Thromboelastometry-guided coagulation management

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Introduction

Transfusion of packed red blood cells (PRBC), fresh frozen plasma (FFP), cryoprecipitate, and platelet concentrates is strongly associated with increased morbidity and mortality in cardiovascular surgery, patients with myocardial infarction, and critically ill patients [1,2]. This includes transfusion-related acute lung injury, transfusion-associated circulatory overload, ischaemic postoperative morbidity, and sepsis [1]. Furthermore, blood transfusion is associated with prolonged hospital stay as well as increased hospital costs [2].

Based on a five-year experience in point-of-care (POC) supported coagulation management in liver transplantation [3] we developed and implemented an algorithm including POC supported coagulation management in cardiovascular surgery, based on first line therapy with specific coagulation factor concentrates such as fibrinogen concentrate and prothrombin complex concentrate (PCC) combined with POCthromboelastometry(ROTEM®) and whole blood impedance aggregometry (Multiplate®) [4]. To assess the impact of this approach on transfusion requirements, we compared transfusion rates before and after implementation of this new practice pattern.

Methods

In a retrospective cohort study including 3,865 patients we analysed the incidence of intra-operative allogeneic blood transfusions (primary endpoints) before and after algorithm implementation [5].

Thromboelastometry: As the mainstay method of our POC supported coagulation management we used thromboelastometry (ROTEM®, Tem International GmbH, Munich, Germany). Thromboelastometry is much less sensitive to movement artifact compared to the classical thromboelastography system enabling its mobile use in the operating room. It provides four independent measuring channels and assays with different activators, and additives are commercially available to detect and differentiate specific haemostatic defects such as hyperfibrinolysis, heparin and protamine effects, hypofibrinogenaemia and fibrin polymerization disorders, coagulation factor deficiencies, and thrombocytopenia. For interpretation of thromboelastometric assays we used the following variables as part of our POC supported coagulation management algorithm: CT is the time from adding the start reagent to the citrated blood sample until the clot starts to form (clot firmness of 2 mm). Prolongation of CT may be a result of coagulation factor deficiencies or anticoagulants such as heparin, dependent on the test used. Maximum clot firmness (MCF) represents the greatest amplitude of the thromboelastometric trace and reflects the "strength" of the clot. A low MCF is indicative of decreased platelet concentration and/or function, decreased fibrinogen concentration and/or fibrin polymerization disorders, or low activity of factor XIII. A mechanically weak clot represents a severe bleeding risk [6]. In order to shorten the time to treat, we replaced in our algorithm MCF by the amplitude of clot firmness after 10 minutes (A10) [7]. A10 correlates well with MCF but allows for a 10 to 15 minutes shorter decision time for therapeutic interventions. Clot

lysis index 60 (CLI60) represents the percentage of clot firmness in relation to the MCF remaining at 60 min after CT. CLI60 values below 85% are indicative of systemic hyperfibrinolyis.

Whole blood impedance aggregometry: Platelet aggregation was measured by impedance aggregometry, also called multiple electrode aggregometry (MEA) (Multiplate®, VerumDiagnostica GmbH, Munich, Germany). Platelet dysfunction mediated by antiplatelet drugs like aspirin, non-steroidal anti-inflammatory drugs, platelet P2Y12 receptor antagonists, GpIIb/IIIa receptor antagonists or by CPB itself can be detected by whole blood impedance [4]. MEA results closely correlate both with early stent thrombosis and mortality after implantation of drug-eluting coronary stents as well as with bleeding complications after stent implantation or cardiac surgery [8-10]. Therefore, MEA complements in an ideal way thromboelastometry in peri-operative POC coagulation diagnostics. In MEA, the increase in impedance is measured over a period of six minutes after stimulation of platelets by arachidonic acid (ASPItest®), collagen (COLtest®), adenosine diphosphate (ADPtestÒ), or thrombin receptor activating peptide 6 (TRAPtest®). The area under the curve (AUC) is used as the main variable for platelet aggregation and is expressed in AU x min (arbitrary unit x minute).

Principles of the POC supported coagulation management algorithm: POC testing and haemostatic therapy was only done in patients at high risk for bleeding or with clinically relevant diffuse bleeding after heparin reversal with protamine. According to our POC supported coagulation management algorithm haemostatic therapy was performed with the following prioritization, if indicated by POC measurements: 1. Optimization of haemostatic preconditions, 2. Reversal of residual heparin effects with protamine, 3. Fibrinogen substitution, 4. PCC administration, 5. FFP transfusion, 6. Platelet transfusion, 7. Factor XIII, and 8. rFVIIa administration as a rescue therapy. Further details of the principles of our POC supported coagulation management have been described previously [3-5].

Results

Following algorithm implementation the incidence of any allogeneic blood transfusion (52.5 vs. 42.2%; P<0.0001), packed red blood cells (PRBC) (49.7 vs. 40.4%; P<0.0001), and fresh frozen plasma (FFP) (19.4 vs. 1.1%; P<0.0001) decreased, whereas platelet transfusion increased (10.1 to 13.0%; P=0.0041). Yearly transfusion of PRBC (3276 vs. 2959 units; P<0.0001) and FFP (1986 vs. 102 units; P<0.0001) decreased as did the median number of PRBC and FFP per patient. The incidence of fibrinogen concentrate (3.73 vs. 10.01%; P<0.0001) and prothrombin complex concentrate administration (4.42 vs. 8.9%; P<0.0001) increased as did their amount administered per year (179 vs. 702g; P=0.0008 and 162 x 10^3IU vs. 388 x 10^3IU; P=0.0184, respectively). Despite a switch from aprotinin to tranexamic acid, an increase in use of dual antiplatelet therapy (2.7 vs. 13.7%; P<0.0001), patients' age, proportion of females, emergency cases, and more complex surgery, the incidence of massive transfusion (≥10 units PRBC) (2.5 vs. 1.26%; P=0.0057) and unplanned re-exploration (4.19 vs. 2.24%; P=0.0007) decreased. Composite thrombotic/thromboembolic events (3.19 vs. 1.77%; P=0.0115) decreased but in-hospital mortality did not change (5.24 vs. 5.22%; P=0.98).

Conclusions

Implementation of a coagulation management algorithm based on early, first line therapy with fibrinogen concentrate and/or PCCs combined with POC testing using thromboelastometry and impedance aggregometry was associated with a marked decrease in the incidence of allogeneic blood

transfusion and of transfusion requirements when compared to temporal controls. This was despite a patient population that was sicker and more likely to bleed. Furthermore, the incidence of massive transfusion, re-exploration and thrombotic/thromboembolic adverse events also decreased significantly.

References

1. Marik PE, Corwin HL. Efficacy of red blood cell transfusion in the critically ill: A systematic review of the literature. Crit Care Med 2008; 36: 2667-74
2. Murphy GJ, Reeves BC, Rogers CA, Rizvi SIA, Culliford L, Angelini GD. Increased mortality, postoperative morbidity, and cost after red blood cell transfusion in patients having cardiac surgery. Circulation 2007; 116: 2544-52
3. Görlinger K. Coagulation management during liver transplantation. Hämostaseologie 2006; 26 (3 Suppl 1): S64-76
4. Görlinger K, Jambor C, Hanke AA, Dirkmann D, Adamzik M, Hartmann M, Rahe-Meyer N. Perioperative coagulation management and control of platelet transfusion by point-of-care platelet function analysis. Transfus Med Hemother 2007; 34: 396-411
5. Görlinger K, Dirkmann D, Hanke AA, Kamler M, Kottenberg E, Thielmann M, Jakob H, Peters J. First-line therapy with coagulation factor concentrates combined with point-of-care coagulation testing is associated with decreased allogeneic blood transfusion in cardiovascular surgery: a retrospective, single-center cohort study. Anesthesiology 2011; 115: 1179-91
6. Reinhöfer M, Brauer M, Franke U, Barz D, Marx G, Lösche W. The value of rotation thromboelastometry to monitor disturbed perioperative haemostasis and bleeding risk in patients with cardiopulmonary bypass. Blood Coagul Fibrinolysis 2008; 19: 212-9
7. Görlinger K, Dirkmann D, Weber CF, Rahe-Meyer N, Hanke AA. Algorithms for transfusion and coagulation management in massive haemorrhage. Anästh Intensivmed 2011; 52: 145-59
8. Rahe-Meyer N, Winterhalter M, Boden A, Froemke C, Piepenbrock S, Calatzis A, Solomon C. Platelet concentrates transfusion in cardiac surgery and platelet function assessment by multiple electrode aggregometry. Acta Anaesthesiol Scand 2009; 53: 168-75
9. Sibbing D, Braun S, Morath T, Mehilli J, Vogt W, Schömig A, Kastrati A, von Beckerath N. Platelet reactivity after clopidogrel treatment assessed with point-of-care analysis and early drug-eluting stent thrombosis. J Am Coll Cardiol 2009; 53: 849-56
10. Solomon C, Hartmann J, Osthaus A, Schöchl H, Raymondos K, Koppert W, Rahe-Meyer N. Platelet concentrates transfusion in cardiac surgery in relation to preoperative point-of-care assessment of platelet adhesion and aggregation. Platelets 2010; 21: 221-8