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Clinical Review

IS PLATELET TRANSFUSION EFFECTIVE IN PATIENTS TAKING ANTIPLATELET AGENTS WHO SUFFER AN INTRACRANIAL HEMORRHAGE?

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☐ **Abstract—Background: Patients taking antiplatelet agents (APAs) with intracranial hemorrhage (ICH) may be treated with platelet transfusion. Objectives: We conducted a systematic review of the use of platelet transfusion in the management of APA-related ICH. Methods: We searched the Cochrane, Medline, Embase, and CINAHL databases. Included studies were randomized, case-controlled, or cohort studies comparing outcomes in adult patients with APA-related ICH who received or did not receive platelet transfusion. Study quality was measured using appropriate scores. The primary outcome of interest was in-hospital mortality rate. Secondary outcomes included rates of craniotomy, neurological, medical, or radiological deterioration; mean length of hospital stay, delayed mortality, and functional status at discharge. We reported proportions, medians with interquartile ranges, and pooled odds ratios with their 95% confidence intervals. p values < 0.05 were considered statistically significant. Results: There were no randomized controlled trials. Seven retrospective cohort studies (four traumatic, three primary ICH) were included. For APA-related traumatic ICH, the pooled odds ratio (OR) for in-hospital mortality with platelet transfusion was 1.77 (95% confidence interval [CI] 1.00–3.13). There were no statistically significant differences for secondary outcomes except for proportion with medical decline (6/44 vs. 2/64; p = 0.006). For APA-related primary ICH, the pooled OR for in-hospital mortality with platelet transfusion was 0.49 (95% CI 0.24–0.98). There were no statistically significant differences for most secondary outcomes between the two groups. These studies had important methodological limitations. Conclusions: The evidence for platelet transfusion in APA-related ICH was inconclusive due to methodological limitations.** © 2015 Elsevier Inc.

☐ **Keywords—intracranial hemorrhage; antiplatelet agents; platelet transfusion**

INTRODUCTION

Antiplatelet agents (APAs) are indicated for prevention of cardiovascular diseases like transient ischemic attack, stroke, and myocardial infarction. It has been estimated that up to 36.2% of the American population over the age of 35 years are on APAs (1). Common classes of APAs used are cyclooxygenase-1 inhibitors like aspirin, phosphodiesterase inhibitors like dipyridamole, adenosine diphosphate 2 receptor antagonists including ticlopidine, clopidogrel, and prasugrel, as well as cyclopentyltriazolopyrimidine agents like ticagrelor (2). With the exception of ticagrelor, which is a reversible inhibitor of platelet function, the inhibition of platelet activity by other APAs and bleeding times, however, take approximately 5 days to normalize after discontinuation (3–5).

As the population ages, it is increasingly common to encounter older patients in the emergency department (ED) with traumatic or spontaneous intracranial hemorrhage (ICH). Although Spektor et al. reported no difference in rates of ICH evacuation and mortality between patients on APAs and controls with traumatic ICH, other

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studies reported conflicting results (6–10). In these studies, preinjury use of APAs was associated with increased mortality rates (21.6–56% vs. 7.8–10%) and rates of craniotomy (55.2% vs. 40.1%) or rebleed (5% vs. 1%) (7–10). Similarly, studies on the effect of APAs use on spontaneous ICH outcome have also produced conflicting results (11–20).

Intravenous platelet transfusion has been used to treat patients with traumatic or spontaneous ICH and preinjury APA use.

The aim of this evidence-based report is to identify and summarize the relevant literature for the effectiveness of platelet transfusion in treating ICH among patients with preinjury exposure to APAs.

METHODS

We identified relevant studies by searching the Cochrane Library (1946 through June 2014), MEDLINE (1946 through June 2014), Embase (1980 through June 2014), and CINAHL (1980 through June 2014) databases using the search expression {Exp platelet transfusion} AND [anti-platelet therapy] OR [anti-platelet agents] AND [intracranial hemorrhage] OR [head injury]. Titles and abstracts were reviewed to identify papers potentially addressing the research question. Full texts of these were obtained and reviewed. A hand search of the reference lists of published papers was also conducted.

Studies were included if they were randomized or case controlled or cohort studies comparing outcomes in adult patients with APA-related traumatic or primary ICH who were treated, vs. those who were not treated with platelet transfusion; with results available in English. Study quality was measured using the Jadad score for randomized studies or the Newcastle-Ottawa Scale for case-controlled or cohort studies (21,22).

Two reviewers independently screened suitable articles using our inclusion criteria. They discussed and decided on the finally included articles. The Jadad or Newcastle-Ottawa score for each of these finally included articles was assigned after discussion between them.

The primary outcome of interest was in-hospital mortality rates between the group with platelet transfusion and the other with no transfusion. Secondary outcomes included rates of acute clinical deterioration like craniotomy, neurological, or other medical deterioration requiring intensive care monitoring or intervention, radiological progression on repeat computed tomographic (CT) scan of the head, mean length of hospital stay (LOS), and delayed mortality and chronic clinical morbidity; that is, functional status at hospital discharge or follow-up between the two groups.

We reported proportions, medians, and their interquartile ranges (IQRs). For the analysis, we calculated the weighted rate of primary outcome in the platelet-transfused group vs. the other with no transfusion. We reported p values, odds ratios (ORs), and 95% confidence intervals (CIs) for outcomes measured. We weighted each of the individual studies according to their respective number of subjects enrolled. p values < 0.05 were considered statistically significant. We chose to take the more conservative approach of pooling studies with a random-effects analysis. We performed all analyses using RevMan version 5 (the Cochrane Collaboration, Copenhagen, Denmark).

RESULTS

We identified 19 papers, of which seven met inclusion criteria. There were no randomized controlled trials or case-controlled studies investigating this topic. There were seven retrospective cohort studies that investigated the effect of platelet transfusion on APA-related ICH in adult patients (23–29). Four such studies were done on APA-related traumatic ICH, and three were on APA-related primary ICH (23–29). All studies on APA-related traumatic ICH were done in Level I trauma centers in the United States with three single-center studies and one conducted in two centers (23–26). Two studies on APA-related primary ICH were conducted in a single center within the United States (US), and the other was a single-center Japanese study (27–29). The APAs used in the US studies were aspirin and clopidogrel or aspirin and clopidogrel or extended release dipyridamole (23–28). In the Japanese study, the APAs used were aspirin, aspirin and clopidogrel, and clopidogrel or ticlopidine alone (29). There were no studies investigating prasugrel or ticagrelor. Details of these papers are shown in Tables 1 and 2 (23–29).

Table 3 reveals the study quality of these seven studies as assessed using the Newcastle-Ottawa score (23–29). The median score was seven (IQR two). Sample sizes ranged from 108 to 328 for traumatic ICH and 66 to 121 for primary ICH. There were only three studies, which specifically stated that information regarding platelet transfusion was obtained from secured records; that is, intensive care unit or blood bank records (23,24,28). In all studies except one, the decision to transfuse platelets was made at the discretion of the attending doctor (24). In the two-center study by Downey et al., platelet transfusion was given at the discretion of the attending doctor in one center, whereas in the other, it was given only if there was laboratory evidence of platelet dysfunction using the Platelet Function Analyzer (PFA)-100® screening test (24).

Of the four studies investigating the use of platelet transfusion in APA-related traumatic ICH, the most common outcome was in-hospital mortality rate (23–26). The in-hospital mortality rates among patients who received