Patient Blood Management in Craniosynostosis Surgery

Claudine Kumba (claudine.kumba@gmail.com)
Hôpital Universitaire Necker Enfants Malades, Assistance Publique Hôpitaux de Paris, APHP, Université de Paris

Short Report

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Abstract

Background: Craniosynostosis surgery is one of the most hemorrhagic interventions, where transfusion rates vary from 20 to 100% depending on the study.

Objective: To describe intraoperative and postoperative outcomes in a secondary analysis of children who underwent craniosynostosis surgery included in the initial retrospective study with the aim of proposing intraoperative implementation optimization protocols for postoperative outcome improvement.

Methods: Secondary analysis. The study was approved by the Ethics Committee.

Results: There were 69 children with a median age of 10 [0-207] months.

Eight (11.6%) patients had intraoperative and/or postoperative complications. One patient (1.5%) had intraoperative hemorrhagic shock, and two patients (2.9%) had intraoperative broncholaryngospasm. One patient (1.5%) had postoperative anaphylaxis. One patient (1.5%) had postoperative hemorrhagic shock. One patient (1.5%) had postoperative respiratory failure. Two patients (2.9%) had postoperative neurologic failure. One patient (1.5%) had neuro-meningeal sepsis. One patient (1.5%) had a re-operation. There was no in-hospital mortality.

Fourty-eight patients (69.6%) had intraoperative transfusions.

Conclusion: Transfusion protocols guided with point-of-care tests should be included in patient blood management programs in craniosynostosis surgery.

Introduction

Cranial vault remodeling surgery is one of the most hemorrhagic interventions where transfusion rates vary from 20 to 100% depending on studies (1, 2, 3). Depending on the type of craniosynostosis, intraoperative blood loss has been reported to be higher in syndromic cranial vault remodeling where venous anomalies play a major role in this outcome (4, 5). Tranexamic acid and higher fibrinogen levels have demonstrated reduction in transfusion requirements and blood loss in craniosynostosis surgery (6, 7).

It has been reported that transfusion with all types of blood products was one of the independent predictors of adverse postoperative outcome in terms of morbidity and length of hospital stay (8, 9). Hospitalization costs were increased in transfused patients than in non-transfused (10). Preoperative, intraoperative and postoperative hemoglobin levels have been correlated to postoperative morbidity, length of hospital stay and length of mechanical ventilation in surgical pediatric patients (11). Transfusion can be a necessary therapeutic intervention in hemorrhagic settings and it is important to assess the benefits and risks when deciding to administer blood product in patients. Several physiopathology mechanisms underly adverse outcomes correlated to transfusion (12). Firstly, transfusion can be related to infectious risks due to transfusion-transmitted viruses, bacterial

contamination, vector-borne bacteria, parasites and prions (12). Secondly, transfusion can be related to immunological risks which can lead to transfusion-related acute injury known as TRALI; immunological risks can lead to febrile nonhemolytic transfusion reactions, to allergic and anaphylactic reactions, hemolytic transfusion reactions, transfusion-related immunomodulation known as TRIM, posttransfusion purpura and transfusion associated graft versus host disease (12).

Finally, transfusion can be related to non-infectious and non-immunological risks which can be due to mis-transfusion, can express as transfusion-associated circulatory overload known as TACO and as coagulopathy complications in massive transfusion (12).

The incidence of transfusion related acute lung injury in critically ill patients has been reported to be 6.9%. Reported predictors of TRALI were mechanical ventilation, sepsis and high risk of mortality ill score (13). The hypothesis underlying TRALI is the presence of antibodies or other inflammation mediators in blood products (13).

Transfusion related immunomodulation is probably due to complex reactions which lead to a dual pro-inflammatory and immunosuppressive response (14).

Transfused patients are generally critically ill and critical illness is associated with acute inflammation and immunosuppression.

We described here intraoperative and postoperative outcomes in a secondary analysis of patients who underwent craniosynostosis surgery included in the initial retrospective study (9). This outcome description in this potential hemorrhagic setting had the objectives to propose intraoperative implementation optimization protocols for postoperative outcome improvement.

Methods And Materials

Secondary analysis of patients who underwent cranial vault remodeling in the initial retrospective study (9).

The study was approved by the Ethics Committee of Necker Enfants Malades University Hospital under the registration number 2017-CK-5-R1 on 21 March 2017.

Patients were retrospectively included from the 1 January 2014 to 17 May 2017.

Inclusion criteria were all children included in the initial study and who underwent craniosynostosis surgery and age less than 18 years old.

Exclusion criteria were patients included in the initial study who did not undergo craniosynostosis surgery and aged more than 18 years old.

Statistics were analyzed with XLSTAT 2020.4.1. software. Continuous variables were expressed as medians with ranges or means with standard deviations. Categorial variables were described in

proportions.

In our hospital, patients who underwent craniosynostosis surgery were managed intraoperatively according to a defined protocol. All patients were monitored with an arterial and central venous catheter, an indwelling bladder catheter, a naso-gastric tubing, a high-volume fluid administrating device, a Bair Hugger®, a core temperature probe. Induction of anesthesia was performed with sevoflurane, sufentanil at 0.3–0.5 µg/kg bolus intravenously (IV) with a short acting non-depolarizing muscle relaxant such atracurium at 0.5 mg/kg bolus IV. Airway was secured with oro-tracheal intubation. Antibiotic prophylaxis was performed with cefazolin at 50 mg/kg bolus IV. Maintenance of anesthesia was realized with sufentanil as an IV infusion of 0.3–0.5 µg/kg/h with sevoflurane. All patients received tranexamic acid as a 10mg/kg IV bolus followed by an IV infusion of 10mg/kg/h up-to 6 hours postoperatively. A maintenance infusion with a crystalloid (isopedia®) at 3 ml/kg/h if the patient weighed less than 10 kg and 5 ml/kg/h if the weight was above 10 kg. Hemoglobin levels were regulary assessed. Fluid therapy was managed by monitoring central venous pressure, arterial blood pressure and pulse pressure variation with colloids (voluven® or plasmion®) administered as 20–30 ml/kg bolus, packed red blood cells (PRBC) and albumin. Fresh frozen plasma (FFP) as 15 ml/kg and concentrated platelet units as 0.1–0.2 UI/kg (CUP) were administered if transfusion requirements were above the total circulating blood volume. The volume of transfused packed red blood cells was determined as followed: PRBC in ml = Target hematocrit levels-Initial hemotocrit levels/ Weight in kg.

After surgery, the patient was transferred sedated and intubated in the post-interventional care unit (PACU) or the pediatric intensive care unit (PICU) for surveillance.

Postoperative analgesia was realized with intravenous morphine and oral morphine, intravenous acetaminophen and intrarectal ibuprofen. Patients could start oral intake feeding 4 hours after extubation. Blood draining systems were removed on postoperative day 2. All patients received intravenously 5mg/kg iron (venofer®) as an infusion. Patients were discharged from the PICU when hemoglobin levels equaled or were above 12g/dL.

Results

Table illustrates the general characteristics.

There were 69 children with a median age of 10 [0-207] months. There were thirty-six (52.2%), sixteen (23.2%), fourteen (20.3%) and three (4.3%) American Society of Anesthesiologists grade one, two, three and four patients, respectively. Four (5.8%) patients had emergency intervention, and sixty-five (94.2%) had elective surgery. Eight (11.6%) patients had intraoperative and/or postoperative complications. One patient (1.5%) had intraoperative hemorrhagic shock, and two patients (2.9%) had intraoperative broncholaryngospasm. One patient (1.5%) had postoperative anaphylaxis. One patient (1.5%) had postoperative hemorrhagic shock. One patient (1.5%) had postoperative respiratory failure. Two patients (2.9%) had postoperative neurologic failure. One patient (1.5%) had neuro-meningeal sepsis. One patient (1.5%) had a re-operation.

There was no in-hospital mortality.

Fourty-eight patients (69.6%) had intraoperative transfusion with PRBC, FFP or CUP.

Median PRBC volume was 1[0-4] units. The median FFP volume was 0[0-2] units, and the median CUP volume was 0[0-2] units. The mean preoperative hemoglobin level was 12.0±1.2 g/dL, and the mean postoperative hemoglobin level was 11.6±1.6 g/dL.

Median crystalloid volume was 0[0-1000] ml. Median colloid volume was 250[30-2050] ml.

The median length of intensive care unit stay (LOSICU) was 3[1-90] days. The median length of hospital stay (LOS) was 2[0-8] days. The median total length of hospital stay (LOSICU+LOS=TLOS) was 5[2-90] days. The median length of mechanical ventilation (LMV) was 0[0-79] days.

Table 2 illustrates co-morbidities.

The most common comorbidity was Crouzon syndrome in six patients (8.7%), followed by obstructive apneic syndrome in three patients (4.3%), Apert syndrome, asthma, Chiari's malformation, congenital heart disease, and former preterm birth in two patients (2.9%).

Discussion

Intra-operative transfusion rate in this secondary cohort was 69.6%. Most of the patients received PRBC and or FFP units. Cranial vault modeling being a potential hemorrhagic surgery, intraoperative transfusion with point of care viscoelastic assays need to be included in patients who undergo this intervention. It has been proven that point of care tests to guide transfusion in hemorrhagic surgery like craniosynostosis reduce transfusion requirements (6, 15, 16). Figures 1 to 3 illustrate algorithms with rotational thromboelastometry (ROTEM) in different age groups. ROTEM parameters in children have been described with ROTEM delta version (17). These algorithms can be applied in other potential hemorrhagic settings to guide blood product administration (18, 19). In this secondary cohort, intra-operative hemorrhagic shock rate was 1.5%. Syndromic craniosynostosis has been reported to be correlated to higher intraoperative blood loss emphasizing the necessity of integrating point of care tests for transfusion optimization in these patients (4). Cranial vault surgery concerns most of the time small infants, blood loss in these patients can occur acutely and rapidly thus anticipating this situation is mandatory. Rates of intraoperative hemorrhagic shock in children vary according to surgical settings and age and has been reported to vary between 0 to 5.6% (20, 21, 22, 23, 24, 24). In small children blood product requirements can rapidly reach total circulating blood volume and massive transfusion is very likely in potential hemorrhagic situations. Transfusion and massive blood product administration are predictors of adverse postoperative outcome which have to be put into balance with the risk of anemia which is also a predictor of postoperative unfavorable evolution in surgical children (10, 11, 12, 13, 14, 25, 26, 27). Preoperative and intraoperative hemoglobin levels have been negatively correlated to postoperative outcome and LOS with low preoperative hemoglobin levels below 6 g/dL and intraoperative

hemoglobin levels below 5g/dL being related to higher LOS (11). Postoperative hemoglobin levels have been positively correlated to LMV with hemoglobin levels higher than 12 g/dL being related to higher LMV. Restrictive transfusion strategies compared to liberal strategies in critically ill patients did not increase adverse outcome. Maintaining a hemoglobin level target of 12 g/dL or more maybe not necessary in all patients and should be assessed according to patients global status and co-existing co-morbidities like congenital heart disease, prematurity, sepsis etc…

Preoperative erythropoietin has been reported to reduce blood product transfusion in craniosynostosis surgery, integrating this molecule with iron supplementation in blood transfusion management protocols in this surgery could contribute to reduce the rate of intraoperative transfusions (29).

Crystalloid and colloid fluid therapy just like transfusion need to be guided with validated variables and tools in the pediatric population for optimal fluid and hemodynamic management (30, 31, 32, 33).

Conclusion

Transfusion protocols guided with point of care tests should be included in patient blood management programs in craniosynostosis surgery. Targeting higher postoperative hemoglobin levels in all patients is not necessary and should be assessed depending on patient co-morbidities. Restrictive transfusion strategies are alternatives to liberal practices to reduce transfusion rates.

Declarations

Conflict of Interest: The author declared no conflicts of interest.

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Author contributions: Claudine Kumba conceptualized and designed the study and drafted the initial manuscript. She designed the data collection instruments, collected data, carried out initial and final analyses.

Ethics Approval: This study received approval from the Ethics Committee of Necker on 21 March 2017 under registration number 2017-CK-5-R1 and waived patient consent.

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Tables

Table 1 General characteristics

Characteristic	N=69
Median age months [range]	10 [0-207]
ASA I n (%)	36 (52.2)
ASA II n (%)	16 (23.2)
ASA III n (%)	14 (20.3)
ASA IV n (%)	3 (4.3)
Emergency surgery n (%)	4 (5.8)
Elective surgery n (%)	65 (94.2)
Re-operation n (%)	1 (1.5)
Patients with intra-operative and or postoperative complications (organ failure or sepsis) n (%)	8 (11.6)
Intra-operative hemorrhagic shock n (%)	1 (1.5)
Intra-operative broncho-laryngospasm n (%)	2 (2.9)
Postoperative anaphylaxis n (%)	1 (1.5)
Postoperative hemorrhagic shock n (%)	1 (1.5)
Postoperative respiratory failure n (%)	1 (1.5)
Postoperative neurologic failure n (%)	2 (2.9)
Postoperative neuro-meningeal sepsis n (%)	1 (1.5)
In-hospital mortality n (%)	0 (0)
Transfusion n (%)	48 (69.6)
Median packed red blood cells units [range]	1 [0-4]
Median fresh frozen plasma volume units [range]	0 [0-2]
Median concentrated platelet units [range]	0 [0-2]
Mean preoperative hemoglobin levels ± standard deviation in g/dL	12.0±1.2
Mean postoperative hemoglobin levels ± standard deviation in g/dL	11.6±1.6
Median crystalloid volume in ml [range]	0[0-1000]
Median colloid volume in ml [range]	250[30-2050]
Median length of intensive care unit stay in days [range]	3[1-90]
Median length of hospital stay in days [range]	2[0-8]
Median total length of hospital stay in days [range]	5[2-90]
Median total length of mechanical ventilation in days [range]	0[0-79]

Table 2 Co-morbidities

bidity	Number of patients (%)
-Chotzen syndrome	1(1.5)
formation syndrome with congenital heart disease tabolic disease	1(1.5)
yndrome	2(2.9)
oid cyst	1(1.5)
	2(2.9)
malformation	2(2.9)
ital coagulation disorder	1(1.5)
ital heart disease	2(2.9)
ı syndrome	6(8.7)
y	1(1.5)
pre-term	2(2.9)
ebral tumor	1(1.5)
tive apneic syndrome	3(4.3)
sm	1(1.5)
omalacia	1(1.5)

Figures

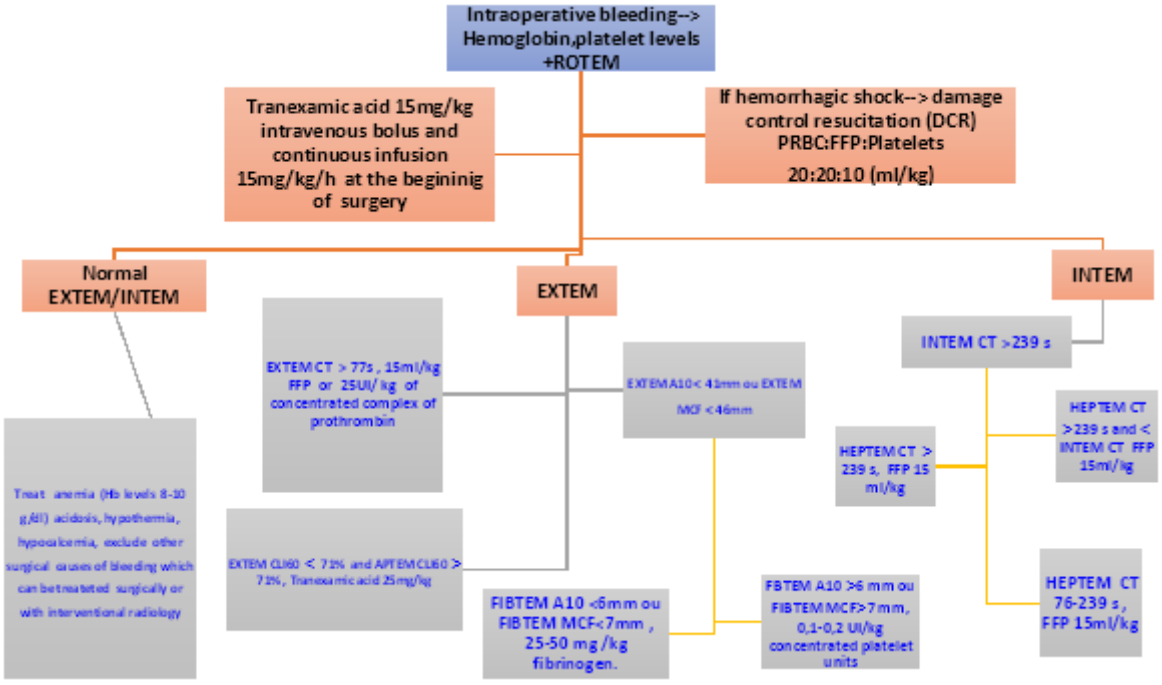

Figure 1

ROTEM algorithm in children between enfant 0-24 months. CT=coagulation time in seconds, A10= clot firmness at 10 minutes, MCF =maximum clot firmness, CLI60= lysis index in % 60 minutes after CT, ML= maximum lysis in %, FFP=fresh frozen plasma, PRBC=packed red blood cells, Hb=hemoglobin

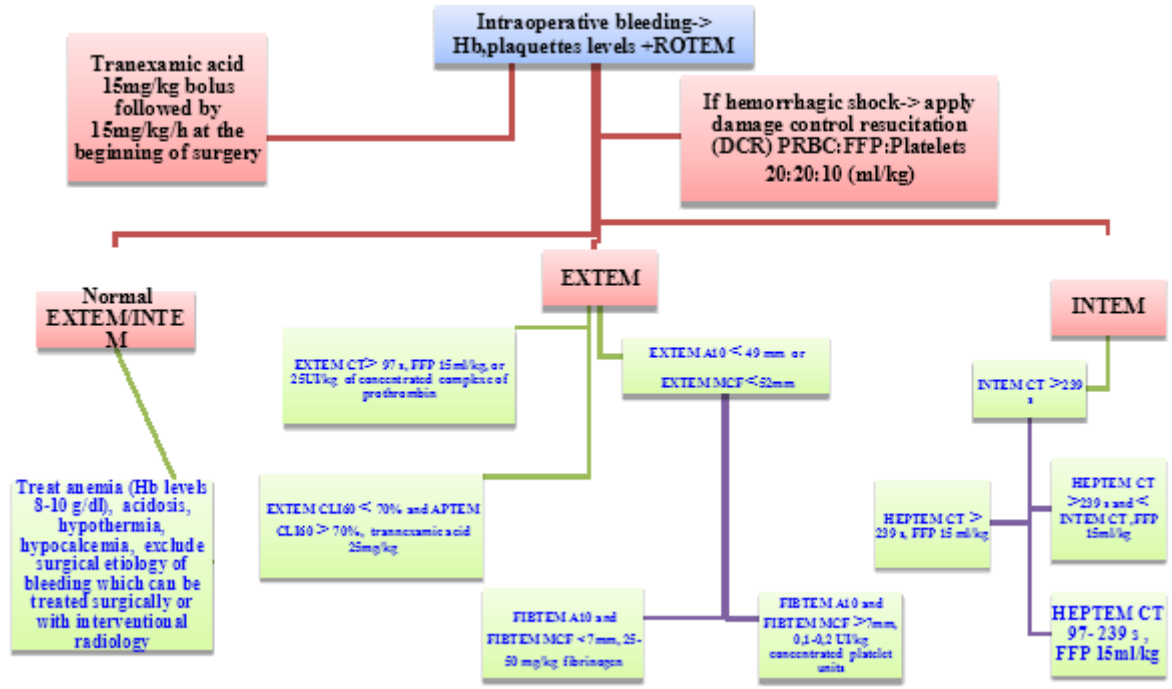

Figure 2

ROTEM Algorithm in children 2-16 years. CT=coagulation time in seconds, A10= clot firmness after 10 minutes, MCF =maximum clot firmness, CLI60= lysis index in % 60 minutes after CT, ML= maximum lysis in %, FFP=fresh frozen plasma, PRBC=packed red blood cells, Hb=hemoglobin

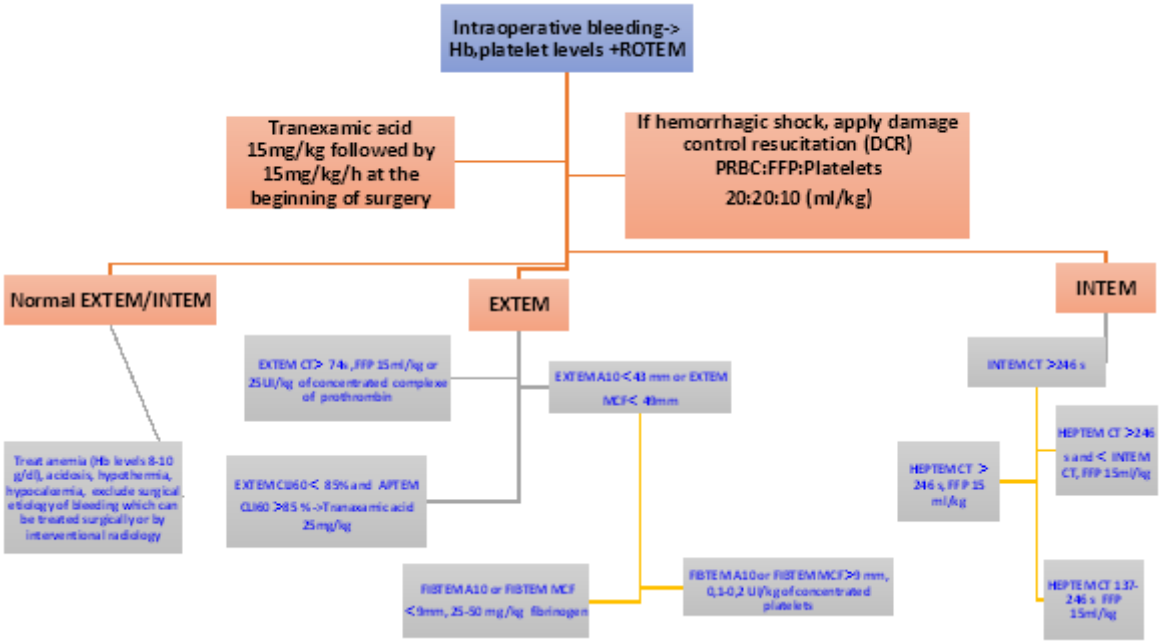

Figure 3

ROTEM Algorithm >16 years. CT=coagulation time in seconds, A10= clot firmness at 10 minutes, MCF =maximum clot firmness, CLI60= lysis index in % 60 minutes after CT, ML= maximum lysis in %, FFP=fresh frozen plasma, PRBC=packed red blood cells, Hb=hemoglobin