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Enhanced Recovery Protocol after Fronto-orbital Advancement Reduces Transfusions, Narcotic Usage, and Length of Stay

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Background: Enhanced recovery after surgery (ERAS) protocols utilize multi-modal approaches to decrease morbidity, narcotic usage, and length of stay. In 2013, we made several changes to our perioperative approach to children undergoing complex craniofacial procedures. The goal of this study was to analyze our protocol for children undergoing fronto-orbital advancement (FOA) for craniosynostosis.
Methods: A retrospective chart review was performed after IRB approval, for children who underwent fronto-orbital advancement for craniosynostosis from 2010 to 2018. The ERAS protocol, initiated in December 2013, involves hemoglobin optimization, cell-saver technology, tranexamic acid, specific postoperative fluid titration, and a transfusion algorithm. The analgesic regimen focuses on narcotic reduction through the utilization of scheduled acetaminophen, ibuprofen, or ketorolac, and a dexmedetomidine infusion with opioids only for breakthrough pain.
Results: Fifty-five ERAS protocol children and 23 control children were analyzed. ERAS children had a decreased rate (13/53 versus 23/23, $P < 0.0001$) and volume of intraoperative transfusion (183.4 mL versus 339.8 mL, $P = 0.05$). Fewer ERAS children required morphine/dilaudid (12/55 versus 22/23 $P < 0.0001$) and for children who required morphine, fewer doses were required (2.8 versus 11, $P = 0.02$). For ERAS protocol children who required PO narcotics, fewer doses were required (3.2 versus 5.3, $P = 0.02$). ERAS children had a decreased length of stay (2.3 versus 3.6 nights, $P < 0.0001$). No patients were re-admitted due to poor oral intake, pain, hemodynamic, or pulmonary concerns.
Conclusions: Our ERAS protocol demonstrated a reduction in the overall and intraoperative allogenic blood transfusion rate, narcotic use, and hospital length of stay. This is a safe and effective multimodal approach to managing complex craniofacial surgical recovery. *(Plast Reconstr Surg Glob Open 2020;8:e3205; doi: 10.1097/GOX.0000000000003205; Published online 28 October 2020.)*

INTRODUCTION

Enhanced recovery after surgery (ERAS) protocols utilize multi-modal approaches perioperatively, with the goal of decreasing patient morbidity, narcotic usage, and hospital length of stay to result in an improved patient experience.[1–5] ERAS protocols typically begin preoperatively with the deliverance of medications aimed at reducing postoperative nausea, emesis, and pain, as these factors have shown to increase the length of stay and negatively impact patient satisfaction.[6–8] Intraoperative interventions include the use of gabapentin and local anesthetic, as the utilization of a multimodal analgesia cocktail has been shown to decrease postoperative nausea, vomiting, drowsiness, and impaired sleep.[1,7–13] Although widely adopted in other fields of surgery, there have been minimal reports of ERAS implementation in plastic surgery [4,5,14–19] and there are few published reports analyzing the outcomes of these pathways in craniofacial surgery.

Craniosynostosis is commonly treated with 1 of the 2 main surgical approaches (strip craniectomy or cranial vault remodeling) that aim to treat the skull deformity and the negative effects of the growth restriction on development. Compared with the variety of strip-craniectomy–based procedures (isolated, spring-assisted, distraction), cranial vault remodeling may be associated with significant blood volume loss. Additionally, amongst cranial vault remodeling

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procedures, fronto-orbital advancement (FOA) has been associated with an increased rate of blood transfusions and a prolonged hospital length of stay.[20,21] There has yet to be a detailed report of management for complex craniofacial children from an anesthesia or intensive care perspective.[22,23] Additionally, most postoperative protocols rely on direct patient examination by a provider that may only occur at certain time points, such as morning rounds, which can delay decision-making and the advancement of a child's recovery. However, protocols and order sets that allow for decisions to be increasingly made by the bedside nursing team can allow for expedited changes based on the child's evolving recovery.

In 2013, our division made several changes to our perioperative approach for children undergoing complex craniofacial procedures. Our perioperative pathway and postoperative order set was analyzed with a focus on outcomes including rate and volume of blood transfusions, narcotic pain medication requirements, and hospital length of stay. The goal of this study was to analyze our experience in utilizing this protocol for children with craniosynostosis undergoing FOA.

METHODS

Chart Review

A retrospective chart review was performed after IRB approval for all children who underwent FOA for craniosynostosis from 2010 to 2018, with all staff surgeons. Charts were reviewed for patient demographics, preoperative hemodynamic optimization, operative course, intra- and postoperative resuscitation, postoperative pain medication requirements, length of stay, and perioperative hemoglobin levels. For continuous independent variables (eg, age), a non-parametric correlation analysis was performed. For discrete independent variables, either a chi-square or Kruskall-Wallis test was performed to assess for differences between cohorts.

Pre-enhanced Recovery after Surgery

The Enhanced Recovery after Surgery protocol was initiated in December 2013. Before ERAS introduction, preoperatively, patients did not receive iron supplementation or erythropoietin. Intraoperatively, cell saver (CS) was not utilized, there was not as much focus on maintaining a warm environment, and tranexamic acid (TXA) was not used. Postoperatively, acetaminophen and ibuprofen were not scheduled, dexmedetomidine was not used, and fluids were not titrated down rapidly based on high urine output (UOP). Additionally, there was no agreed upon transfusion threshold amongst the various team members involved in the care (plastic surgeons, neurosurgeons, anesthesiologists, and intensivists). This group of consecutive patients served as the control cohort.

Enhanced Recovery after Surgery

Preoperative

At a preoperative clinic visit, around 6 months of age, a baseline hemoglobin is obtained, and all children less than 18 months of age are offered recombinant EPO to increase red cell mass.[24] After obtaining informed consent, recombinant EPO (600 units/kg) is initiated 3 weeks before surgery, and on average, requires 2–3 weekly doses. Hemoglobin level is checked before each injection, and EPO is held when the level is ≥15g/dL. Baseline laboratory values, a complete blood count, coagulation panel, and basic metabolic panel are obtained preoperatively. In preparation for surgery, 20 mL/kg of packed red blood cells are prepared and divided into smaller aliquots (10 mL/kg per aliquot) to avoid over transfusion and waste, as well as to reduce donor exposures.

Intraoperative

Our team consists of 2 plastic surgeons and 2 neurosurgeons who work together routinely. Once the patient is under anesthesia, at least two proportionally large size peripheral IV catheters (≥22 gauge) are obtained to allow for volume resuscitation. Central venous access is not routinely secured unless adequate peripheral intravenous access cannot be obtained, as central venous pressure monitoring has not demonstrated any reduction in the frequency or duration of hypotension during cranial vault remodeling,[25] is consistently a poor predictor of fluid responsiveness in children,[26] and can be associated with significant complications.[27] An arterial line is inserted, typically utilizing the radial artery. Cefazolin at 50 mg/kg is used for surgical site infection prevention before incision and re-dosed every 3 hours. If the patient is allergic to penicillin/cephalosporin, clindamycin 10 mg/kg is chosen and re-dosed every 6 hours.

Care is exercised to ensure that the operating room is warmed to around 72°F. A radiant heater is utilized for infants during the induction period and line placement. The distance between the patient and the radiant heater is adjusted per manufacturer's recommendation to avoid over heating or skin burns. All children are positioned on an under-body forced air-warming mattress upon arrival to the operating room. An intravenous fluid/blood warmer is also used.

Cell-saver technology is utilized to recycle blood that is lost during the procedure. Additionally, CS allows for an objective measurement of blood loss with the understanding that not all blood can be captured by the machine, and thus, it is an underestimation. At one-fourth total blood volume loss, banked blood is brought to the operating room in a cooler even if it is not to be given. At one-third total blood volume loss, due to blood loss and dilution, and coagulation factors are checked. The final decision to transfuse is based on multiple factors, such as hematocrit, hemodynamics, UOP, stage of procedure, and the availability of CS. Factors contributing to this decision include hemoglobin < 6.5 g/dL and profuse and persistent bleeding. In addition, attempts are made to stay within 10%–15% of the preoperative vital signs. CS blood is always utilized preferentially over allogenic transfusions. UOP is also monitored and maintained at 1 mL/kg per hour at minimum. We utilize TXA at a loading dose of a 25 mg/kg infusion over 15 min, followed by an infusion of 5 mg/kg per hour until closure. A dexmedetomidine drip is initiated at closing and continued postoperatively. Postoperatively, the drip is titrated to effect and maintained until the first postoperative morning.

Postoperative Approach

Children typically spend 1 night in the pediatric intensive care unit (PICU), during which, continuous cardiorespiratory and pulse oximetry are monitored. Fluids are titrated by UOP, and maintenance fluids are discontinued for most patients by the morning after surgery before morning rounds. Perioperative antibiotics are continued for two postoperative doses. Scheduled acetaminophen is delivered at 15 mg/kg intravenously every 6 hours. Ketorolac or ibuprofen are given every 6 hours. The decision to give one over the other is at nursing discretion, as there is not a concern for postoperative hemorrhage.[28] Oxycodone and morphine are available and are given as needed at nursing discretion. Decision on which pain medication to utilize is nurse-driven and based on protocol parameters. The algorithm is summarized in Figure 1 and presented in Table 1.

RESULTS

Fifty-five children treated with the ERAS protocol, and 23 control children were analyzed. There was no difference between the cohorts in regard to sex, age, and weight at the time of surgery. All ERAS protocol children aged less than 18 months received EPO and 40 received TXA intraoperatively ($P < 0.0001$). There were no observed side effects to EPO ERAS protocol children received more crystalloid intraoperatively both volume and volume/kg ($P < 0.0001$). There was no difference in colloid resuscitation between the cohorts. Of the 55 ERAS protocol children, 54 received CS during surgery. There was no difference in estimated blood loss (EBL) between the cohorts. Fewer ERAS protocol children required blood transfusion intraoperatively, and those that did require transfusion required a lesser volume (13/55 versus 23/23, 183.4 mL versus 339.8 mL, $P < 0.0001$ and $P = 0.05$, respectively). There was no difference between the cohorts in regard to postoperative transfusion incidence or volume. ERAS protocol children had a higher preoperative hemoglobin (13.5 g/dL versus 12.5 g/dL, $P < 0.0001$), a lower postoperative hemoglobin (9.6 g/dL versus 11.7 g/dL, $P < 0.0001$), a lower nadir hemoglobin (8.7 g/dL versus 10.3 g/dL, $P < 0.0001$), and lower hemoglobin at discharge (9 g/dL versus 11.4 g/dLm, $P < 0.0001$). No patients were re-admitted due to poor oral intake, pain, and hemodynamic or pulmonary concerns. Patient results and demographics are presented in Table 2.

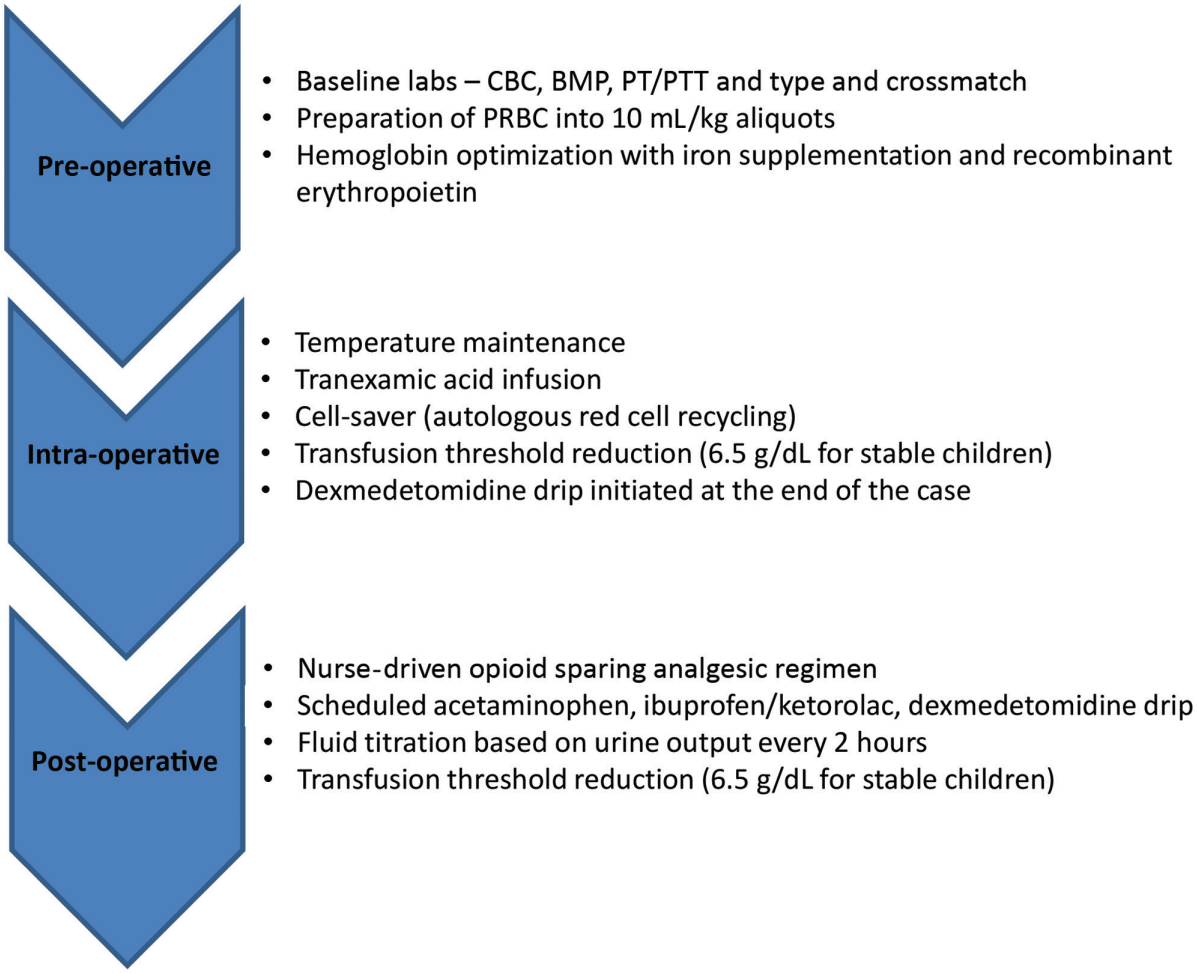

Fig. 1. Overview of the ERAS protocol.

Table 1. Postoperative Protocol for Patients after Craniosynostosis Surgery

POD	Location	Monitoring	Respiratory Status	Urine Output	Incision Care	Diet	Labs	Fluids	Medication	Expectations	Other
0	PICU	Continuous cardio-respiratory, pulse ox	FiO2: 40% via face shield for SAT < 93%. Decadron only if airway issues, up to 4 doses in 24 h	Foley catheter Make changes to IVF every 2 h; if less than 1 mL/kg/h, consider increasing IVF. If less than 2 mL/kg/h, decrease by half and then half again. If still >2 mL/kg/h, saline lock.	Clean with saline twice daily and cover with bacitracin/mupirocin.	Ad lib	CBC/BMP starting at 1800,0000. If Hg < 6.5, evaluate for diluted blood sample and repeat CBC. If not dilute, transfuse.	D5LR at maintenance rate	Ancef 30 mg/kg/dose for 2 doses q8h. Acetaminophen 15 mg/kg IV q6h. Ketorolac/ibuprofen: ketorolac 0.25 mg/kg IV q6h or ibuprofen 10 mg/kg PO q6h. Ativan 0.05 mg/kg IV up to 0.5 mg q6h for pain/anxiety if no dexmedetomidine. Oxycodone 0.05 mg/kg PO q6h prn. Morphine 0.05 mg/kg q4h prn, max 2–4 mg. Zofran 0.15 mg/kg IV q8h prn up to 4 mg. May add Phenergan 12.5 mg/kg IV.	Intermittent tachycardia without hypotension. UOP > 1 mg/kg/h. Purposeful movement of all extremities. Eyes unlikely to open completely. Significant edema/ecchymosis expected. Emesis not uncommon. No need to hold PO. Fevers not uncommon. No workup needed.	Head of bed at 30 degrees. Parents may hold when cleared by PICU staff.
1	PICU /transitional care	Continuous cardio-respiratory, pulse ox	FiO2: 40% via face shield for SAT < 93%.	Discontinue foley.	Clean with saline twice daily and cover with bacitracin/mupirocin.	Ad lib	CBC/BMP 0600. If Hg < 6.5, evaluate for diluted blood sample and repeat CBC. If not dilute, transfuse.	Saline lock	Acetaminophen 15 mg/kg PO q6h prn. Ketorolac/ibuprofen: ketorolac 0.25 mg/kg IV q6h or ibuprofen 10 mg/kg PO q6h. Try to stagger acetaminophen and ketorolac/ibuprofen every 3 h Ativan 0.05 mg/kg IV up to 0.5 mg q6h for pain/anxiety if no dexmedetomidine. Oxycodone 0.05 mg/kg PO q6h prn. Zofran 0.15 mg/kg IV q8h prn up to 4 mg. May add Phenergan 12.5 mg/kg IV.	Intermittent tachycardia without hypotension. UOP > 1 mg/kg/h Purposeful movement of all extremities. Eyes unlikely to open easily. Significant edema/ecchymosis expected. Emesis not uncommon. No need to hold PO. Fevers not uncommon. No workup needed.	Head of bed at 30 degrees. Parents may hold. Remove arterial line, extra IVs. Ok to transfer if no concerns and Hg > 6.5
2	Transitional care	Continuous cardio-respiratory, pulse ox	FiO2: 40% via face shield for SAT <93%.	Foley out	Shampoo lightly, do not comb	Ad lib	Not typically obtained	Saline lock	Acetaminophen 15 mg/kg PO q6h prn. Ketorolac/ibuprofen: ketorolac 0.25 mg/kg IV q6h or ibuprofen 10 mg/kg PO q6h. Oxycodone 0.05 mg/kg PO q6h prn. Zofran 0.15 mg/kg IV q8h prn up to 4 mg. May add Phenergan 12.5 mg/kg IV.	Intermittent tachycardia without hypotension. UOP > 1 mg/kg/h Purposeful movement of all extremities. Eyes unlikely to open. Peak edema/ecchymosis. Emesis not uncommon. No need to hold PO. Fevers not uncommon. No workup needed.	Discharge today if goals met (ie, pain controlled, vital signs stable, tolerating PO intake, parents amenable and ready)

Table 2. Patient Demographic and Results

Metric	ERAS (n = 55) (mean, range, SD)	Control (n = 23) (mean, range)	*P*
Men/Women	24 (43.6%)/21 (38.2%)	10 (43.5%)/13 (56.5%)	0.61
Age at surgery (years)	2.8, 0.6–16, 3.7	1.5, 0.3–6, 1.4	0.11
Weight at surgery (kg)	14.9, 6.3–67, 13.8	10.6, 6.1–27.1, 4.4	0.15
Patients receiving EPO	35 (63.6%)	0 (0%)	<0.0001*
Patients receiving TXA	40 (72.7%)	0 (0%)	<0.0001*
Patients receiving crystalloid	55 (100%)	23 (100%)	1
Crystalloid (mL)	1178.1, 370–3800, 691.1	519.8, 190–2100, 392.8	<0.0001*
Crystalloid (mL/kg)	91.4, 17.1–147.7, 26.6	49.4, 12.3–107.5, 26.1	<0.0001*
Patients receiving colloid	22 (40%)	10 (43.5%)	0.8
Colloid (mL)	185.9, 20–1000, 165.6	146.9, 50–350, 92.2	0.49
Colloid (mL/kg)	13.5, 1.9–26.9, 6.4	12.4, 5.9–27.6, 5.7	0.645
Patients receiving cell saver	54 (98.2%)	0 (0%)	<0.0001*
Cell saver (mL)	115.6, 14–586, 113.7	0	<0.0001*
Cell saver (mL/kg)	8.5, 1.8–37.7, 5.9	0	<0.0001*
EBL	322.7, 75–1400, 271.1	341.7, 100–1800, 345.7	0.80
EBL (mL/kg)	24.9, 5.3–77.3, 14.3	33, 11.5–141.7, 27.3	0.09
Patients receiving intraoperative transfusion	13 (23.6%)	23 (100%)	<0.0001*
Intraoperative transfusion (mL)	183.4, 80–300, 67.8	339.8, 75–1400, 268.3	0.05
Patients receiving postoperative transfusion	2 (3.6%)	4 (17.4%)	0.6
Postoperative transfusion (mL)	100, 70–130, 30	221.3, 115–500, 161.5	0.38
Patients receiving any transfusion	15 (27.2%)	23 (100%)	<0.0001*
Preoperative Hg	13.5, 10.9–15.7, 1.1	12.5, 10.9–13.8, 0.7	<0.0001*
Postoperative Hg immediate	9.6, 6.3–15.1, 1.7	11.7, 9.4–13.6, 1.2	<0.0001*
Lowest Hg	8.7, 6.3–14.2, 1.7	10.3, 5.7–13.5, 2.1	0.0007*
Discharge Hg	9, 6.4–14.2, 1.6	11.4, 8.1–13.5, 1.3	<0.0001*
Patients receiving ketorolac	22 (40%)	1 (0.7%)	<0.0001*
Patients receiving ibuprofen	55 (100%)	14 (60.9 %)	<0.0001*
Ibuprofen doses	5.4, 1–17, 3.2	6.9, 1–19, 5.2	0.18
Patients receiving morphine/dilaudid	12 (21.8%)	22 (95.7%)	<0.0001*
Morphine/dilaudid doses	2.8, 1–8, 1.8	11, 2–49, 11.9	0.02*
Patients receiving PO narcotics	36 (65.5%)	17 (73.9%)	0.6
PO narcotic doses	3.2, 1–12, 2.3	5.3, 1–15, 4.1	0.02*
LOS	2.3, 1–7, 0.8	3.6, 2–17, 3.2	0.006*
PICU stay	1.1, 1–4, 0.5	1.7, 1–14, 2.6	0.1

* $P < 0.05$

ERAS protocol children had a higher incidence of ketorolac and ibuprofen utilization ($P < 0.0001$), but for children who received ibuprofen, there was no difference in dosing. Fewer ERAS protocol children required morphine/dilaudid (12/55 versus 22/23, $P < 0.0001$), and for children who required morphine, fewer doses were required (2.8 versus 11, $P = 0.02$). There was no difference in the number of children who required PO narcotics, but for ERAS protocol children who required PO narcotics, fewer doses were required (3.2 versus 5.3, $P = 0.02$). ERAS protocol children had a decreased overall length of stay (2.3 versus 3.6 nights, $P < 0.0001$), but there was no difference in length of PICU stay (1.1 versus 1.7, $P = 0.1$). Patient results and demographics are presented in Table 2.

Subgroup analysis was performed between ERAS protocol children who did and did not require perioperative transfusion. There was no difference in age or weight at time of surgery between the cohorts. A similar number of children received EPO preoperatively. There was no difference in intraoperative resuscitation between the cohorts. EBL was higher in the cohort requiring transfusion (470 mL versus 287.5 mL, $P = 0.03$, 22 mL/kg versus 34.4 mL/kg, $P = 0.006$). Children who did not receive a transfusion trended toward a lower nadir hemoglobin (8.4 g/dL versus 9.4 g/dL, $P = 0.06$) and discharge hemoglobin was higher in children who received a transfusion (10.1 g/dL versus 8.7 g/dL, $P = 0.005$). Results are presented in Table 3.

To eliminate outliers in regard to age and patients undergoing secondary surgery, a subgroup analysis was also performed for children less than 18 months at the time of surgery. Thirty-five ERAS protocol children and 15 control children were analyzed. There was no difference between the cohorts in regard to sex, age, and weight at the time of surgery.

All ERAS protocol children received EPO and CS during surgery. There was no difference in EBL between the cohorts. Fewer ERAS protocol children required intraoperative blood transfusion (10/35 versus 15/15, $P < 0.0001$), and those that did require transfusion required a lesser volume (170 mL versus 282.3 mL, $P = 0.01$). There was no difference between the cohorts in regard to postoperative transfusion incidence or volume (2 children per cohort and 100 mL versus 135 mL, $P = 0.6$ and 0.3, respectively). For ERAS protocol children who required morphine or PO narcotics, fewer doses were required (3.1 versus 10.6, $P = 0.0005$ and 3.3 versus 6.4, $P = 0.007$, respectively). ERAS protocol children had a decreased overall length of stay (2.2 versus 3.7 nights, $P = 0.02$) but there was no difference in PICU stay (1.1 versus 1.9, $P = 0.2$). Subgroup analysis of children aged less than 18 months at the time of surgery is presented in Table 4.

DISCUSSION

Pediatric cranial vault remodeling is associated with numerous potential postoperative complications,

Table 3. Subgroup Analysis of Patients Requiring Transfusion

Metric	No ERAS Transfusion (n = 42) (mean, range, SD)	ERAS Transfusion (n = 13) (mean, range, SD)	*P*
Men/Women	17 (405%)/25 (59.5%)	6 (46.2%)/7 (53.8%)	0.76
Age at surgery (years)	2.8, 0.6–16.1, 3.5	2.9, 0.8–14.8, 4.5	0.93
Weight at surgery (kg)	15.4, 7.6–67, 13.5	14.5, 6.3–64, 15.4	0.84
Patients receiving EPO	25 (59.5%)	10 (76.9%)	0.3
Patients receiving TXA	31 (73.4%)	9 (69.2%)	0.73
Patients receiving crystalloid	42 (100%)	13 (100%)	1.0
Crystalloid (mL)	1201, 370–3800, 636.2	1211, 600–3250, 886.2	0.96
Crystalloid (mL/kg)	91.4, 17.1–147.7, 29.3	91.4, 50.8–117.7, 18.2	1.0
Patients receiving colloid	22 (52.4%)	10 (76.9%)	0.2
Colloid (mL)	168, 20–250, 77.3	256.9, 50–1000, 292.3	0.19
Colloid (mL/kg)	13.7, 1.9–26.9, 6.5	13.7, 4.1–26.3, 6.5	1
Patients receiving cell saver	42 (100%)	13 (100%)	1
Cell saver (mL)	106, 14–495, 90.6	161.8, 18–586, 168	0.13
Cell saver (mL/kg)	7.8, 1.8–23.7, 4.6	10.8, 2.1–37.7, 9	0.11
EBL	287.5, 75–1400, 225.1	470, 150–1300, 371	0.03*
EBL (mL/kg)	22, 5.3–67, 13.0	34.4, 19.7–77.3, 15.6	0.006*
Postoperative Hg	9.2, 6.3–13.2, 1.4	10.8, 7.4–15.1, 2.2	0.003*
Lowest Hg	8.4, 6.3–11.9, 1.4	9.4 6.5–14.2 2.3	0.06
Discharge Hg	8.7, 6.4–12, 1.3	10.1, 6.9–14.2, 2.1	0.005*

*$P < 0.05$.

Table 4. Subgroup Analysis of Patients 18 Months and Younger at the Time of Surgery

Metric	ERAS (n = 35) (mean, range, SD)	Control (n = 15) (mean, range, SD)	*P*
Men/Women	18 (51.4%)/17 (48.6%)	10 (66.7%)/5 (3.3%)	0.4
Age at surgery (years)	0.9, 0.6–1.4, 0.15	0.7, 0.3–1.5, 0.3	0.2
Weight at surgery (kg)	9, 6.3–12.3, 1.12	8.6, 6.1–12.2, 1.6	0.4
Patients receiving EPO	32 (91.4%)	0 (0%)	0.0001*
Patients receiving TXA	24 (68.6%)	0 (0%)	0.0001*
Patients receiving crystalloid	35 (100%)	15 (100%)	1
Crystalloid (mL)	848.9, 370–1300, 207.7	403.1, 200–550, 100.7	0.0001*
Crystalloid (mL/kg)	95.9, 38.9–147.7, 24.6	47.6, 22.5–67.2, 12.7	0.0001*
Patients receiving colloid	35 (100%)	9 (60%)	0.0003*
Colloid (mL)	117.1, 20–250, 60	106.7, 50–250, 58.9	0.6
Colloid (mL/kg)	12.9, 2.6–26.9, 6.1	11.3, 5.9–20.5, 4.1	0.5
Patients receiving cell saver	35 (100%)	0 (0%)	0.0001*
Cell saver (mL)	80.9, 14–366, 63	0	0.0001*
Cell saver (mL/kg)	8.8, 1.8–37.7, 6.3	0	0.0001*
EBL	246.3, 80–750, 137	262.3, 100–500, 116.7	0.7
EBL (mL/kg)	27.3, 8.4–77.3, 13.4	31.6, 11.5–61, 15.6	0.3
Patients receiving intraoperative transfusion	10 (28.6%)	15 (100%)	0.0001*
Intraoperative transfusion (mL)	170, 80–300, 65.5	282.7, 150–500, 123	0.01*
Patients receiving postoperative transfusion	2 (5.7%)	2 (13.3%)	0.6
Postoperative transfusion (mL)	100, 70–130, 30	135, 120–150, 15	0.3
Preoperative Hg	13.7, 10–9–15.7, 1.0	12.3, 10–9–13.5, 0.8	0.0001*
Postoperative Hg immediate	9.6, 6.3–15.1, 1.8	11.8, 9.4–13.6, 1.3	0.0001*
Lowest Hg	8.8, 6.3–14.2, 1.9	10.5 5.8–13.5, 2.2	0.008*
Discharge Hg	9.2, 6.4–14.2, 1.8	11.4, 8.1–13.5, 1.5	0.0001*
Patients receiving ketorolac	19 (54.2%)	0 (0%)	0.0002*
Patients receiving ibuprofen	35 (100%)	8 (53.3%)	<0.0001*
Ibuprofen doses	4.7, 1–12, 2.6	8.6, 1–19, 5.5	0.004*
Patients receiving morphine/dilaudid	32 (91.4%)	14 (93.3%)	1
Morphine/dilaudid doses	3, 1–8, 1.9	10.6, 2–49, 11.2	0.0005*
Patients receiving PO narcotics	25 (71.4%)	12 (80%)	0.7
PO narcotic doses	3.3, 1–12, 2.4	6.4, 1–15, 4.4	0.007*
LOS	2.2, 1–7, 0.9	3.7, 2–17, 3.6	0.02*
PICU stay	1.1, 1–4, 0.5	1.9, 1–14, 3.2	0.2

* $P < 0.05$.

including infection, bleeding, CSF leak, and death.[29–32] There have yet to be detailed reports of management for complex craniofacial children, beginning with preoperative assessment and optimization to anesthesia, intraoperative management, and intensive care recovery.[22,23] As cranial vault remodeling can be associated with significant morbidity and a prolonged length of stay, analyzing surgical techniques and approaches is critical to improving and optimizing recovery. In this study, we chose to analyze only children undergoing FOA, as this complex surgical approach has been associated with a historically high rate of transfusion requirement and hospital length of stay, even within cranial vault remodeling.[20,21] As recently as 2018, the average EBL in surgery for craniosynostosis has been reported as high as 77% of the circulating volume with 90% of patients requiring transfusions.[33]

Our protocol to optimize hemodynamic outcomes begins with preoperative assessment of hemoglobin. The majority of children (35/55) in our ERAS protocol met the inclusion criteria for EPO and were given it

preoperatively (32/35). EPO is one of the most widely studied approaches to blood conservation in craniofacial surgery.[34] However, EPO is expensive and requires multiple preoperative visits.[35] Fearon et al. performed a randomized control trial (RCT) in which children received either EPO at 600U/kg for 3 weeks preoperatively plus iron at 4 mg/kg per day or just iron. Children who received EPO had a lower rate of transfusion than those who did not receive EPO.[36] Krayewski et al. utilized the combination of EPO at 600 U/kg for 3 weeks preoperatively in combination with cell-saver in an RCT. Patients treated in this manner demonstrated lower transfusion rates despite EBL comparable to the control arm. Additionally, of the 80% of the patients with intervention arm that received CS blood at the end of the case, approximately 31% would have required allogeneic transfusion if recycled blood was not available.[37] These positive results have been demonstrated in other retrospective studies, as well.[38–42] Our children tolerated EPO well and this is similar to the experience of others, as demonstrated in a multi-center review of 369 children.[34]

Intraoperatively, blood loss is minimized with the utilization of TXA, an anti-fibrinolytic agent that competitively blocks the conversion of plasminogen to plasmin. By doing so, it inhibits the proteolytic action of plasmin on fibrin clot and platelet receptors to inhibit fibrinolysis at the surgical wound.[43–45] A meta-analysis performed in 2013 analyzed 4 studies in 3 articles with 138 children, where the role of TXA in reducing packed red blood cells' transfusion and blood loss during pediatric craniosynostosis surgery was investigated. This study demonstrated that intraoperative administration of TXA could significantly reduce blood loss and the need for packed red blood cell transfusion. However, the subgroup analysis on randomized controlled trials showed that TXA did not significantly reduce blood loss during surgery compared with the placebo.[46] Forty of our ERAS children received TXA, which was correlated with a reduction in EBL compared with that of control children. However, as ERAS children had a completely different perioperative approach compared with control children, one of which was TXA, it is difficult to determine the impact that TXA directly had on EBL or transfusion rates.

Blood loss is recycled with the use of a CS machine that allows for autologous blood donation. Of the various techniques to minimize allogeneic blood exposure, intraoperative CS was one of the earliest adopted and is the most widely used and reviewed.[47] However, this technique can be expensive and some have cited that it is inefficient in infants and small children.[48] Somewhat confounding the evidence is the different type of CS machines available and investigated. Even though EBL was similar between our cohorts, children treated with a CS had a lower incidence and volume of intraoperative transfusion requirements, likely due to blood volume autotransfused. Jimenez et al. performed an RCT on children treated with CS in addition to hemostatic approaches and found that children treated with this combination had a decreased transfusion volume.[49] Krayewski et al. utilized the combination of EPO at 600U/kg for 3 weeks preoperatively in combination with CS in an RCT. Children treated in this manner demonstrated lower transfusion rates despite EBL comparable to the control arm.[37] Fearon et al. performed a prospective, non-controlled study on children treated with CS in conjunction with EPO and found that only 18/60 children required allogeneic blood.[50] Thus, CS appears to be an effective means by which to reduce allogenic blood requirements.

Transfusions are associated with risks such as metabolic acidosis, bacterial or viral contamination, fluid overload, acute lung injury and transfusion reactions, and should not be driven solely by laboratory values if a patient is hemodynamically stable.[51–56] Others have proposed protocols to reduce transfusion incidence after cranial vault remodeling by instituting transfusion thresholds. Stricker et al. implemented a protocol that included projected drain output and specific transfusion thresholds and was able to demonstrate that this reduced the prevalence of postoperative transfusion despite similar hematocrits and drain outputs to historical controls.[57] Nguyen et al. instituted an algorithm that dictated when to send labs based on operative results, as well as how the results should guide resuscitation. This approach, along with intraoperative aminocaproic acid (ACA), resulted in a decrease in EBL and transfusion volume of packed red blood cells and fresh frozen plasma (FFP).[58] Haas et al. utilized a patient blood management protocol that was created in collaboration with the anesthesia and hematology teams. Using this protocol, while there was no reduction in the amount of transfused blood required, there was a total avoidance of FFP and a reduction in platelets versus children treated off protocol. This also led to a reduction in cost of 7.1% per patient.[59] Similarly, in our cohort, no children treated with the ERAS protocol required fresh frozen plasma or platelets. In our cohort, while there was no difference in colloid resuscitation between ERAS and control children, children treated with the ERAS protocol received more crystalloid, partly explaining the lower postoperative hemoglobin. Additionally, it may have assisted with lowering the transfusion rate, as hemodynamics were maintained by this additional resuscitation fluid.

Children treated with the ERAS protocol were placed on a dexmedetomidine drip postoperatively to increase comfort and decrease pain medication requirements. Almost half of children treated in the ERAS protocol received ketorolac at the nurse's discretion. As we have demonstrated previously, ketorolac is a safe medication in this population, and does not increase risk of bleeding or blood transfusions, and reduces the need for opioids.[28] Children treated with the ERAS protocol required less morphine/dilaudid and oral narcotics. Thus, this demonstrates the success of our perioperative protocol to provide opioid-sparing pain control.

It has been previously demonstrated that implementation of a preoperative clinical pathway for children undergoing surgery for non-syndromic single-suture craniosynostosis resulted in a decreased ICU stay without an increase in morbidity. However, this study largely assessed postoperative strategies such as when to perform

neurological examinations, draw labs, and thresholds for transfusion.[60] In our study, while the length of stay in the PICU was not decreased, the overall length of stay was decreased in the ERAS cohort. Our study was not powered to detect a difference in PICU length of stay, as this duration is typically only 1–2 nights. Thus, a further reduction would likely only be possible if some children were not admitted to the ICU after FOA, which, at this time, is not a protocol that our institution has adopted.

To eliminate outliers in regard to age and patients undergoing secondary surgery, a subgroup analysis was performed on children aged less than 18 months at the time of surgery. Similar findings were demonstrated in this analysis with decreased transfusion rates, opioid requirements, and length of stay, indicating that this protocol can be applied to even our most vulnerable subgroup of children undergoing FOA.

In conclusion, analysis of our ERAS pathway for patients undergoing FOA demonstrated that this approach led to a reduction in overall and intraoperative allogenic blood transfusion rate, reduction in narcotic use, and hospital length of stay. We will continue to use and improve upon this protocol for children undergoing FOA, as well as other complex craniofacial procedures. We hope this report encourages other institutions to adopt a comprehensive perioperative pathway to enable safe and effective expedited recovery for these children.

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