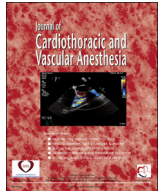




Contents lists available at ScienceDirect

ScienceDirect

journal homepage: www.jvcaonline.com

Original Article

Postoperative Bleeding After Change in Heparin Supplier: A Cardiothoracic Center Experience



Mirela Bojan, MD, PhD^{*,1}, Andreas Fischer, PharmD[†],
Ashok Narayanasamy, MD[‡], Paul Yea, RODP, SCP[§],
Eleanor Dunnett^{||}, Andrea Kelleher, MD[¶]

^{*}Department of Anesthesiology and Critical Care, Necker-Enfants Malades University Hospital, Paris, France

[†]Critical Care and Cardiothoracic Surgery, Pharmacy Department, Barts Heart Centre, Barts Health NHS Trust, St. Bartholomew's Hospital, London, United Kingdom

[‡]Department of Anesthesiology, Royal Sussex County Hospital, Brighton, United Kingdom

[§]Department of Anesthesiology, Papworth Hospital, NHS Foundation Trust, Cambridge, United Kingdom

^{||}Department of Cardiac Surgery & TCV, Royal Brompton & Harefield Hospital, London, United Kingdom

[¶]Department of Anesthesiology, Royal Brompton & Harefield Hospital, London, United Kingdom

Objective: Unfractionated heparin is a mixture of glycosaminoglycans with different pharmacologic and pharmacokinetic properties. The literature suggests that blood loss after cardiac surgery is related to both elevated postoperative heparin concentrations and the potency of different heparin brands.

Design: An audit of the observed increase in the incidence of cardiac surgery-related bleeding after change in heparin supplier. Patient characteristics were compared between groups before and after a change in heparin brands.

Setting: Tertiary cardiothoracic center.

Participants: All patients undergoing cardiac surgery between August 1, 2011, and April 30, 2012.

Interventions: None.

Measurements and Main Results: Two hundred eighty patients underwent surgery before a change in heparin brands and 216 after a change. Their preoperative and intraoperative characteristics were similar. Postoperative chest tube drainages and blood transfusions were significantly greater after the change in heparin brands (postoperative chest drainage 476.8 ± 393.1 v 344.8 ± 323.2 mL/6 h and $1,062.2 \pm 738.8$ v 841.8 ± 567.4 mL/24 h, respectively; both $p < 0.001$) despite the administration of larger amounts of protamine, fresh frozen plasma/platelet transfusions, and cryoprecipitate. Heparin recirculation within 24 hours of bypass was noted in about 70% of the samples tested using either anti-factor X activity or the thromboelastography ratio between nonheparinase R and heparinase-modified R and was not associated with the heparin brand. The likelihood ratio chi-square test for nested models identified an added predictive value of the heparin brand when included as a predictor of bleeding (chest drainage > 800 mL/6 h) in a model comprising recirculation, assessed using either an elevated anti-factor X activity or ratio between nonheparinase R and heparinase-modified R.

Conclusion: It is likely that the observed increase in postoperative bleeding was related to the pharmacologic properties of the new heparin brand rather than a higher incidence of heparin recirculation.

© 2017 Elsevier Inc. All rights reserved.

Key Words: cardiopulmonary bypass; bleeding; blood coagulation/anticoagulation

¹Address reprint requests to Mirela Bojan, MD, PhD, Department of Anesthesiology and Critical Care, Necker-Enfants Malades University Hospital, 149 rue de Sèvrès, 75743 Paris Cedex 15, France.

E-mail address: mirela.bojan@nck.aphp.fr (M. Bojan).

Postoperative bleeding is a common complication after cardiac surgery with cardiopulmonary bypass (CPB), with nearly 20% of patients experiencing significant bleeding after surgery and 2% to 8% requiring re-exploration for excessive

bleeding.^{1–3} There is increasing evidence that bleeding that requires transfusions is independently associated with postoperative morbidity, such as sepsis, acute respiratory distress syndrome, renal failure and death.^{4–7}

Unfractionated heparin is a mixture of glycosaminoglycans, which vary in their pharmacologic and pharmacokinetic properties.⁸ The literature suggests that blood loss after CPB is linked to both postoperative heparin concentrations and the use of different heparin brands.^{9–13} Due to the short pharmacokinetic half-life of protamine and nonspecific binding and release of heparin from plasma proteins,¹² heparin may recirculate for several hours after neutralization with protamine. Nevertheless, associations between heparin recirculation and postoperative bleeding are controversial.^{14–16} More recent reports have highlighted the differences among heparin brands in terms of potency^{9,11,13} and linked them with the risk of postoperative bleeding.¹¹

This analysis aimed to audit the observed increase in the incidence of postoperative bleeding after adult cardiac surgery that occurred at a British tertiary cardiothoracic center. It investigated whether the increase in postoperative bleeding was due to a higher potency of the new heparin brand or to excessive heparin recirculation.

Methods

This was a retrospective cohort analysis, auditing the observed increase in the incidence of postoperative bleeding after adult cardiac surgery at the beginning of 2012 at the Royal Brompton Hospital London, UK. The investigation used data from all cardiac procedures performed between August 1, 2011, and April 30, 2012, stored in the institutional database. The heparin brand was switched from Heparin Leo (LEO Pharma, Ballerup, Denmark) to Heparin Wockhard (Wockhardt, Wrexham, UK) starting December 20, 2011. The institutional Ethics Committee waived the need for specific patient consent with regard to the use of records for this research after the deidentification of patient information.

Demographic characteristics, medical history, and prior medication, intraoperative, postoperative, and survival data were extracted from the institutional database. The institutional protocol was to induce anesthesia with a combination of fentanyl, propofol, or sodium thiopental and maintain with fentanyl and propofol. Tranexamic acid was administered before and during CPB. The initial heparin loading dose ranged between 300 and 400 IU/kg to achieve systemic heparinization. The activated clotting time (ACT) was used as a monitor of intraoperative heparinization in whole-blood samples by means of a Hepcon (HEP) System (Medtronic, Minneapolis, MN), located in the operating room. Additional heparin was given if the ACT was < 450 seconds before CPB. Nonpulsatile CPB was performed in moderate hypothermic conditions in all patients. Cardiomy suction was used in all patients, and cardiomy blood was treated by cell salvage and transfused. Protamine was administered to neutralize heparin after CPB. Heparin reversal first was assessed using the ACT and by the activated partial thromboplastin time (aPTT).

Additional tests for the detection of residual plasma heparin were performed at the physician's discretion—thromboelastography (TEG) and/or plasma heparin concentration measurements (HEP). TEG was performed using a TEG 5000 Hemostasis Analyser System (Haemonetics, Braintree, MA). Whole-blood samples (360 μ L) were placed into 2 cuvettes containing, respectively, kaolin and kaolin with heparinase. The ratio between non-heparinase R and heparinase-modified R (R/HR) was taken to be a measure of residual plasma heparin. Plasma heparin concentration was assessed using the anti-factor X activity (anti-FXa). Most anti-Xa assays were performed on the day after surgery, whereas most TEG assays were performed within the first hours after bypass (the TEG analyzer was located in the operating room). All coagulation tests performed within 24 hours of CPB (ie, in the operating room, on admission to the intensive care unit, and on the day after surgery) were collected for this analysis. Allogeneic packed red blood cells were administered if the hematocrit value was < 21% to 25%. Fresh frozen plasma was infused if, in the presence of significant bleeding, abnormal values for prothrombin time, international normalized ratio, or TEG parameters were noted after protamine administration. Platelet concentrates were transfused at the physician's discretion in the presence of bleeding. The anticoagulation protocol, the transfusion protocol, and monitoring were the same across the inclusion period.

Statistical Analysis

Patient data were separated into the following 2 groups: patients who underwent surgery with bypass before December 20, 2011 (the before group), and those who underwent surgery starting December 20, 2011 (the after group). Demographic, preoperative, intraoperative, and postoperative data were compared between groups using the Student *t*-test, the Mann Whitney test, or the chi-square test, as appropriate. Postoperative bleeding was defined as the upper decile of the postoperative chest tube drainages within 6 hours of CPB. Plasma heparin is detected using anti-FXa assay > 0.01 IU/L and whole-blood heparin by an R/HR ratio 10% above normal. Nevertheless, because the analysis of the literature failed to identify a threshold for the definition of heparin recirculation, anti-FXa and R/HR ratios were analyzed as continuous variables.

Associations among postoperative bleeding, heparin brand, and heparin recirculation were explored using nested logistic regression models. The models included as predictors of bleeding either the heparin brand (the brand model) or heparin recirculation. Heparin recirculation was assessed using the anti-FXa level or the R/HR ratio, generating 2 recirculation models (the HEP and the TEG models). Another 2 models included both the brand and the recirculation variables (the brand + HEP and the brand + TEG models). Then the likelihood ratio chi-square statistic for nested models¹⁷ was used to explore the added predictive value of the recirculation variables when included in the brand model and the added predictive value of the brand when included in the recirculation models. If bleeding was due to heparin brand alone, then adding

Download English Version:

<https://daneshyari.com/en/article/5582259>

Download Persian Version:

<https://daneshyari.com/article/5582259>

[Daneshyari.com](https://daneshyari.com)