Peri-operative Dual Antiplatelet Therapy for the Coil Embolization of Unruptured Brain Aneurysms: The efficacy and the side effect

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Background and purpose

- Optimal dose and duration of antiplatelet therapy before / after the coil embolization of unruptured aneurysm has not been established, yet.
- The dual antiplatelet therapy (DAPT) using aspirin and clopidogrel started 3 to 7 days before operation has been a commonly used antiplatelet protocol, although few studies have done to evaluate the relationship between the duration of the pre-operative DAPT and its efficacy / side effects.
- In the present study, the different durations of the pre-operative DAPT and their related “efficacy / side effect” was retrospectively analyzed.

Methods

- This retrospective study included unruptured brain aneurysm patients who underwent coil embolization with general anesthesia between September 2014 and July 2017 at our hospital.
- Dual antiplatelet agents (aspirin 100mg daily and clopidogrel 75mg daily) were prescribed prior to surgery to some extent according to the facility standards as follows;
Three days prior ; September 2014 – June 2015
Seven days prior ; July 2015 – July 2017

- Patients were eligible if the platelet aggregation profiles were evaluated on the day of procedure.
- The patients were categorized into 3 different groups depending on the duration of the DAPT:
Group A (within 3days), Group B (4-6 days) and Group C (7 days or longer).
- We performed Kruskal Wallis analysis to compare the maximum aggregation rate between the 3 groups. Relationship between the duration of the DAPT and 1) the maximum aggregationrate, 2) the rate of symptomatic / asymptomatic stroke, 3) rate of hemorrhagic event were evaluated.

Results

- A total of 380 unruptured brain aneurysm patients (female, n=283 (74%); median age, 61 y) were included in the present study. (Table 1)
- Diffusion weighted image performed the day after the operation showed that 272 (72%) patients had high intensity lesion (any high intensity lesion), and 13 (3.4%) represented symptomatic infarction.
- The both adenosine diphosphate (ADP) and collagen aggregation rate were significantly decreased according to the longer DAPT period. (Figure 2)
- The symptomatic infarction after operation tended to decrease with longer DAPT period (Figure 3). Compared to the group A, the risk ratio for symptomatic infarction was 0.64 in group B, and 0.46 in group C.
- Hemorrhagic event in each group were as follows. In group A, aneurysm rupture during procedure;1. In group B, bleeding of puncture site; 9, aneurysm rupture during procedure; 1. In group C, bleeding of puncture site; 17, aneurysm rupture during procedure; 1, intracerebral hemorrhage; 1, retroperitoneal hematoma; 1.

	total (n=380)	Group A (n=90)	Group B (n=55)	Group C (n=235)
Female sex	283 (74)	66 (73)	44 (80)	173 (74)
Age, years	61 (51-69)	61 (50-70)	61 (47-68)	61 (52-69)
Backgrounds				
Hypertension	160 (42)	38 (42)	20 (36)	102 (43)
Dyslipidemia	53 (14)	16 (18)	8 (15)	29 (12)
Diabetes mellitus	22 (6)	4 (4)	4 (7)	14 (6)
Ischemic heart disease	10 (3)	2 (2)	1 (2)	7 (3)
Old cerebral infarction	11 (3)	3 (3)	1 (2)	7 (3)
Chronic kidney injury	13 (3)	7 (8)	2 (4)	4 (2)
Laboratory data				
ADP aggregation, %	50 (42-56)	54 (50-59)	52 (45-59)	47 (41-54)
Collagen aggregation, %	44 (35-53)	51 (43-57)	45 (33-56)	41 (33-49)
Aneurysm distribution				
Anterior circulation	326 (86)	80 (89)	51 (57)	195 (83)
Maximum diameter, mm	5.6 (4.8-7.7)	6.0 (4.7-8.1)	5.5 (5.1-6.5)	5.6 (4.8-7.9)
Neck diameter, mm	4.6 (3.6-6.0)	4.6 (3.2-6.0)	4.0 (3.5-5.1)	4.7 (3.7-6.1)
Operation				
Number of coils	8 (6-12)	8 (5-12)	7 (6-9)	8 (6-12)
Amount of contrast, mL	200 (170-250)	200 (159-240)	200 (165-220)	210 (170-253)
Operation time, min	235 (205-261)	240 (210-280)	230 (208-248)	235 (205-265)
Volume embolization ratio, %	25.4 (22.1-28.5)	23.3 (20.6-27.0)	26.5 (22.5-29.8)	26.2 (22.8-28.5)
Adjunctive technique				
Double catheter technique	232 (61)	54 (60)	33 (60)	145 (62)
Balloon assist technique	64 (17)	21 (23)	10 (18)	33 (14)
Stent assist technique	90 (24)	12 (13)	12 (22)	66 (28)

Table 1. Characteristics of the patients

Data are presented as n (%) and median (interquartile range).
Duration of DAPT; Group A: ≤3days, Group B; 4-6 days, Group C: ≥7 days.
Abbreviations: ADP, adenosine diphosphate.

Figure 1. Platelet aggregometer (absorbance method) and its results.

Aggregation-inducing substances (ADP, collagen) are added to plasma, and record changes of absorbance. Maximum aggregation rate within 7 minutes is evaluated. ADP is associated to clopidogrel, and the value of maximum aggregation rate ≤46% is considered to be effective. Collagen is associated to aspirin, and the value of maximum aggregation rate ≤64% is considered to be effective.

Figure 2. Maximum aggregation rate by oral administration period of DAPT. The longer oral administration period becomes, the lower maximum aggregation rate becomes in both aspirin (collagen) and clopidogrel (ADP).

Figure 3. Proportion of patients with symptomatic infarction by oral administration period. The incidence of symptomatic infarction inclined to become lower when the oral administration period becomes longer.

Discussion

- The risk of postoperative thromboembolic complications were evaluated with different DAPT periods. The results of study indicated the possibility of reducing the risk of thromboembolic complications by initiating the DAPT at least 7 days prior to surgery.
- In previous studies, the period of DAPT, and the types or amounts of agent used varied ^(1,2,3).
- Since the occurrence rate of complications are relatively small, further investigation with increased number of patient with more statistical power is required.

Conclusion

Longer DAPT period significantly reduced both the ADP and collagen aggregation.
The rate of symptomatic thromboembolic event tended to decrease with longer DAPT period.