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Original Article

Hypothermia, pH, and Postoperative Red Blood Cell Transfusion in Massively Transfused Adult Cardiac Surgery Patients: A Retrospective Cohort Study

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Objective: To determine the relationships between hypothermia and pH at surgery end and postoperative red blood cell (RBC) transfusion in massively transfused adult cardiac surgery patients.
Design: Retrospective cohort study.
Setting: Single tertiary care, academic medical center.
Participants: A total of 395 adult patients having cardiac surgery with cardiopulmonary bypass who were massively transfused during an 8-year period. Patients were excluded if they did not receive an antifibrinolytic drug during surgery.
Interventions: None.
Measurements and Main Results: Body temperature and pH at surgery end were recorded. Postoperative RBC transfusion, a surrogate for postoperative bleeding, was the study's primary outcome. Secondary outcomes were postoperative fresh frozen plasma (FFP) transfusion, postoperative platelet transfusion, reoperation for bleeding, and mortality. Patients with hypothermia did not have more postoperative RBC transfusion ($p = 0.56$), but patients with acidosis or alkalosis received more RBCs after surgery ($p = 0.04$). There were no differences in secondary outcomes between groups. In multivariate analysis, both acidosis and alkalosis were independently associated with postoperative RBC transfusion ($p = 0.01$ and $p < 0.0001$).
Conclusion: Hypothermia at surgery end has no association with postoperative RBC transfusion in massively transfused cardiac surgery patients, but pH derangements are associated with increased postoperative transfusion. Thus, normalization of blood pH may be important in reducing postoperative bleeding in massively transfused cardiac surgery patients.

Key Words: hypothermia; bleeding; cardiac surgery; acidosis; alkalosis

MASSIVELY TRANSFUSED CARDIOTHORACIC surgery patients often have significant bleeding after surgery, and optimal targets for intraoperative hemostatic resuscitation have not been identified.[1] In multitrauma patients, a "lethal triad" of acidosis, hypothermia, and coagulopathy has been described, but it is unclear if this is relevant to cardiothoracic surgery patients.[2,3] Massively transfused patients are particularly at risk for hypothermia and acidosis because transfused blood products are often colder than body

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temperature, and red blood cell (RBC) storage solutions become progressively acidotic over time.[4] These factors may paradoxically worsen coagulopathy and potentiate postoperative bleeding.[5]

At present, there is a paucity of studies examining the relationships between body temperature, blood pH, and postoperative bleeding in adult cardiothoracic surgery patients with massive transfusion. The authors hypothesized that massively transfused cardiothoracic surgery patients with hypothermia and acidosis at the end of surgery would have more postoperative bleeding (estimated by postoperative RBC transfusion) than patients with normal body temperature and normal pH.

Methods

Patients

Secondary data analysis was performed using an existing cohort of massively transfused cardiothoracic surgery patients. The original cohort was comprised of all patients who had cardiothoracic surgery with cardiopulmonary bypass (CPB) and required massive intraoperative transfusion between January 1, 2006, and December 31, 2014, at a single institution. Massive intraoperative transfusion was defined as receiving at least 8 RBC units during surgery.[1] Patients who did not receive antifibrinolytic drugs during surgery were excluded from the analysis.

Definitions

Study variable definitions were based upon Society of Thoracic Surgeons database specifications (versions 2.61 and 2.73) (www.sts.org). The following variables were collected: age, sex, weight, height, diabetes mellitus, dyslipidemia, hypertension, history of end-stage renal disease requiring dialysis, baseline creatinine, infectious endocarditis, chronic lung disease, peripheral vascular disease, cerebral vascular disease, previous cardiac intervention, congestive heart failure within 2 weeks of surgery, prior myocardial infarction, left ventricular ejection fraction, preoperative beta-blocker use, preoperative statin use, preoperative warfarin use, preoperative heparin use, preoperative aspirin use, preoperative glycoprotein IIb/IIIa inhibitor use, preoperative thienopyridine use, type of surgery, urgency of procedure, CPB time, preoperative international normalized ratio (INR), preoperative hemoglobin, preoperative platelet count, antifibrinolytic use, intraoperative transfusion, postoperative transfusion, reoperation for bleeding, and in-hospital mortality.

In addition to these variables, the authors collected body temperature and blood pH at the time of surgery end. Body temperature in the authors' center is typically measured at 2 sites in cardiothoracic surgery patients: either the nasopharynx or esophagus, and the bladder. Nasopharyngeal or esophageal temperatures at case end were recorded except in cases when they were not available, and in those cases, temperatures from alternative sites were recorded.

Transfusion Practices

Transfusions were administered at the discretion of anesthesiologists, cardiac surgeons, and intensivists and were not specifically protocolized. Lower limit transfusion thresholds for patients with acute bleeding at the authors' institution are RBC transfusion for a hemoglobin level less than 7 mg/dL, fresh frozen plasma (FFP) transfusion for an INR greater than 1.5, platelet transfusion for a platelet count less than 100,000 platelets/μL, and cryoprecipitate transfusion for a fibrinogen level less than 200 mg/dL. Three antifibrinolytics were used during the study period: Epsilon-aminocaproic acid (EACA), tranexamic acid (TXA), and aprotinin. The majority of patients received EACA as a 10-g bolus and 1 g/h infusion until 6 hours after surgery. TXA was used in a small number of patients and aprotinin was used only during the early study period before safety concerns arose in 2007. Aprotinin was dosed as a 1,000,000-kallikrein inhibitory unit (KIU) bolus and 250,000 KIU/h.

Outcomes

The study's primary outcome was postoperative RBC transfusion. Secondary outcomes were postoperative FFP transfusion, postoperative platelet transfusion, reoperation for bleeding, and in-hospital mortality.

Statistical Analysis

Statistical analyses were performed using SAS 9.3 (Cary, NC). Patient variables were examined using histograms and frequency tables. Categorical variables were reported as the number and % of patients. Continuous variables were reported as the median value and 25th to 75th percentile value.

To examine hypothermia's impact on postoperative bleeding, patients were categorized as hypothermic (body temperature < 36ºC) at the time of surgery end or not hypothermic (body temperature ≥ 36ºC). Postoperative RBC transfusion was compared between groups using the Wilcoxon Rank Sum Test. A p value less than 0.05 was considered significant. For secondary outcomes, either the Wilcoxon rank sum test, Kruskal–Wallis test, or the Chi-squared test was used to compare FFP and platelet transfusion or reoperation and mortality rates. A Bonferroni correction was used to account for the fact that 4 secondary outcomes were tested. A p value less than 0.01 was considered significant for secondary outcomes. To examine the relationships between pH, postoperative RBC transfusion, and secondary outcomes, the same analyses were performed using 3 pH groups: pH < 7.35, pH 7.35 to 7.45, and pH > 7.45.

Multivariate Poisson regression was performed to determine whether there were independent associations between body temperature, blood pH, and postoperative RBC transfusion. Postoperative RBC transfusion was modeled as the dependent variable. Independent variables were selected for model inclusion by first testing for univariate association with postoperative RBC transfusion. Variables that had a univariate

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