Acute Subdural Hematoma in Patients With Medication Associated With Risk of Hemorrhage

Hirofumi OYAMA,1 Akira KITO,1 Hideki MAKI,1 Kenichi HATTORI,1 Tomoyuki NODA,1 and Kentaro WADA1

1Department of Neurosurgery, Ogaki Municipal Hospital, Ogaki, Gifu

Abstract

The characteristics of 90 cases of acute subdural hematoma were analyzed in 25 patients taking medication related to bleeding tendency, the bleeding tendency group, and 65 patients without such medication, the control group. Acute subdural hematoma was significantly associated with over-turning or without accident in the bleeding tendency group (92%) compared with the control group (56.9%). The time from trauma to admission was significantly longer in the bleeding tendency group (32.7 hours) compared with the control group (9.7 hours). The mean Glasgow Coma Scale score on admission was 13.0 points in the bleeding tendency group and was significantly better than 10.9 points in the control group. The international normalized ratio of prothrombin time on admission was 3.59 in the patients treated with warfarin. All patients taking warfarin received reversal agents and this value decreased significantly to 1.38. In the bleeding tendency group, hematoma size increased in 20% after the operation, almost the same as in the control group (25%). Although good recovery tended to be observed less frequently in the bleeding tendency group than in the control group, the mean age of the bleeding tendency group was significantly higher than that of the control group, so the prognosis might be affected by this age-related factor. Cautious diagnosis, follow-up imaging, and strict management are mandatory in patients with bleeding tendency.

Key words: acute subdural hematoma, warfarin, antiplatelet drug, factor IX complex, fresh frozen plasma

Introduction

Patients receiving anticoagulant and anti-aggrega-
tion therapy are at risk for acute subdural hemato-
ma.4,6) Patients who develop acute subdural hemato-
ma frequently have different clinical courses and
worse outcome than unaffected patients.3) This
study reviewed 90 cases of acute subdural hemato-
ma, including 25 cases with previous medication
related to bleeding tendency, and discusses the clin-
ical course, treatment, and outcome.

Patients and Methods

This study analyzed 90 patients with acute subdural
hematoma, 52 males and 38 females aged 7 months
to 90 years (mean 69.4 years), hospitalized in the
acute phase over the past 5 years. This study includ-
ed patients with hematoma in the subdural space of
convexity, interhemisphere, and tentorial surface,
and excluded patients with acute hemorrhage in the
cavity of chronic subdural hematoma. Soon after ad-
mission, all patients taking warfarin received revers-
al agents [human factor IX complex, fresh frozen
plasma, and vitamin K [menatetrenone]] in an at-
tempt to reverse coagulopathy. Platelets were ad-
ministered only to patients taking antiplatelet ther-
apy who required surgery.

Twenty-five patients had previously taken medica-
tion related to the bleeding tendency and formed the
bleeding tendency group (Table 1). The medication
potentially associated with hemorrhage included
warfarin with/without antiplatelet medication in 17
patients, one or two types of antiplatelet medication
in 8 patients (5 treated with one antiplatelet drug
and 3 with two antiplatelet drugs). Sixty-five patients
had not taken medication potentially associated
with hemorrhage, and formed the control group.

Results

The mean age of the bleeding tendency group was
significantly higher than that of the control group (Table 1). The international normalized ratio of prothrombin time (PT-INR) on admission was 3.59 ± 3.47 (mean ± standard deviation) in the 17 patients treated with warfarin, 1.24 ± 0.62 in the 8 patients treated with antiplatelet drugs, and 1.06 ± 0.14 in the control group, so was significantly higher in the patients treated with warfarin compared to the control group (Mann-Whitney’s U test, p < 0.001). After the patients treated with warfarin had received reversal agents such as human factor IX complex, fresh frozen plasma, and/or vitamin K, the PT-INR decreased significantly to 1.38 ± 0.43 (paired t-test, p = 0.017).

The trauma was caused by over-turning in 46 patients, falling in 12, traffic accident in 16, beating in 1, shaking in 1, and no accident in 14. If the cause of the trauma was not identified, the patients were classified as no accident. The incidence of over-turning or no accident in the bleeding tendency group was significantly higher than that in the control group (Table 1). The time from trauma to admission was significantly longer, and the mean Glasgow Coma Scale score on admission was significantly better in the bleeding tendency group than in the control group.

The hematoma size increased in 2 of 65 patients (3.1%) in the control group before operation. In the bleeding tendency group, the hematoma increased in 3 of 25 patients (12%), so was rather more common compared with the control group (no significance). Surgery was performed in 5 patients of the bleeding tendency group, and in 12 patients of the control group. Surgery was contraindicated by non-evacuated mass lesion and diffuse injury II in the computed tomography classification of the Traumatic Coma Data Bank. The hematoma size increased in 3 of 12 patients (25%) in the control group after the operation. The hematoma size increased in 1 of 5 patients (20%) in the with bleeding tendency
group, almost the same compared with the control group. The Glasgow Outcome Scale score showed no difference between the bleeding tendency group and the control group (Table 2) (Mann-Whitney’s U test, \( p = 0.257 \)). However, good recovery tended to be observed less frequently in the bleeding tendency group (0%) than in the control group (10.8%).

**Table 2 Glasgow Outcome Scale scores in the bleeding tendency group and the control group**

<table>
<thead>
<tr>
<th>Glasgow Outcome Scale</th>
<th>Bleeding tendency group (n = 25)</th>
<th>Control group (n = 65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good recovery</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Moderate disability</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>Severe disability</td>
<td>12</td>
<td>25</td>
</tr>
<tr>
<td>Vegetative state</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Dead</td>
<td>6</td>
<td>14</td>
</tr>
</tbody>
</table>

Glasgow Outcome Scale scores showed no difference between the bleeding tendency group and the control group (Mann-Whitney’s U test, \( p = 0.257 \)). However, good recovery tended to be observed less frequently in the bleeding tendency group (0%) than in the control group (10.8%).

**Discussion**

Many cases of warfarin-related acute subdural hematoma have been reported. The PT-INR is related to the risk of the major hemorrhagic complications in the whole body. Major hemorrhagic complications often occur in patients with normal values (PT-INR 2.2 to 3.5) and the frequency (6.6% per year) is significantly higher than that in patients with low values (PT-INR 1.5 to 2.1; 0% per year).\(^{13} \) Major hemorrhage occurs in 4.4% of patients with an PT-INR of 2.30–3.56.\(^{13} \) The hemorrhagic tendency does seem to increase with addition of antiplatelet drugs. Hemorrhagic complication occurs in 6.2% of patients who receive aspirin and warfarin.\(^{5} \) Major bleeding complications occur with aspirin and warfarin in 6.9% of patients with PT-INR of 2.5 to 3.\(^{10} \) The PT-INR was quite high (mean 3.59) in the warfarin-treated cases of the present series. Therefore, careful adjustment of the dosage is important to maintain PT-INR in the range of 1.5 to 2.1 in patients treated with warfarin.

Patients treated with 2 types of anti-platelet drugs are very susceptible to hemorrhagic complications.\(^{3} \) The CURE study found no significant difference in major bleeding between the groups with clopidogrel or placebo (placebo 2.4%, clopidogrel 2.7%).\(^{7} \) However, hemorrhagic complications increased with administration of two antiplatelet drugs. Hemorrhagic complications occurred in 1.8% of the patients who received only aspirin, but in 5.5% of the patients who received aspirin and ticlopidine.\(^{5} \) The present study found that 62.5% of the patients had been treated with one antiplatelet drug and 37.5% of the patients had been treated with two antiplatelet drugs. Two types of antiplatelet drugs prevent ischemic attacks more effectively, but the risk of the hemorrhage must be considered.

Acute subdural hematoma can occur without trauma or after minor trauma in patients taking anticoagulant or anti-aggregation agents. One study found anticoagulation-related acute subdural hematoma occurred in 25% of patients without trauma, 37.5% with minor trauma without loss of consciousness, 16.7% with cerebral concussion, and 16.7% with cerebral contusion.\(^{5} \) The present study found that acute subdural hematoma without an accident or with over-turning occurred at a significantly higher rate among the bleeding tendency group (92%) compared with the control group (56.9%). Therefore, head CT should be performed proactively to check for intracranial hemorrhage even after minor head injury.

The initial symptom in ordinary cases of acute subdural hematoma was rapidly progressive disruption of consciousness.\(^{11} \) However, progression was slow in patients who received anticoagulant or anti-aggregation therapy. One study found that these patients deteriorated due to delayed acute subdural hematoma from 9 hours to 3 days after traumatic brain injury.\(^{3} \) Similarly, the time from trauma to admission was significantly longer in the bleeding tendency group (mean 32.7 hours) compared with control group (mean 9.7 hours) in the present series. Therefore, cautious follow up using head CT is recommended in patients who received anticoagulant or anti-aggregation therapy. The symptoms are relatively mild at onset in these patients.\(^{3,6} \) The Glasgow Coma Scale score on admission was 2.1 points better in the bleeding tendency group compared with control group in the present series.

Intracranial hematoma often rebleeds following evacuation, leading to a fatal outcome inpatients taking anticoagulant or anti-aggregation agents, so strict management of the general condition is important.\(^{4} \) Patients taking warfarin should receive reversal agents in an attempt to reverse coagulopathy soon after admission. Platelets should also be administered to patients taking antiplatelet agents. The conventional treatment with fresh frozen plasma and vitamin K often fails to achieve the desired correction of coagulopathy in urgent neurosurgical settings.\(^{2,9,11} \) Recombinant coagulation factor VIIa or human factor IX complex concent-
treat provide rapid correction of coagulation to a level that allows safe neurosurgical intervention without significant delay. In the present series, patients taking warfarin received reversal agents such as human factor IX complex concentrate, fresh frozen plasma, and/or vitamin K.

Oral anticoagulant and anti-aggregation therapy does not increase the risk of postoperative hematoma reaccumulation if the patients receive reversal agents or platelets transfusion. In the present series, preoperative enlargement of the hematoma occurred more frequently in the bleeding tendency group (12%) compared with the control group (3.1%). However, postoperative enlargement of the hematoma happened almost at the same rate in these two groups (20% in the bleeding tendency group, 25% in the control group). The PT-INR value suitable for surgery was reported to be less than 1.25–1.4 in patients receiving anticoagulant therapy. In the present patients treated with warfarin, the PT-INR decreased to 1.38 after receiving reversal agents such as human factor IX complex, fresh frozen plasma, and/or vitamin K.

The present study found no difference in outcome between the bleeding tendency group and the control group. Good recovery tended to be observed less frequently in the bleeding tendency group than in the control group, but the mean age of the bleeding tendency group was significantly higher than that of the control group, so the results might be affected by this age-related factor.

References

Address reprint requests to: Hirofumi Oyama, MD, Department of Neurosurgery, Ogaki Municipal Hospital, 4–86 Minaminokawa–cho, Ogaki, Gifu 503–8502, Japan. e-mail: oya3776@arrow.ocn.ne.jp

Neurol Med Chir (Tokyo) 51, December, 2011