Journal of Clinical Neuroscience 38 (2017) 79–83

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Case study

Influence of antithrombotic agents on the recurrence of chronic subdural hematomas and the quest about the recommencement of antithrombotic agents: A meta-analysis

Yangshuo Wang, Jingru Zhou, Cungang Fan, Dongliang Wang, Feng Jiao, Bo Liu, Qingjun Zhang *

Department of Neurosurgery, Peking University People's Hospital, Beijing, China

ARTICLE INFO

Article history:
Received 17 June 2016
Accepted 3 December 2016

Keywords:
Anticoagulation
Antiplatelet
Antithrombosis
Chronic subdural hematoma
Recurrence

ABSTRACT

Antithrombotic agents (AT), including anticoagulants and antiplatelets, are risk factors of chronic subdural hematomas (CSDHs). However, the use of AT has not been clearly associated with postoperative recurrence (PR) in the literature before. Furthermore, the association between the resumption of AT and postoperative complications also requests research. Databases including Pubmed, Embase and Cochrane were searched for patients presenting with CSDH on anticoagulant or antiplatelet medication. Ten studies were included to analyze the association between the use of AT and PR: The meta-analysis showed that the use of AT, both anticoagulants (OR = 2.20, 95%CI [1.45, 3.33]; $P = 0.0002$) and antiplatelets (OR = 1.64, 95%CI [1.17, 2.30]; $P = 0.004$), could increase the PR rate. Two studies were included to analyze the relationship between the resumption of AT and postoperative complications. The meta-analysis showed that after the patients on AT resumed their medication, the risk of PR did not increase (OR = 0.33, 95%CI [0.13, 0.80]; $P = 0.01$), and the occurrence of thromboembolism events had no statistical significance (OR = 1.30, 95%CI [0.26, 6.50]; $P = 0.75$). This meta-analysis demonstrated that AT were risk factors for the recurrence of CSDH. Recommencement of AT did not appear to increase the risk of postoperative hemorrhage, and could reduce the risk of thromboembolism. Thus, appropriate postoperative resumption of anticoagulants or antiplatelets may be safe. Still, more evidence is needed to answer the question about whether and how to resume AT.

1. Introduction

In the worldwide, the number of people over the age of 60 is projected to reach almost 2 billion by 2050, representing 22 percent of the world's population [3]. Therefore, as a disease of the elderly, the prevalence of chronic subdural hematomas (CSDH) is expected to rise in the future for sure.

Despite aging, risk factors thought to contribute to the occurrence of CSDH also include male sex, history of falls, minor head injury, use of antithrombotic agents (AT, including anticoagulant or antiplatelet therapy), chronic alcohol use, epilepsy, low intracranial pressure states, and haemodialysis [14]. In warfarinised patients, the risk of developing a CSDH was at least 42.5 times higher, and aspirin could also increase the risk [24]. The recurrence rate for CSDH ranged from 9% to 33% in the recent literature [7], and the contemporary consensus is that the reoperation rate is 10–20% [14]. There are variable predictors of CSDH postoperative recurrence (PR), including patient characteristics such as age [4], bilateral CSDH [29], radiographic variables such as preoperative hematoma width and morphology [6], and surgical and perioperative factors such as brain re-expansion and postoperative persistence of midline shift [14,26].

Preoperative AT, including anticoagulant and antiplatelet medication, is also considered a possible predictor of CSDH recurrence. However, the use of AT has not been clearly associated with PR in the literature. Chon et al. and Leroy et al. found increased recurrence with anticoagulants [6,16], Forster et al. and Wada et al. showed increased recurrence with antiplatelets [8,30], and several others found no increase in recurrence with either anticoagulants or antiplatelets [1,17,19,22,23,26,27,29].

With the increasing numbers of elderly people, the number of patients who are treated with AT is also increasing [25]. Therefore,

Abbreviations: ASDH, acute subdural hematomas; AT, antithrombotic agents; CSDH, chronic subdural hematomas; INR, international normalized ratio; PR, postoperative recurrence; NOS, Newcastle-Ottawa Scale.

* Corresponding author. Fax: +86 88324852.
E-mail addresses: wysh1227@163.com (Y. Wang), zhangqj4852@163.com (Q. Zhang).

http://dx.doi.org/10.1016/j.jocn.2016.12.001
0967-5868/

it is of importance to analyze the correlation between AT and the recurrence of CSDH. This systematic review and meta-analysis studied this problem from two parts: the first part, the association between the use of AT and postoperative recurrence; the second part, the association between the recommencement of AT and postoperative complications including recurrence and thromboemoblic events.

2. Methods

2.1. Selection criteria

The selection criteria for studies to be included were as follows:

1. Study design: Prospective and retrospective observational studies, comparison group and specific study data were necessary.
2. Population: Patients with traumatic or atraumatic CSDH who were on AT (anticoagulants or antiplatelets) on admission.
3. Management: All patients underwent surgical treatment including burr hole evacuation, twist drill or craniotomy.
4. Outcome: Studies should include specific data about the incidence of recurrences (requiring reoperation) and thrombotic events during the follow-up period.

2.2. Search strategy

Databases including Pubmed, Embase and Cochrane were searched using the key words: "chronic subdural hematoma", "antithrombotic", "anticoagulant" and "antiplatelet". The last search time was May, 2016. All studies included were clinical studies published in the English language.

2.3. Selection of studies and data extraction

The titles and abstracts of the studies identified by the search strategy were screened by two researchers independently (Y.S.W and J.R.Z). They assessed all identified studies using the selection criteria, and resolved disagreement by discussion. If agreement could not be reached, they consulted an additional researcher (D. L.W) to make the final decision. All data in this meta-analysis were extracted from the texts, tables and figures of the studies met the selection criteria.

2.4. Statistical analysis and quality assessment

Statistical analysis was performed using RevMan software version 5.3. The odds ratio (OR) and 95% confidence level (Cl) were analyzed. Heterogeneity among studies was assessed by the I^2 statistic. The methods and findings reported in this meta-analysis were based on the PRISMA guidelines [20].The quality of studies were assessed using the Newcastle-Ottawa Scale (NOS), which provided a quantitative assessment based on study participant selection, comparability and outcome [32]. Funnel plots were also conducted to assess the potential publication bias if the included studies were more than ten in each analysis.

3. Results

The initial search resulted in 233 papers. Nine repeated studies were excluded. After screening titles and abstracts, 176 papers were excluded. In the remained 48 studies, 12 retrospective studies were in accordance with the inclusion criteria. The study characteristics were summarized in Table 1. Among the 12 studies, ten studies were selected to analyze the association between the use of AT and PR, and two studies could be used to discuss the recommencement of AT.

Among the ten studies, eight were in the anticoagulant group, and nine studies were included in the antiplatelet group (seven studies included both anticoagulant and antiplatelet therapy). (Fig. 1) In these ten observational studies, four concentrated on the influence of AT on the outcome of CSDH [1,19,24,30]. The others analyzed multiple risk factors for CSDH recurrence. Anticoagulant or antiplatelet medication was considered as one of the risk factors [6,16,23,26,27,29].

In total, seven studies aimed to research the resumption of AT were found, but only two studies met the inclusion criteria. The sample size was 256. The detailed exclusion reasons of the five studies were list below: no comparison group [13,33], review article [5], providing only statistic result without specific data [23], researching CSDH together with acute and subacute subdural hematomas [18]. The studies excluded would be analyzed in the discussion part because articles on this field were not many.

Funnel plots to assess potential publication bias was not performed in any analysis due to the included studies were less than ten.

3.1. Use of anticoagulants or antiplatelets increases the PR rate of CSDH patients

3.1.1. Anticoagulants

Eight studies examined the PR rate of CSDH patients on anticoagulants. The heterogeneity was very low among the studies (I^2 = 8%, P = 0.37). The overall effect of the studies showed significant association (Z = 3.71; P = 0.0002). Meta-analysis of included studies demonstrated a strong relationship between anticoagulants and PR rate (OR = 2.20; 95%CI [1.45, 3.33]; P = 0.0002) (Fig. 2).

3.1.2. Antiplatelets

Associations between antiplatelets and PR were evaluated in nine studies. The overall effect of the studies was statistically significant (Z = 2.85; P = 0.004). Summary result implied positive correlation between antiplatelets and PR rate (OR = 1.64; 95%CI [1.17, 2.30]; P = 0.004), with low heterogeneity (I^2 = 25%; P = 0.22) (Fig. 3).

3.2. PR and thromboembolic events incidences are unaffected by the resumption of AT

Two studies were included. One studied acetylsalicylic acid and warfarin separately [10], the other specified on warfarin [9]. In Guha's study, the median time of resumption was 52 days, and 24.4% restarted in two weeks. The median time of recurrence was 16.2 days. In Gonugunta's study, 50% of the resumption time was 3–5 days, and all recurrences occurred within three weeks after operation. The detailed data were shown in Table 2. The heterogeneity was low (I^2 = 23%; P = 0.27). The overall effect was statistically significant (Z = 2.45; P = 0.01). Meta-analysis revealed a reversed relationship between the use of AT and PR rate (OR = 0.33; 95%CI [0.13, 0.80]; P = 0.01).

Both of the two studies also counted postoperative thromboembolic events, but thrombosis only appeared in Guha's study, no thrombotic events happened in Gonugunta's study. In the restart group (totally 113 patients), three patients resulted in thrombotic events, and all three of the thrombotic events happened before the recommencement of AT. In contrast, two patients in the no restart group (totally 109 patients) developed thrombosis, which was not statistically significant (OR = 1.30; 95%CI [0.26, 6.50]; P = 0.75). The median time of thromboembolic events was 2.7 days after operation.