

Safety of Preprocedural Antiplatelet Medication in Coil Embolization of Ruptured Cerebral Aneurysms at the Acute Stage

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Summary

Preoperative antiplatelet medication for aneurysm coil embolization during acute subarachnoid hemorrhage (SAH) is not common. However, recent advances in neurointerventional devices make antiplatelet medication necessary for SAH surgery. We tested the hypothesis that preprocedural antiplatelet therapy in the acute stage of SAH prevents complications due to ischemia or induced bleeding.

We retrospectively reviewed 35 consecutive ruptured cerebral saccular aneurysms that underwent coiling at our institute. Two hundred milligrams of aspirin and 150 mg of clopidogrel were administered to the patients at least two hours before coiling. Systemic heparinization was given after sheath insertion. Procedure-related thrombus formation on digital subtraction angiography, and clinical evidence of ischemia and procedure-related stroke on CT were reviewed.

The median patient age was 69 years. Five males and 30 females were included. Seventy-seven percent of patients were Hunt-Hess grades 1 to 3. Assist techniques were used in 20 cases (57%). We inserted one extracranial internal carotid artery stent, but no intracranial stent. Intraoperative thrombosis occurred in one case (2.9%), with no clinical symptoms. Postoperative cerebrospinal fluid drainage was done in three cases, but we experienced no bleeding complications.

Preoperative antiplatelet therapy leads to a low rate of thromboembolic events in coiling during acute stage SAH, and this strategy had no adverse influence on bleeding complications.

Introduction

Ischemic complication is a major problem in coil embolization of cerebral aneurysms¹⁻³. In coil embolization of unruptured cerebral aneurysms, preoperative treatment with antiplatelet medicines and intraoperative systemic heparinization are commonly applied⁴⁻⁶. Even though intraprocedural thrombi that require additional treatment occur in 5-11% of ruptured cerebral aneurysm coilings, anticoagulation and antiplatelets for coil embolization of ruptured cerebral aneurysm in the acute stage remain controversial^{1,4,5}. Based on the International Subarachnoid Aneurysm Trial (ISAT) subanalysis, only 8% of ISAT participant centers used antiplatelets during coiling, and 47% of centers never used antiplatelets during coiling⁷. During the acute stage of subarachnoid hemorrhage, however, hypercoagulopathy and hyperfibrinolysis occurred in plasma⁸⁻¹⁰.

Recently, a vascular reconstruction device for coil embolization and a flow-diverting device were used in the acute stage of subarachnoid hemorrhage (SAH) in combination with antiplatelet medicines. A covered stent has also been used for large or giant intracranial an-

eurysms, in combination with antiplatelet medicines¹¹⁻¹⁴. The application of antiplatelet medicines preoperatively is not considered minor therapy for ruptured cerebral aneurysms. Golshani et al. reported that preprocedural administration of 300 mg clopidogrel reduced thromboembolic complications in stent-assisted coil embolization of ruptured cerebral aneurysms without increasing intracerebral hemorrhage¹⁵.

The aim of this study was to determine whether the application of precoiling antiplatelet treatment prevents ischemic complications and is not associated with bleeding complications.

Material and Methods

This study was approved by the Hirosaki University Ethics Committee, with written informed consent provided by patients and/or families.

We reviewed 35 consecutive ruptured cerebral saccular aneurysms that had coiling performed at our institute from January 2007 through January 2012. All patients were treated within 72 hours after aneurysm rupture. We excluded dissecting aneurysms and cases of parent artery occlusion. Aneurysmal neck clipping is first-line therapy at our institute; coiling cases are thus associated with specific medical problems (e.g. lung edema, advanced age, posterior circulation).

More than two hours before the coil embolization, 200 mg of aspirin and 150 mg of clopidogrel were administered to patients preoperatively via a transoral or a trans-nasogastric tube. From the day after the coiling we administered 100 mg of aspirin per day up to 30 days after the onset of SAH.

Systemic heparinization was done during the operation, keeping activated clotting time at about twice the preoperative value.

The definition of clotting was based on the absence of contrast medium during angiography, and a periprocedural ischemic event was defined by the onset of clinical symptoms, except for symptomatic vasospasm, with the use of CT limited to ruling out intracerebral hemorrhage as the cause of symptoms. Not all cases were available for MRI study due to medical conditions; procedure-related ischemic lesion was determined by CT taken the day after coiling.

All events were diagnosed and the Glasgow Outcome Scale was evaluated 30 days after SAH by blind co-authors NM and MN, and a consensus meeting was held.

Results

Five male and 30 female patients were included (Table 1). Median age of patients was 69 years (IQR: 57-79, range 42-94). Seventy-seven percent of patients were Hunt-Hess grades 1 to 3 (Table 2). Posterior circulation aneurysms amounted to forty percent.

Assist techniques were done in 20 cases (57%); 11 balloon assist cases, six triple coaxial catheter cases, two double catheter cases, one long sheath case (Tables 1 and 2). We performed one extracranial internal carotid artery stenting as a rescue mechanical dissection, due to the guiding catheter. In this case alone, an additional 150 mg of clopidogrel were administered (Table 1). Asymptomatic branch occlusion with thrombus occurred in one case (2.9%), but this thrombus disappeared within a few minutes and no new ischemic lesion appeared (Table 1).

Postoperative cerebral ventricle drainage was done in two cases and lumbar drainage in one case (Table 1). Postoperative complications occurred in five cases (14% of patients): coil migration, cerebral infarction due to chronic internal carotid artery occlusion, vasospasm, brainstem edema and cardiogenic cerebral embolism (Table 1). No bleeding complications arose. Seventy-seven percent of patients achieved a good recovery or moderate disability on the Glasgow Outcome Scale.

Discussion

This report reveals for the first time that preoperative dual antiplatelet therapy did not increase bleeding complications in the coiling of ruptured cerebral aneurysms, while the incidence of thromboembolic complications was relatively low compared to recent reports^{1,3-5}.

Aspirin and Clopidogrel doses of 200 mg and 150 mg, respectively, are lower than commonly used loading doses at many institutes. We administered those medicines at least two hours before coiling. Two hundred milligrams of aspirin inhibit the platelet aggregation response within two hours^{16,17}. The dose of clopidogrel

Table 1 Analyzed cases.

| Age/ Gender | HH | Aneurysm Location | Size (mm) | Neck (mm) | Assist technique | Intraoperative event | CSF drainage | Postoperative complication | GOS @ 30 days |
|----------------|----|----------------------|------------------|--------------|---------------------|---------------------------|-----------------|--|---------------------|
| 42/F | 2 | PC | 4.3 × 3.2 × 2.5 | 3 | Balloon | No | No | Coil migration from another aneurysm | MD |
| 49/F | 3 | VA | 4 × 3 × 2.7 | 2 | Balloon | No | No | No | GR |
| 51/F | 2 | BA | 4.5 × 2.4 × 2.3 | 2.3 | No | No | No | No | GR |
| 73/F | 3 | Acom | 5.2 × 3.4 × 3 | 3 | No | No | No | No | MD |
| 75/M | 3 | Acom | 5 × 4.2 × 4 | 3 | No | No | No | Cerebral infarction due to chronic IC occlusion | SD |
| 77/F | 3 | IC | 8.7 × 7.3 × 5.3 | 5.4 | Balloon | No | No | No | SD |
| 79/F | 3 | IC | 22 × 19 × 19 | 10 | Double catheter | No | No | Vasospasm | SD |
| 79/F | 4 | IC | 5.5 × 4.1 × 5.3 | 4 | Balloon | No | No | No | MD |
| 43/F | 4 | Acom | 7.6 × 7.2 × 5 | 4 | No | No | No | No | VS |
| 48/F | 3 | VA | 7.1 × 5.2 × 5 | 4 | Balloon | Aneurysm perforation | Yes (CVD) | No | MD |
| 56/F | 3 | Acom | 4.6 × 3.1 × 3 | 1.5 | No | No | No | No | GR |
| 57/F | 4 | IC | 9.6 × 3.9 × 3.8 | 2.5 | Balloon | No | No | No | GR |
| 57/F | 1 | MC | 6.9 × 5.9 × 5.9 | 2.7 | No | No | No | No | GR |
| 57/M | 2 | IC | 6.2 × 5.8 × 4.3 | 4 | Balloon | No | No | No | GR |
| 58/M | 2 | Acom | 8.7 × 7.1 × 5.5 | 4 | No | No | Yes (CVD) | No | GR |
| 61/F | 2 | Acom | 6.2 × 3.9 × 3.7 | 3 | No | No | No | No | GR |
| 62/F | 3 | BA | 6.1 × 5.5 × 5.1 | 4 | No | No | No | No | GR |
| 64/F | 4 | BA | 14.5 × 13.7 × 13 | 10 | Support catheter | Branch occlusion | No | No | SD |
| 64/F | 2 | VA | 16 × 12 × 12 | 8 | Balloon | No | No | Brainstem edema | MD |
| 67/F | 4 | IC | 15 × 12 × 11 | 7 | Balloon | No | No | No | GR |
| 68/F | 3 | Acom | 6.8 × 5 × 5 | 4 | No | No | No | No | GR |
| 68/F | 1 | BA | 5.8 × 3.3 × 3 | 3 | No | No | No | No | GR |
| 69/F | 2 | VA | 5.1 × 3.4 × 3.2 | 2 | Long sheath | No | No | No | GR |
| 70/M | 3 | BA | 7 × 6 × 5.7 | 5 | Balloon | No | No | Cardiogenic cerebral embolism | MD |
| 75/M | 3 | BA | 4 × 3 × 2.7 | 2.7 | No | No | No | No | GR |
| 79/F | 2 | IC | 5 × 4.8 × 4.5 | 4 | Balloon | No | No | No | MD |
| 79/F | 3 | IC | 10 × 6.4 × 5 | 5 | Support catheter | No | No | No | GR |
| 80/F | 2 | BA | 14.5 × 13 × 14 | 11 | Double catheter | No | Yes (LD) | No | MD |
| 82/F | 5 | IC | 4.1 × 4 × 3.7 | 3 | No | No | No | No | MD |
| 83/F | 4 | PICA | 4.6 × 3.5 × 3.4 | 2 | Support catheter | No | No | No | SD |
| 84/F | 3 | IC | 16 × 12 × 10 | 9 | No | Cervical IC dissection | No | No | MD |
| 87/F | 2 | IC | 9.8 × 6 × 5.9 | 4 | Support catheter | No | No | No | SD |
| 89/F | 4 | Acom | 7.7 × 5.7 × 5.7 | 3.5 | Support catheter | No | No | No | SD |
| 94/F | 2 | IC | 8.2 × 7.2 × 7.2 | 4 | No | No | No | No | GR |
| 94/F | 3 | BA | 5.1 × 5 × 4.9 | 4.1 | Support catheter | No | No | No | MD |

Acom: anterior communicating artery, BA: basilar artery, CSF: cerebrospinal fluid, CVD: cerebral ventricle drainage, GOS: Glasgow Outcome Scale, GR: good recovery, HH: Hunt-Hess grade, IC: internal carotid artery, LD: lumbar drainage, MC: middle cerebral artery, MD: moderately disabled, PC: posterior cerebral artery, PICA: posterior inferior cerebellar artery, SD: severely disabled, VA: vertebral artery, VS: vegetative survival.

Table 2 Summary of analyzed cases.

| | |
|--|-----------------------|
| Number of cases (Male / Female) | 35 (5 / 30) |
| Median age (IQR, Range) | 69 (57 - 79, 42 - 94) |
| Hunt-Hess grade (1 : 2 : 3 : 4 : 5) | 2 : 11 : 14 : 7 : 1 |
| Assist technique (No: Balloon : Triple coaxial catheter : Double catheter : Long sheath) | 15 : 11 : 6 : 2 : 1 |
| Intraoperative event* (No: Thrombosis : Perforation : Dissection : Coil migration) | 32 : 2 : 1 : 1 : 0 |
| Intraoperative thrombosis (No : Yes) | 34 : 1 |
| CSF drainage (No : Yes) | 32 : 3 |
| Bleeding complications (No : Yes) | 35 : 0 |
| Glasgow Outcome Scale at 30 days (GR : MD : SD : VS : D) | 16 : 11 : 7 : 1 : 0 |
| <p>*: One case had two complications. CSF: cerebrospinal drainage GR: good recovery, MD: moderately disabled, SD: severely disabled, VS: vegetative survival, D: dead.</p> | |

used is half that previously reported and is adequate to prevent thrombus formation with dual antiplatelet and systemic heparinization. Preprocedural administration of 300 mg clopidogrel reduced thromboembolic complication in stent-assisted coil embolization of ruptured cerebral aneurysms without increasing intracerebral hemorrhage, but after stent deployment integrin inhibitor and 600 mg clopidogrel could not prevent thromboembolic complications in 16% cases^{15,18}. An impairment of antiplatelet-aggregating activity has been known to occur in the acute stage of SAH¹⁹. However, in cases of unruptured aneurysms, the response to preinterventional clopidogrel exhibited great variability and the rate of thromboembolic adverse events related to platelet reactivity was wide-ranging²⁰. During acute stage SAH, the instability of the platelet response and an altered coagulation response make estimates of coagulate function difficult. Thus, prophylactic antiplatelet therapy before coiling in acute stage SAH is effective in the prevention of thromboembolic events.

After deployment of the first coil, intravenous administration of acetylsalicylic acid reduced the rate of thromboembolic events in coil embolization of ruptured and unruptured cerebral aneurysms²¹. Moreover, systemic application of glycoprotein IIb/IIIa antagonist resolved intraprocedural thrombus formation during coil placement in SAH¹. Application of antiplatelets during acute stage SAH is seldom done at present. But Meckel et al. reported antiplatelet and

anticoagulation management for stent-assisted coiling of ruptured cerebral aneurysm in the acute stage, and no thromboembolic complication occurred¹³. Development of useful new devices for intervention can change treatment strategies in terms of devices used conventionally and medications. Application of antiplatelet medicines preoperatively will represent most cases of treatment of complicated aneurysms.

A prospective, randomized study with a large number of patients could therefore lead to the detection of improvement in clinical outcome resulting from antiplatelet therapy prior to coiling.

Conclusion

We report for the first time that preoperative antiplatelet therapy did not influence adverse bleeding complications during and after coiling for acute stage SAH. The incidence of thromboembolic complications was relatively low.

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