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Influence of antiplatelet therapy on postoperative recurrence of chronic subdural hematoma: A multicenter retrospective study in 719 patients

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ABSTRACT

Objective: The present study tested the hypothesis of whether antiplatelet agents (APA) induce chronic subdural hematoma (CSDH) recurrence via a platelet aggregation inhibitory effect.
Method: We examined risk factors for CSDH recurrence, focusing on APA, in 719 consecutive patients who admitted to three tertiary hospitals and underwent burr-hole craniostomy and irrigation for CSDH. This was a multicenter, retrospective, observational study.
Results: Age, sex, history of diabetes mellitus, hypertension, chronic renal failure, alcohol consumption habits, consciousness disturbance on admission, or preoperative CT density was not associated with recurrence. Subdural drainage was significantly associated with less recurrence. Preoperative oral APA administration was significantly associated with more recurrence. The recurrence rate of CSDH in non-APA group was 11% if surgery was performed on admission. However, if surgery was performed immediately after discontinuation of oral APA administration, the recurrence rate in APA group significantly increased to 32% (p value < 0.0001; odds ratio, 3.77; 95% confidence interval, 1.72–8.28). The effect of APA on CSDH recurrence gradually diminished as the number of days until initial surgery, after stopping APA, increased.
Conclusion: Antiplatelet therapy significantly influences the recurrence of CSDH.

1. Introduction

Chronic subdural hematoma (CSDH) is routinely encountered by neurosurgeons. There are many different treatment methods ranging from conservative management with oral steroids, twist drill craniostomy [1], craniostomy with or without a closed drainage system, and craniotomy with extensive membranectomy. We have been applying burr-hole craniostomy and irrigation with or without closed-system subdural drainage as the primary treatment method based on our past experience. We occasionally manage cases requiring re-operation for CSDH recurrence within a month after the initial surgery.

Risk factors for CSDH recurrence have been examined in several prior reports. However, few statistically significant risk factors have been identified [2–11]. Preoperative oral warfarin administration [2–14] and postoperative drainage [15] have already been suggested to significantly influence recurrence. To the best of our knowledge, however, except for the report by Rust et al. [14], antiplatelet agents (APA) have consistently been shown to have no impact on CSDH recurrence [16–18]. Intuitively, it seems that preoperative antiplatelet therapy would affect recurrence, though the evidence remains inconclusive. Thus, we conducted this study to examine whether APA show associations with CSDH recurrence.

While a protocol allowing the effects of warfarin to temporarily be reversed has been established, it is not possible to reverse the inhibitory effects of APA, underscoring the importance of managing risks associated with these drugs.

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We herein report risk factors for CSDH recurrence, focusing mainly on APA.

2. Materials and methods

2.1. Study design

We conducted a retrospective observational study using data from 719 consecutive patients admitted to 3 tertiary hospitals, Sanmu Medical Center (168 patients), Kimitsu Chuo Hospital (347), and Chiba Cardiovascular Center (204) in Japan, between January 1, 1996 and February 1, 2006 and who underwent burr-hole craniostomy and irrigation with or without drainage for CSDH.

In general, burr-hole craniostomy and irrigation with or without drainage is the first choice for surgery for CSDH in above mentioned hospitals. Twist-drill craniostomy was not adopted. Craniotomy with extensive membranectomy was considered as a second option if burr-hole irrigation failed. The indication for surgery was symptomatic CSDH proven by CT scan. Presenting symptoms included headaches, confusion, disorientation, drowsiness, hemiparesis, ataxia, seizures and aphasia. Patients were included if they were aged 20 years or older and presented to the department of neurosurgery at the 3 above mentioned hospitals with surgical indication.

Primary outcome was defined as the recurrence rate of CSDH in the APA and non-APA group. The recurrence rate was defined as the rate of re-operation for recurrent CSDH after previous primary burr-hole irrigation with or without drainage. Recurrence was defined as the development of symptoms attributed to ipsilateral hematoma (i.e., same side as the initial surgery) proven by CT scan within 3 monthes of the initial surgery. The criteria for re-operation were cases in which the patient's original neurological deficit increased, recurred, or worsened, or new neurological deficits appeared, as evidenced by CT scan, necessitating further burr-hole surgery or craniotomy [1,19].

Secondary outcome was defined as contribution of other risk factors to the recurrence rate of CSDH.

Data from patients meeting the following exclusion criteria were not analyzed:

1. Taking warfarin.
2. *Organized CSDH*: Patients who could not be irrigated by the operating surgeon because of old solid clots, for whom drain insertion was judged unsafe and whose CT showed presence of huge residual CSDH 1 day after surgery.
3. *Multilocular CSDH*: Patients who could not be sufficiently irrigated by the operating surgeon because of septa, for whom drain insertion was judged unsafe and whose CT showed presence of huge residual CSDH 1 day after surgery.
4. Thrombocytopenia (i.e., platelet count < 50,000/μL) due to cirrhosis or thrombocytosis (i.e., platelet count > 2,000,000/μL) due to leukemia.

CSDH patients who were surgical candidates were immediately hospitalized. Oral APA administration was discontinued on admission. In principle, the patient was not to resume oral APA for one month after surgery.

All the data were obtained from medical charts, surgical reports and CT reviews.

This study was approved by the ethics committee of our hospital.

2.2. Patient demographics

We examined 10 factors: age, sex, history of diabetes mellitus (DM), hypertension (HT), chronic renal failure (CRF), alcohol consumption habits, consciousness disturbance on admission, preoperative computed tomography (CT) density (classified into 5 types: hypo/iso/high/mixed density and niveau), preoperative oral APA administration and postoperative drainage. The neurosurgeon completed an admission proforma about presenting symptoms and the 10 conditions mentioned above. DM, HT and CRF were defined by current treatment for the respective conditions. An alcohol consumption habit was defined as drinking 1 or more units of liquor daily. Consciousness level <15 on the Glasgow Coma Scale (GCS) was taken to indicate consciousness disturbance. CT studies were reviewed based on the characteristics of the hematoma. The density of the hematoma was compared to that of the brain parenchyma. An APA was defined as an agent that has a platelet aggregation inhibitory function as the main effect. The type, dose, and compliance of APA were examined. If an APA was discontinued before admission, the duration from cessation to admission was checked.

2.3. Operative method

In the 3 aforementioned hospitals, essentially the same surgical techniques for craniostomy with or without the closed drainage system were employed for CSDH. The surgical protocol starts with local anesthesia, followed by hematoma evacuation and irrigation with normal saline through one or two burr holes. We generally adopted the 1 burr-hole technique. We only adopted the 2 burr-hole technique when the hematoma cavity was large or many septa were expected, making irrigation difficult. For closed system subdural drainage, a subdural catheter was connected to a plastic bag fixed on the bed located approximately 10 cm below the patient's external acoustic meatus. Drainage was continued for 24–48 h after surgery depending on the amount to be drained [35]. When drain was removed, the fluid color inside usually became xanthochromic. However, while closed system subdural drainage was performed in principle, the surgeon decides whether or not to adopt this method depending on the situation.

2.4. CT analysis

CT studies were performed in all patients to confirm the diagnosis prior to the operation. Routine postoperative CT was performed one day and then again one week after surgery. Neurological assessment and CT follow-up were performed for several months postoperatively.

2.5. Statistical analysis

Data are given as means ± standard deviation. Results were analyzed for statistical significance using the unpaired Student's *t*-test. The Pearson's chi-square test and the Fisher's exact test were employed for univariate analyses and the logistic regression model for multivariate analyses. Differences were considered significant if the probability value was <0.05. Statistical analyses were performed using IBM SPSS statistical software version 19.0 (IBM Japan Ltd., Tokyo, Japan).

3. Results

The trial profile is shown in Fig. 1. A total 719 patients who were candidates for burr-hole surgery were immediately hospitalized, and underwent burr-hole irrigation with or without drainage. Meanwhile, 32 patients were excluded: 16 were taking warfarin, 9 had organized CSDH (7 were observed after surgery and 2 underwent craniotomy subsequently), 2 had multilocular CSDH, 4 had thrombocytopenia due to cirrhosis, and 1 had thrombocytosis due to leukemia. 6 patients dropped out. Ninety-two patients who took APA were classified into 2 groups according to the duration from