Thrombosis Research 153 (2017) 85–89

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Full Length Article

Predictors of postoperative bleeding in children undergoing cardiopulmonary bypass: A preliminary Italian study

Luca Spiezia [a], Guido Di Gregorio [b], Elena Campello [a], Sara Maggiolo [a], Giacomo Bortolussi [c], Giovanni Stellin [c], Paolo Simioni [a,*], Vladimiro Vida [c]

[a] Thrombotic and Haemorrhagic Diseases Unit, Department of Medicine, University of Padua, Padua, Italy
[b] Cardiac Anaesthesia Unit, Department of Medicine, University of Padua, Padua, Italy
[c] Paediatric and Congenital Cardiac Surgery Unit, Department of Cardiac, Thoracic and Vascular Sciences, University of Padua, Padua, Italy

ARTICLE INFO

Article history:
Received 8 January 2017
Received in revised form 15 March 2017
Accepted 21 March 2017
Available online 22 March 2017

Keywords:
Cardiac surgical procedures
Consumptive coagulopathy
Haemorrhage

ABSTRACT

Background: Several characteristics such as demographics, pre-existing conditions, surgical procedure, perioperative coagulopathy may predispose children undergoing cardiopulmonary bypass (CPB) to bleeding complications. As yet, studies on risk factors for postoperative bleeding have brought mixed results. The purpose of our study was therefore to retrospectively evaluate the parameters able to predict postoperative bleeding in a group of consecutive children undergoing cardiac surgery involving CPB.

Methods: We collected demographic and perioperative laboratory data, as well as intraoperative transfusion requirements and blood loss during the first 24 h after surgery in a group of consecutive children (aged ≥1 month) scheduled for cardiac surgery with CPB at Padua University Hospital between June 2014 and April 2015. Cases were patients who experienced a 24-h postoperative blood loss ≥80th percentile. Univariate and multivariate logistic regression analyses were performed to determine the independent parameters associated with a high 24-h postoperative chest tube drainage volume.

Results: Eighty-three children (M:F 38:45; age range 1–168 months) were enrolled. Age < 7.7 months (p 0.015), postoperative platelets $<109 \times 10^9$/L (p 0.003) and postoperative D-dimer ≥2350 μg/L (p 0.007) were the variables most significantly and independently associated with excessive 24-h postoperative blood loss.

Conclusions: Although preliminary, our study identified younger age, lower postoperative platelet count and higher D-dimer plasma levels as possible risk factors for postoperative bleeding. As for coagulation parameters, our results suggested consumptive coagulopathy might cause a strong predisposition to postoperative bleeding in children. Large-scale prospective studies would provide insight into the early diagnosis and treatment of CPB-related coagulopathies.

1. Introduction

Children undergoing cardiac surgery with cardiopulmonary bypass (CPB) have an increased bleeding risk [1]. As a result, these patients require higher transfusion rates and are associated with higher morbidity and mortality rates [2]. Multiple concomitant mechanisms are involved in the development of the hypocoagulable state that fosters bleeding-related complications [3]. The main factors which concur to generate the acquired postoperative coagulopathy are: a) the patients' demographics and pre-existing/underlying conditions (e.g. age < 12 months and/or weight < 8 kg, cyanotic heart disease, etc.); b) the complexity and the duration of the surgery; c) the CPB procedure itself which activates the haemostatic system; d) hypothermia; e) blood dilution; and f) massive anticoagulation. In regard to the identification of CPB-related coagulopathies, traditional coagulation parameters are used in concert with whole blood point-of-care (POC) techniques such as thromboelastometry/graphy which are bed-side whole blood viscoelastic monitoring systems able to overcome some of the limitations faced while using more traditional coagulation tests [4]. Specifically, thromboelastometry/graphy allows to simultaneously study the integrated interactions among the different components (red blood cells, platelets, leukocytes and plasmatic factors) involved in the dynamics of clot formation, stabilization and lysis. The benefits of these tests are twofold: i) the identification of CPB-related coagulopathies [5–7]; ii) the management of perioperative bleeding complications [8–11].

Several studies have been published on the possible involvement of various factors (e.g. patients' demographics, pre-existing conditions, surgical procedure, pre- and postoperative traditional laboratory parameters and POC tests, and intraoperative transfusion rates) in determining a predisposition to postoperative bleeding in children

* Corresponding author at: Thrombotic and Haemorrhagic Diseases Unit, Department of Medicine, University of Padua, Via Giustiniani 2, 35128 Padua, Italy.
E-mail address: paolo.simioni@unipd.it (P. Simioni).

http://dx.doi.org/10.1016/j.thromres.2017.03.021
0049-3848/

undergoing cardiac surgery with CPB. However, the results have all been inconclusive [12–18]. The aim of our study was therefore to identify the parameters capable of predicting the 24-h postoperative drainage volumes from chest tube in relation to demographic and surgical characteristics, in a group of consecutive children undergoing cardiac surgery with CPB.

2. Methods

2.1. Data collection

Upon notification of the Ethical Committee of the Padua Hospital, Padua, Italy, we performed a retrospective analysis of medical records and computerized hospital data of all consecutive patients (age range from 1 month up to 14 years) who underwent elective CPB surgery in our Paediatric and Congenital Cardiac Surgery Unit between June 2014 and April 2015. Exclusion criteria were: congenital coagulation disorders, severe liver and/or kidney dysfunction, emergency procedures, reoperations, Jehovah's witnesses beliefs and incomplete blood samples data. Aspirin, when used, was discontinued 24 h before surgery. We gathered demographic characteristics, surgical data, perioperative transfusion requirements and blood loss volumes during the first 24 h for each enrolled patient. Clinically significant postoperative bleeding was defined as drainage volume from chest tube ≥16 mL/kg during the first 24 h after surgery, which corresponds to the 80th percentile of the blood loss in our population. Cases were children who experienced a 24-h postoperative blood loss volume ≥ 16 mL/kg and controls those with a 24-h postoperative blood loss volume < 16 mL/kg.

2.2. Blood samples and laboratory tests

Blood samples were obtained from each patient at two different time points: a) at least 30 min prior to surgical incision; b) within 15 min after reaching an activated clotting time (ACT) value <150 s. Two BD vacutainer tubes (Becton Dickinson, Franklin Lakes, New jersey) containing sodium citrate 109 Mmol/L (3.8% sodium citrate) and one containing Ethylenediaminetetraacetic acid (EDTA) 5.4 mg were collected. White Blood Cells (WBC, $\times 10^9$/L), haemoglobin (Hb, g/L), haematocrit (Hct, %), platelet count (Plts, $\times 10^9$/L), prothrombin time (PT, %), activated partial thromboplastin time (aPTT, *sec*), fibrinogen (Fibr, mg/dL), antithrombin (AT, %) and D-dimer (μg/L) were performed according to the standard procedures. The INTEM, EXTEM and FIBTEM assays were obtained through the ROTEM® apparatus (Tem International GmbH, München, Germany). The following ROTEM® parameters were considered: i) Clotting time (CT, *sec*), the time from the beginning of the coagulation analysis until an increase in amplitude of 2 mm; ii) Clot Formation Time (CFT, *sec*), the time elapsed for an increase in amplitude of the thromboelastogram from 2 to 20 mm. The CFT reflects the measurement of the propagation phase of whole blood clot formation; iii) Maximum Clot Firmness (MCF, mm), the maximum amplitude in millimetres reached in thromboelastogram; iv) Maximum lysis (ML, %), defined as the ratio between the lowest amplitude after reaching MCF and the MCF itself.

2.3. Anaesthesia and blood products management

The same team of paediatric heart surgeons and anaesthetists in accordance with the institutional protocols managed all patients enrolled in the study. In particular, anaesthesia was induced with intravenous fentanyl (5–10 mcg/kg), sodium thiopental (3 mg/kg) and rocuronium bromide (0.6 mg/kg). The maintenance was achieved with a continuous pump of midazolam (0.5 mg/kg/h), fentanyl (2 mcg/kg/h) and cisatracurium (0.2 mg/kg/h). Before aortic cannulation, 300 IU/kg unfractionated heparin (UFH) was administered to achieve an ACT >400 s; at the end of CPB, UFH was reversed with protamine to achieve an ACT <150 s. The priming solution consisted of crystalloid fluid (normal saline solution with Na-gluconate, Fresenius Kabi, Verona, Italy), 18% mannitol (weight/0.036), sodium bicarbonate (1 mL/kg if hematic prime) and packed red blood cells (RBCs) to achieve a predictive Hct value of 30% after dilution, for children weighing up to 10 kg. No blood products were added to the priming solution for patients weighing over 10 kg. In order to maintain the colloid oncotic pressure in all patients, 20% human albumin (50 mL) was added to the priming solution. Tranexamic acid (median dosage 5 mg/Kg) was administered either before surgery or after CPB at the discretion of the anaesthetists. The transfusion regiments during the procedure were based on blood loss volumes, surgical field assessment and laboratory tests. Weaning from CPB was initiated after patients had been rewarmed to a rectal temperature > 36 °C upon which modified ultrafiltration was performed to achieve an Hct >30%. After the termination of the CPB, packed RBCs were administered to either achieve an Hct >24% or arterial oxygen saturation > 90%. The surgeons and the anaesthetists relied on the thromboelastometry profiles [19] of bleeding children to manage the postoperative transfusion of platelet concentrates, Fresh Frozen Plasma (FFP) and fibrinogen. In particular, i) 40 mg/kg of fibrinogen was administered to patients with MCF in FIBTEM <9 mm; ii) 10–15 cm^3/kg of FFP to patients with CT prolongation in INTEM and/or EXTEM; iii) 10 mL/kg of platelets to patients with MCF in INTEM and/or EXTEM <40 mm and with MCF in FIBTEM >10 mm.

3. Statistical analysis

Data were analysed using the PASW Statistics 17.0.2 (SPSS Inc.) for Windows. Continuous variables are expressed as mean ± standard deviation (SD). Categorical variables are presented as number and

Table 1
Demographics, surgical data and blood products use.

	Bleeders	Non-bleeders	*p*-Value
Patients, n	19	64	–
Age, months (range)	16.4 (2.9–128)	43.2 (1.1–160)	**0.004**
Male, n (%)	7 (37)	31 (48)	0.37
Weight, kg	8.3 ± 6.9	14.2 ± 11.8	**0.01**
Cyanotic disease, n (%)	7 (37)	16 (25)	0.31
SpO_2, %	88 ± 11	92 ± 9	0.17
Aortic clamp duration, min	85 ± 43	62 ± 32	0.08
CPB duration, min	158 ± 95	106 ± 45	**0.036**
RACHS, n	3 ± 1	2 ± 1	0.08
Aspirin before surgery, n (%)	3 (16)	5 (8)	0.28
RBCs prime, n (%)	14 (74)	25 (39)	**0.008**
Tranexamic acid, n (%)			
Before CPB	2 (11)	14 (22)	0.27
After protamine	2 (11)	10 (16)	0.58
Patients exposed to BP, n (%)			
Intraoperative			
RBCs	13 (68)	29 (45)	0.08
FFP	11 (58)	17 (27)	**0.011**
Platelet	3 (16)	2 (3)	**0.041**
Fibrinogen	2 (11)	16 (25)	0.18
Postoperative (first 24 h)			
RBCs	14 (74)	17 (27)	<**0.001**
FFP	14 (74)	16 (25)	<**0.001**
Platelet	0	2 (3)	–
Fibrinogen	5 (26)	3 (5)	**0.005**
Amount of BP given, mL/kg			
Intraoperative			
RBCs	46.8 ± 37.8	31.3 ± 24.4	0.19
FFP	30.7 ± 10.8	27.3 ± 21.1	0.58
Platelets	5.1 ± 0.2	7.5 ± 3.5	0.51
Fibrinogen, mg/kg	25.4 ± 18.3	39.3 ± 23.1	0.46
Postoperative (first 24 h)			
RBCs	20.2 ± 10.6	10.3 ± 6.0	**0.006**
FFP	30.0 ± 19.3	12.1 ± 8.2	**0.005**
Platelets	–	13.0 ± 1.2	–
Fibrinogen, mg/kg	46.0 ± 25.9	31.5 ± 9.1	0.30

SpO_2, oxygen saturation; CPB, cardiopulmonary bypass; BP, blood products; RBCs, red blood cells; FFP, fresh frozen plasma. Numbers indicate mean ± standard deviation unless stated otherwise. Values in bold show statistical significance.