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Clinical study

The application of point-of-care platelet function assay in guiding platelet transfusion in aspirin-users with intracranial haemorrhages

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ABSTRACT

Background: An increasing number of patients with intracranial haemorrhages are aspirin-users. Neurosurgeons commonly attempt to minimize the risk of re-bleeding by withholding the medication and giving platelet transfusion. However, recent studies raised safety concerns and showed poorer outcome with platelet transfusion when the latter was not guided by changes in platelet function.

Aim of study: To study the temporal pattern and degree of changes in platelet activities following a fixed dose of platelet transfusion in aspirin-users with intracranial haemorrhages.

Methods: Aspirin-users with intracranial haemorrhages underwent baseline aspirin response units (ARU) using the VerifyNow® assay. Those who showed abnormal platelet activity received a single dose of 4 units of platelet concentrate. ARU were then repeated at 4 h, 24 h and 48 h post-transfusion. Patients were classified according to their responses to transfusion.

Results: Twenty patients were recruited. At 4 h after transfusion, 11 (55%) patients had normalised platelet activities while the rest may show delayed or absent of normalization. Overall, eight (40%) patients were 'early and persistent transfusion responders', five 'delayed transfusion responders', and five (25%) had persistently abnormal platelet function. Two (10%) patients who initially responded to transfusion failed to maintain normalized platelet activity.

Conclusion: Platelet activities in aspirin-users showed considerable heterogeneity up to 48 h following a blanket approach of platelet transfusion. The need for repeated transfusion or alternative therapy strongly argues for a guided practice for transfusion based on point-of-care platelet function assay. Future research should also adopt this approach to re-examine the safety and effectiveness of platelet transfusion in these patients.

1. Introduction

Despite the lack of supportive clinical evidence, many neurosurgeons would give platelet transfusion to users of antiplatelet medications with intracranial haemorrhages in a bid to reduce the risk of further bleeding [1–3]. However, the benefit of platelet transfusion in this situation has not been substantiated, [4–7] and transfusion itself is not without risks. Fluid overload, thrombotic events such as myocardial infarction, pulmonary embolism and stroke, and transfusion reactions are potential complications. The PATCH trial published in 2016 also raised serious concerns over the unguided use of platelet transfusion in this regard [8].

Non-responders to antiplatelet agent may potentially account for the ineffectiveness of platelet transfusion in the above studies, and platelet prescription based on platelet activity measurement may serve to avoid unnecessary transfusion and related complications in this subgroup of patients. Even among aspirin responders, retrospective studies have shown that not all would respond to platelet transfusion or respond equally at 1 h [9,10]. Furthermore, it is unknown whether those who initially respond to transfusion would retain normalised platelet activity during the next 6 h when the rate of haematoma expansion is the highest, or at 24-hour when the majority of haematoma expansion takes place [11]. In principle, serial post-transfusion measurements of platelet activity should be performed. With the advent of point-of-care platelet function assays in recent years, this has now become a feasible approach. It is analogous to the use of the International Normalised Ratio (INR) in guiding the reversal of warfarin-induced anticoagulation that has become an established and widely accepted practice.

Abbreviations: ARU, aspirin response unit; INR, international normalised ratio; CT, computer tomography.

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In this study, we aimed to establish the rationale of a guided approach to platelet transfusion by examining the trends of post-transfusion platelet activity using a point-of-care assay in a cohort of aspirin-users. The hypothesis was that post-transfusion platelet activities would show high heterogeneity among patients and variability at different time-points. We found that not only did patients respond differently to the initial transfusion, but that their requirement for additional transfusion also varied widely if normalisation of platelet activity was to be achieved and maintained up to 48 h.

2. Method

This is a prospective, observational, single centre pilot study conducted at an academic neurosurgical unit. We identified adult aspirin-users with intracranial haemorrhages of any aetiology who were deemed unlikely to require neurosurgical intervention. Patients who were concomitantly receiving other antiplatelet or anticoagulation agents, those with other bleeding diathesis requiring transfusion of other blood products, those deemed not in need of platelet transfusion, and those who were mentally incompetent to provide consent were excluded.

An initial baseline VerifyNow® (Accumetrics, San Diego, CA, USA) assay was performed. Patients with an aspirin response unit (ARU) of less than 550 were identified as aspirin-responders; those with ARU ≧550 were non-responders. The reference range was set according to the recommendation of the manufacturer [12]. Only aspirin-responders were recruited into the study and given 4 units of platelet concentrate per our customary practice. Aspirin was withheld. The clinical management of these patients would follow our standard practice, unaffected by the assay results. No further transfusion was given.

VerifyNow® assay was then repeated at 4, 24 and 48 h post-transfusion. At each time-point, we were able to identify patient as 'transfusion responders' or 'transfusion non-responders'. Based on the longitudinal assessment, patients could be further classified into one of 4 categories: 'early and persistent transfusion responders', 'transient transfusion responders', 'delayed transfusion responders' and 'persistent transfusion non-responders'. Fig. 1 illustrates the study flow.

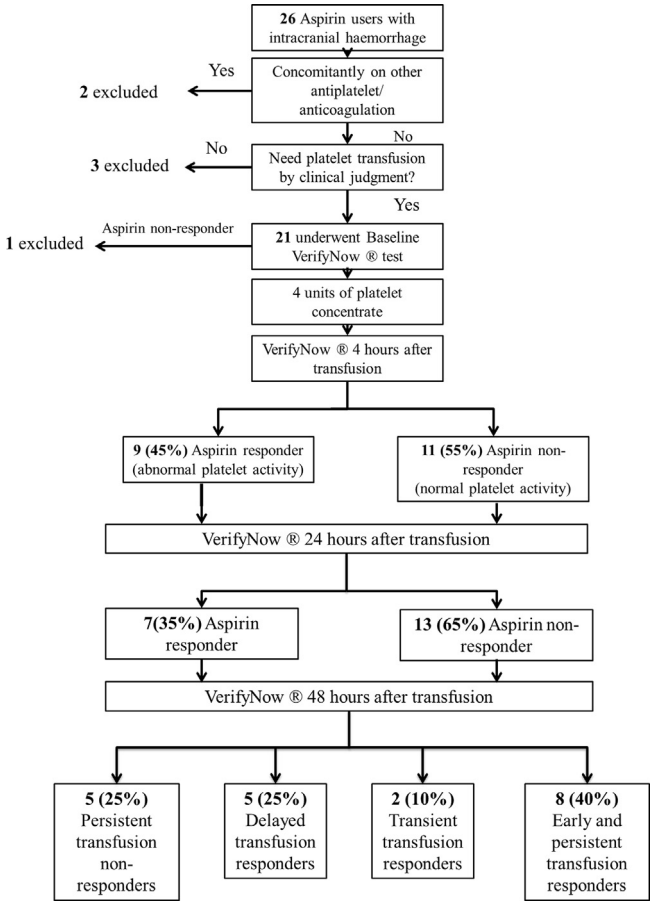

Fig. 1. A flow-chart showing patient recruitment and differential responses to a fixed dose of platelet transfusion.

2.1. Data collection

Data collected included patient demographics, VerifyNow® assay results, pre- and post-transfusion platelet count, creatinine on admission, transfusion-related complications, all-cause mortality rate at 3 months and haematoma progression on computer tomography (CT) scan.

2.2. Informed consent

Written informed consent to collect data and clinical outcomes was obtained from the patient or the legally authorized representative. Patients were informed that the transfusion practice would follow our established practice unaffected by the assay results. Individual patients' test results were not made known to anyone outside the study team, including the attending physician. This study was approved by the hospital's Institutional Review Board.

3. Results

From February 2014 to April 2017, 26 aspirin-users were identified. Six were excluded based on the exclusion criteria, leaving 20 patients recruited for the study. There were 11 male and 9 female patients. The mean age was 80.5 years (range: 65–94). Fifteen patients had a definite history of head injury. Only one patient subsequently required operation for the intracranial haemorrhage.

Table 1 showed the ARU levels at each time point. At 4 h, eleven (55%) patients had ARU above 550. At 24 h, thirteen (65%) patients

Table 1
Aspirin Response Unit (ARU) levels at each time point of VerifyNow® testing.

Patient	Baseline ARU	ARU at 4 h	ARU at 24 h	ARU at 48 h	Platelet activity category
1	449	480	606	643	DR
2	415	514	571	602	DR
3	407	528	569	–[a]	DR
4	480	631	621	591	PR
5	447	613	634	600	PR
6	469	576	464	568	DR
7	391	571	582	642	PR
8	419	588	644	633	PR
9	413	585	508	560	DR
10	404	567	553	544	TR
11	414	585	594	558	PR
12	423	512	581	473	TR
13	495	425	522	533	PN
14	418	514	515	543	PN
15	428	421	524	399	PN
16	549	472	419	440	PN
17	435	602	550	574	PR
18	394	587	622	651	PR
19	406	594	553	571	PR
20	490	536	506	531	PN

[a] Patient 6 did not undergo a third VerifyNow® assay at 48 h. This patient's platelet activity category was determined with data up to 24 h. PR, early and persistent transfusion responder; DR, delayed transfusion responder; TR, transient transfusion responder; PN, persistent transfusion non-responder.