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Assessment of three point-of-care platelet function assays in adult trauma patients

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ARTICLE INFO

Article history:
Received 15 September 2016
Received in revised form
5 January 2017
Accepted 18 January 2017
Available online 27 January 2017

Keywords:
Platelet dysfunction trauma
Platelet function test trauma
Multiplate
VerifyNow
Thrombelastogram platelet mapping

ABSTRACT

Background: Antiplatelet (AP) medication use is common among trauma patients and is associated with poor outcomes. Management options for platelet dysfunction in trauma patients are controversial, expensive, and potentially harmful. Although light transmission platelet aggregometry is considered the standard test to assess platelet function, it is cumbersome and not generally available. Currently, there are no widely accepted platelet function point-of-care tests for acute trauma.

Study design: Prospective observational study from 2014 to 2015. Baseline Multiplate aggregometry aspirin area under the platelet aggregation curve (ASPI AUC), Thrombelastography Platelet Mapping percent inhibition of arachidonic acid (TEG-PM AA), and VerifyNow Aspirin Test (ARU) were compared for ability to detect any AP medication use (aspirin or clopidogrel), platelet dysfunction, and identify patients at risk for intracranial hemorrhage (ICH) progression by calculating the area under receiver operating characteristic curves (AUC), sensitivity, specificity, and positive and negative predictive values. Adenosine diphosphate assays were similarly evaluated.

Results: Sixty-four patients were enrolled, 25 were taking AP medications. AP patients were older (71.6 *versus* 35.0 y, $P < 0.001$) and received more platelet transfusions, but other baseline characteristics were similar. Median ASPI AUC (22.0 *versus* 53.5 $P < 0.001$) and VerifyNow ARU (503.5 *versus* 629.0, $P < 0.001$) were lower, whereas TEG-PM AA (51.8% *versus* 18.3%, $P < 0.001$) was higher in AP patients. Multiplate ASPI AUC, TEG-PM AA percent inhibition, and VerifyNow ARU could identify AP medication use (AUC: 0.90, 0.77, and 0.90, respectively). Adenosine diphosphate assays did not correlate with AP medication use in this population. TEG-PM AA percent inhibition and VerifyNow ARU correlated well with Multiplate ASPI AUC to identify platelet dysfunction (AUC: 0.78, 0.89, respectively). ICH occurred in 29 patients; 12 of which had progression of their injury. ASPI AUC (AUC: 0.50) and VerifyNow ARU (AUC: 0.59) did not correlate, and TEG-PM AA percent inhibition (AUC: 0.66) minimally correlated with progression.

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0022-4804/$ – see front matter
http://dx.doi.org/10.1016/j.jss.2017.01.008

Conclusions: Multiplate, TEG-PM, and VerifyNow are useful point-of-care tests which identify AP medication use and platelet dysfunction in trauma patients. Initial TEG-PM AA percent inhibition may be associated with risk for ICH progression. However, additional large, prospective studies are needed.

Introduction

Antiplatelet (AP) medication use is very common in the United States. As our population ages, the use of these medications continues to increase. Despite the prevalence of these medications, the accurate assessment of platelet function in the trauma population has not been standardized.

Aspirin (acetylsalicylic acid [ASA]) and clopidogrel are the most common AP medications among trauma patients. They function through the irreversible inhibition of platelet aggregation and activation.[1] Severe traumatic injury and traumatic brain injury (TBI) have been shown to decrease platelet aggregation and hemostasis.[2] Furthermore, because of injury acuity, many trauma patients may be unable to recall or relay if they are using AP medications, the type of AP medication, its dose, or most recent administration. Therefore, accurate identification of AP medication use or platelet dysfunction could provide great benefit in this population. It could aid clinical decision-making through bleeding risk stratification, particularly in those patients with intracranial hemorrhage (ICH).[3,4]

Light transmission aggregometry (LTA), developed in 1962, is considered the gold-standard assessment of platelet function.[5] Despite four decades of use, LTA remains cumbersome, time consuming, and largely limited to select facilities with expert technicians.[5] Furthermore, because of the acuity and unexpected nature of trauma, utilization of LTA in this population is nearly impossible. Multiple point-of-care (POC) platelet function tests have been developed to overcome the limitations of traditional LTA. Thrombelastography Platelet Mapping (TEG-PM; Haemoscope Corporation, Niles, IL) is specifically designed to investigate the influence of adenosine diphosphate (ADP)-induced and arachidonic acid (AA)-induced GPIIb/IIIa platelet receptor activation.[6] The Verify Now (Accriva, San Diego, CA) system uses light transduction to assess whole blood platelet adhesion to fibrin-coated beads.[7] It measures the effects of ASA using manufacturer-defined Aspirin Reaction Units (ARU) and clopidogrel using P2Y12 Reaction Units (PRU). Multiplate aggregometry (DiaPharma, West Chester, OH) tests the change in electrical resistance between multiple sensory wires as platelets aggregate over time in response to various platelet aggregation agonists.[4,8,9] Although limited, multiple studies suggest that Multiplate aggregometry may be most comparable to LTA. It tests similar platelet agonists as LTA, and similar to LTA, can be used to monitor cardiovascular patients on AP therapy and to identify patients with high perioperative cardiac surgery bleeding risk.[8,10,32,33] In addition, it has been used to identify platelet dysfunction in trauma patients.[4,11] Despite the availability of multiple POC assays, none has gained widespread acceptance or adoption for use in trauma patients because of limited and often confusing or conflicting literature. To our knowledge, no direct prospective comparisons of these tests against LTA or against each other have been performed in the trauma population.

Given the widespread use of AP medications, the goal of this study was to characterize and compare these POC assays in trauma patients specifically to create a foundation for future studies.[1] Its primary aim was to assess the ability of each assay to identify AP medication use in trauma patients immediately on arrival. The secondary aims were to compare the ability of VerifyNow and TEG-PM with Multiplate aggregometry to identify platelet dysfunction and to determine if any of these tests were predictive of ICH progression. We hypothesized that all POC platelet function assays could identify AP medication use and platelet dysfunction and may be predictive of ICH progression in trauma patients.

Methods

We performed a prospective observational study of trauma patients admitted to Oregon Health & Science University (OHSU) from May 2013 through June 2015. Study approval was granted from the OHSU Institutional Review Board (IRB00009106) and was supported through a grant from the Medical Research Foundation of Oregon.

Based on previously defined criteria, adult trauma patients at risk for coagulopathy and hemorrhage were eligible for this study, and prospectively screened for enrollment immediately on arrival to the Emergency Department.[12,13] Enrollment criteria included Glasgow Coma Scale <10, ICH on initial head computed tomography (CT) scan, systolic blood pressure <90 mm Hg, intubation, base deficit >6 mEq/L, penetrating injury to the torso, groin, or neck, amputation proximal to the ankle or wrist, uncontrolled external hemorrhage, two or more long bone fractures, pelvic fracture, combination trauma with burns (<20% total body surface area). Children aged <15 y, patients with significant burns (>20% total body surface area), prehospital cardiopulmonary resuscitation, and prisoners were excluded.[12,13] Patients on other anticoagulation medications and who were transferred from another facility with >6 h since injury were also excluded. We attempted to enroll subjects consecutively during the study period into two equal groups, an AP group and non-AP group. The AP group included patients currently taking ASA or clopidogrel. To confirm AP medication use, outpatient medication lists were reviewed with the patient, a relative or through outpatient medical records. Therefore, all statistical calculations in this group assumed 100% compliance with these medications. The non-AP group included those who were not taking these medications. Because this was an observational study, patients were not randomized.