Use of Antiplatelet Agents in the Neurosurgical Patient

Amanda S. Zakeri, MD, Shahid M. Nimjee, MD, PhD*

KEYWORDS

• Antiplatelet • Neurosurgery • Aneurysms • Carotid dissection • Carotid stenosis
• Moyamoya disease • Stroke

KEY POINTS

- Antiplatelet therapy is an important part of treating vascular neurologic conditions including carotid artery disease and dissection, intracranial atherosclerotic disease, and moyamoya disease.
- Technological advances in endovascular neurosurgery to treat intracranial aneurysms have resulted in antiplatelet agents being used uniformly electively and increasingly in the acute setting.
- Ischemic stroke has evolved in part to an interventional disease. Medical management may include dual antiplatelet therapy (DAPT) acutely and certainly monotherapy chronically.

INTRODUCTION

Antiplatelet therapy has long been used in a variety of neurosurgical vascular conditions. This article presents relevant literature on the role of antiplatelet therapy in neurosurgical vascular diseases. There is a significant challenge in broadly recommending one or even multiple agents over others. Current literature supports developing an individualized approach to each patient. It is hoped that this serves as a starting point for readers to better understand which regimens have the best evidence to support their implementation in clinical practice and which areas are still under active investigation.

ANEURYSMS

Coil Embolization and Stent-Assisted Coil Embolization for Intracranial Aneurysms

There are currently no randomized clinical trials (RCTs) or published guidelines to support a specific therapeutic regimen or duration of therapy following endovascular treatment of either ruptured or unruptured aneurysms treated with stent-assisted embolization.[1] Because of the risk of thrombosis associated with stent placement, antiplatelet therapy has played an essential role in preventing complications associated with stent-assisted coiling of intracranial arteries. Aspirin (81 or 325 mg) and clopidogrel (75 mg) are commonly used following stent placement but optimal duration of therapy is unknown.

In the setting of unruptured aneurysms treated electively, a retrospective study by Choi and colleagues[2] found that pretreatment with low-dose prasugrel had better efficacy in comparison with clopidogrel for prevention of thrombotic complications without a significant difference in the rate of hemorrhagic events. Patients in the prasugrel group had significantly lower P2Y12 reaction unit (PRU) values and a higher percentage of platelet inhibition. Another retrospective review found 5% increased risk of ischemic events following discontinuation of clopidogrel after 6 weeks.[3] Despite these findings, RCT are necessary to

Disclosure Statement: The authors have nothing to disclose.
Department of Neurological Surgery, Ohio State University Medical Center, N-1014 Doan Hall, 410 West 10th Avenue, Columbus, OH 43210, USA
* Corresponding author.
E-mail address: shahid.nimjee@osumc.edu

Neurosurg Clin N Am 29 (2018) 517–527
https://doi.org/10.1016/j.nec.2018.06.004

determine whether prasugrel provides true benefit over clopidogrel, and ideal duration of therapy remains to be determined.

Antiplatelet therapy may reduce the risk of thromboembolism when administered before or during stent-assisted endovascular treatment of ruptured intracranial aneurysms. A meta-analysis performed by Ryu and colleagues[4] found a greater risk of thromboembolism in patients with ruptured aneurysms compared with unruptured aneurysms when antiplatelet therapy was not administered until after completion of the procedure. There was no increased risk of thrombosis for patients who received either a preprocedural loading dose of aspirin and clopidogrel or modified therapy with glycoprotein (GP) IIb/IIIa inhibitors after stent deployment. It is worth noting that among patients undergoing percutaneous coronary interventions, the addition of short-term intravenous infusion of GP IIb/IIIa antagonists reduced the risk of early arterial or stent thrombosis in large RCTs.[5] This benefit was evident for at least the first month, but more recent evidence suggests that it may persist for at least 6 months.[6–9] In light of these findings, in addition to the review performed by Dornbos and colleagues, it may be beneficial to incorporate the use of GP IIb/IIIa inhibitors when endovascular intervention is indicated for treatment of intracranial aneurysms.

Pipeline Flow Diversion

In 2011, the pipeline embolization device (PED; ev3, Plymouth, MA) was approved for treatment of intracranial aneurysms. Initially, flow diversion with PED gained favor in treatment of aneurysms with morphology unfavorable to current open neurosurgical and endovascular embolization techniques.[10] Specifically, it initially provided an effective alternative approach for large, giant, and nonsaccular aneurysms.[10,11] Now, the role of PED in neurointerventions has expanded to include small, fusiform, and saccular aneurysms. Although an effective treatment, flow diversion stent treatment of aneurysms has been associated with a widely variable risk of thromboembolic (0%–14%) and hemorrhagic (0%–11%) complications.[12] Because of the risk of thrombosis, antiplatelet therapy is essential and a wide variety of treatment strategies have been used without clear evidence of an ideal treatment regimen (**Table 1**).[13] The most common post-PED treatment involved aspirin for at least 6 months in addition to clopidogrel for 3 to 12 months (93% of 1180 patients) with longer duration after PED procedures in the posterior circulation (see **Table 1**).[13] Despite use of dual antiplatelet therapy (DAPT) before and following the procedure, there remains a significant risk of thromboembolic complications (TEC) related to variable therapeutic responses to the standard regimen.[14,15]

Routine assessment of preoperative platelet function test (PFT) is not consistently performed at every center, yet multiple studies have shown potential benefit before treatment with PED.[12,14,16–19] Current methods for this purpose included VerifyNow to obtain PRU with or without aspirin reaction units, light transmission aggregometry to assess aspirin and ADP inhibition percentiles, and/or multiplate platelet-aggregation test to measure aggregation units.[13] Although one systematic review did not find a statistically significant difference in TEC related to PFT, there was a trend toward increased risk of TEC in patients who received no form of PFT.[13] Specifically, one study found an increased risk of thrombotic and hemorrhagic complications associated with PRU greater than 240 or less than 60, respectively, and recommended that target PRU values before PED placement should lie between 60 and 240 and ideally between 70 and 150.[14] Given the lack of formal guidelines, we recommend the routine use of PFT before treatment with PED.

The potential need for PFT is in part caused by the risk for insufficient response to clopidogrel,

Table 1
Preprocedural antiplatelet regimen

Percentage of Patients	Number of Patients	Aspirin Dose (mg)	Aspirin Duration (d)	Clopidogrel Dose (mg)	Clopidogrel Duration (d)
61.7	803	300–325	2–14	75	3 to >10
21.7	351	81	5–10	75	5–10
6.3	82	100–150	5	75	5

Percentage of patients reflects percentage of 1300 patients identified in systematic review whose intracranial aneurysms were treated by PED.

Data from Texakalidis P, Bekelis K, Atallah E, et al. Flow diversion with the pipeline embolization device for patients with intracranial aneurysms and antiplatelet therapy: a systematic literature review. Clin Neurol Neurosurg 2017;161:78–87.