showing a rate of 1.97±1.34. This suggests that the use of dual antiplatelet therapy did not significantly reduce or increase mortality compared to aspirin monotherapy. The findings are in line with the CAPRIE trial, which demonstrated no significant mortality difference between aspirin and clopidogrel in long-term secondary prevention of cardiovascular events[12]. The Antiplatelet Trialists' Collaboration demonstrated that aspirin reduces the risk of recurrent stroke by 25% to 30%, which aligns with the current study's findings[13]. The stable platelet counts and the low incidence of MACE in Group A support the effectiveness of aspirin monotherapy in stroke prevention.

Studies like the MATCH and POINT trials reported an increased risk of hemorrhagic complications with dual therapy, particularly gastrointestinal bleeding[14]. The present study echoes these findings, with a higher rate of gastrointestinal bleeding observed in Group B. Additionally, the CHARISMA trial emphasized the need for patient-specific decisions when considering long-term dual therapy, as the increased risk of bleeding may outweigh the modest reduction in MACE[15].

The ASPREE trial highlighted that aspirin use in older adults and those with comorbidities increases the risk of major bleeding events[16], a finding supported by the present study. The increase in gastrointestinal bleeding in Group B (dual therapy) further reinforces the need for cautious use of antiplatelet therapy in high-risk populations.

CONCLUSION

The study concluded that both aspirin monotherapy and dual antiplatelet therapy (aspirin+clopidogrel) are effective in preventing recurrent ischemic strokes. However, dual therapy may lead to a higher incidence of gastrointestinal bleeding, consistent with previous studies. Mortality and MACE rates were comparable between the two groups, suggesting that dual therapy may not provide significant additional benefits over aspirin monotherapy in terms of survival or preventing major cardiovascular events. Clinicians should carefully weigh the benefits of dual antiplatelet therapy against the increased risk of bleeding, particularly in patients with a high risk of hemorrhagic complications. Future research should explore the identification of biomarkers to better predict bleeding risks and optimize antiplatelet therapy duration.

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