

A Retrospective Look at Packed Red Blood Cell Transfusion in Pediatric Cranioplasty Surgery and Comparison After Use of Vitagel™ Surgical Hemostat

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Abstract

Background and Significance:

Cranioplasty surgery has one of the highest likelihood of blood product transfusion in pediatric patients. There is a considerable risk of blood loss requiring large amounts of blood products for these small patients. Because it is difficult to assess blood loss in these cases, these patients may be transfused with inadequate or excessive volumes of blood products. Vitagel™ Surgical Hemostat is a product that combines microfibrillar collagen and thrombin with fibrinogen and platelets from the patient's plasma. We assessed the amount of packed red blood cell (PRBC) transfusions needed after primary cranioplasty, comparing the patients that received Vitagel™ to patients who did not ; appraising Vitagel™ for overall reduction in blood loss

Methods and Design:

After receiving IRB approval, we conducted a retrospective chart review on all nonsyndromic patients < 3 years of age that underwent primary cranioplasty surgery at Arkansas Children's Hospital (ACH) from January 1, 2010- January 1, 2012. Demographic information reviewed included, age and weight of the patient, suture involved in the cranioplasty repair, length of surgery, urine output, volume of transfused PRBCs and IV fluids each patient received. We also surveyed postoperative volume of PRBC transfusion at 24 and 48 hours. In addition, we compared the amount of PRBC and other blood products transfused between children who received Vitagel™ and those that did not..

Results:

Included in the review were 61 patients that had primary cranioplasty, 18 had Vitagel™ used during the surgery and 43 (control) did not.. The average amount of PRBC given to a patient in the Vitagel™ group was 182 ml (18.4 ml per kg) compared to the control group of 287 ml (33.7 ml/kg). The p-value based on t-tests was 0.02 which showed a significant difference between the two groups favoring the Vitagel™ treated group. Longer surgical time was associated with more PRBC transfusion ; (p-value of 0.001). Vitagel™ use was associated with a decrease in PRBC transfusion volume of 15.6/kg

Discussion

Transfusion protocols at ACH are comparable to other pediatric institutions for blood product use in cranioplasty procedures. We use many of the known strategies to lower the amount of blood products transfused in pediatric cranioplasty repairs. We use some, but not all of these, including optimizing preoperative hematologic conditions, increase control of hemorrhage with surgical technique, and harvesting autologous blood when the patient is > 40 kg and minimizing the volume of crystalloid administered, with early transfusion of fresh frozen plasma. Vitagel™ in our institution has also been shown to decrease the volume of PRBC transfused and we have added it's use to our blood management strategy to minimize the amount of transfusions for this patient population.

BACKGROUND AND SIGNIFICANCE:

Craniosynostosis is the premature fusion of cranial sutures

and is one of the most common congenital craniofacial abnormalities.(1) Cranioplasty is performed at an early age for best cosmetic results, and also to decrease the risks of

increased intracranial pressure when multiple sutures are involve. However, there is a great risk of blood loss requiring large amounts of blood transfusion for these small patients.(2) One study showed that cranioplasty surgery had the second highest likelihood of blood transfusion following liver transplant of all non-cardiac surgeries.(3) The average amount of blood loss can range from 10% - 43% of estimated blood volume (EBV) depending on the type of cranioplasty performed and the number of sutures involved.(2) The complications of massive blood transfusion include hyperkalemia, hypothermia, citrate toxicity, impaired clotting, and infections.

There are many techniques to reduce the amount of blood transfusions for cranioplasty repair. These include optimizing preoperative hematologic conditions by the use of Epogen, intraoperative blood salvage, isovolumic hemodilution, increased control of hemorrhage during surgery, and harvesting autologous blood. (4) Commonly, it is difficult to assess blood loss in these surgeries and these patients may be transfused with inadequate or excessive volumes of blood. (2) Vitagel™ Surgical Hemostat is a FDA approved Class III medical device used to control bleeding. Vitagel™ Surgical Hemostat or Vitagel™, is a product that combines microfibrillar collagen and thrombin with fibrogen and platelets from the patient's plasma. This combination produces a hemostat by forming a collagen/fibrin scaffold with platelets. Intraoperatively, 10 ml of the patient's blood is drawn, centrifused and mixed with Vitagel™ ; preparation takes approximately 5-7 minutes. and Vitagel™ is applied..... at the end of the surgery. Retrospectively analysis was conducted to assess volume of blood transfusion intraoperatively and postoperatively after the use of Vitagel, as well as investigation of the effects of colloid, crystalloid, and surgical time on total blood loss.

METHODS AND DESIGN:

After receiving IRB approval, we conducted a retrospective chart review on all patients < 3 years of age that underwent primary cranioplasty surgery at Arkansas Children's Hospital from January 1 2010 till January 1 1012. We looked at the age and weight of the patient, type of cranioplasty surgery, length of surgery, urine output, amount of transfusion and IV products the patient received. Length of surgery was determined from incision time to the end of surgery, which was documented, in the operative report. Blood loss was analyzed for each patient postoperatively at 24 hours and 48 hours. We compared the amount of packed

red blood cells (PRBC) and other blood products transfused between cases that used Vitagel™ and those that did not. The data was collected from the intraoperative anesthesia records, operative notes, intensive care unit progress notes, flow-sheets, and discharge summaries. Statistical analysis of the demographics and the above categories from the surgeries were analyzed and compared.

RESULTS:

Initially 62 patients had primary cranioplasty performed that were < 3 years old during the study period described. One patient in the Vitagel™ group was excluded because of a surgical complication that led to large inoperative hemorrhage. This patient received 1400 ml of PRBC which was abnormal compared to the other Vitagel™ vs. control results. The remaining data of 61 patients was analyzed in the study.

The summary of the continuous demographic, operative, and post-operative factors is shown on Table 1. The average age of these patients were 10.3 months and the average weight was 8.7 kg. The average surgical time was 236 minutes and the average PRBC given was 256 ml (29.6 ml/kg).

Intraoperative estimate of average blood loss by the anesthesiologist was 292 ml (33.7 ml/kg). Of the 61 patients, 18 had Vitagel™ used during the surgery and 43 (control) did not use Vitagel™ (Table 1). There was no significant difference between the demographics of age, weight, or surgery duration between the Vitagel™ and control group. The average amount of PRBC given to a patient in the Vitagel™ group was 182 ml (18.4 ml per kg) compared to the control group of 287 ml (33.7 ml/kg). The p-value based on t-tests was 0.02, which showed significant difference.

There was also significant difference with the Vitagel™ group receiving less crystalloid and estimated blood loss than the control group. After 48 hours, the average amount of blood loss recorded in the Vitagel™ group was 241 ml (26.2 ml per kg) compared to the control group of 410 ml (48.2 ml per kg); p-value of 0.08. (Table 1)

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Table 1

Summary of continuous demographic, operative, and post-operative factors for the study sample (N=61)

	Overall (N=61)	Control (N=43)	Vitagel (N=18)	P
Age (months)	10.3 (6.2)	10.3 (6.5)	10.3 (6.1)	0.99
Weight (kg)	8.7 (1.6)	8.5 (1.6)	9.2 (1.6)	0.12
Surgery duration (min)	236 (102)	242 (99)	220 (104)	0.45
Colloid	87 (125)	73 (131)	122 (189)	0.31
Crystalloid	623 (478)	697 (509)	445 (323)	0.03
Blood loss	292 (228)	325 (244)	212 (163)	0.04
PRBC	256 (169)	287 (173)	182 (147)	0.02
RBC per kg	29.2 (18.9)	33.7 (19.5)	18.4 (13.6)	0.001
Post-op Blood Loss (6 hours)	102 (68)	106 (71)	94 (53)	0.49
Post-op blood loss (24h)	255 (128)	270 (130)	217 (120)	0.14
Post-op blood loss (48h)	362 (483)	410 (562)	241 (125)	0.08

p-values based on t-tests.

*P <0.05 designates a significant difference between cohorts

The descriptive statistics for the different types of cranioplasty procedure overall and by the treatment groups are shown in Table 2. Nearly half, 47% of the cranioplasty performed were sagittal cranioplasty. Bilateral coronal cranioplasty was the least performed at 8%. There was no association between the Vitagel™ and control groups in terms of the type of cranioplasty performed. (Table 2)

Table 2

Descriptive statistics for procedure type for the overall sample (N=61) and by treatment group.

Procedure (N=60)	Overall (N=60)	Control (N=43)	Vitagel (N=17)	P
Unicoronal	10 (17 %)	8 (19 %)	2 (12 %)	0.57
Bicoronal	5 (8 %)	4 (9 %)	1 (6 %)	
Sagittal	28 (47 %)	20 (47 %)	8 (47 %)	
Lambdoid	7 (12 %)	6 (14 %)	1 (6 %)	
Metopic	10 (17 %)	5 (12 %)	5 (29 %)	

p-value is based on Fisher's exact test.

The summary of the different type of cranioplasty surgery was shown on Table 3. The highest amount of PRBC was given to the bilateral coronal cranioplasty with 408 ml (42 ml per kg) and the least amount of PRBC was given to the sagittal cranioplasty with 196 ml (25 ml per kg). The longest surgery duration was with the unicoronal cranioplasties with the average lasting 353 minutes and the shortest time was sagittal cranioplasties that was averaging about 150.5 minutes. The age and weight were significantly different between the groups with the sagittal cranioplasties having a lower mean age and weight than the other types of

cranioplasties. The p-values were based on one-way analysis of variance (ANOVA). (Table 3)

Table 3

Summaries by procedure (N=60)

	Unicoronal (N=10)	Bicoronal (N=5)	Sagittal (N=28)	Lambdoid (N=7)	Metopic (N=10)	p-value
Age (months)	13.2 (4.7)	11.2 (2.2)	7.6 (5.6)	15.1 (8.8)	11.5 (5.6)	0.01
Weight (kg)	10.0 (1.3)	9.9 (0.6)	7.8 (1.6)	9.4 (1.0)	9.0 (1.3)	<0.001
Surgery time	353 (35)	350 (26)	151 (63)	228 (48)	311 (47)	<0.001
PRBC	342 (94)	408 (257)	196 (166)	232 (113)	307 (138)	0.02
PRBC per kg	34 (12)	42 (27)	25 (20)	24 (11)	36 (18)	0.21

*p-values are based on one-way analysis of variance (ANOVA).

A significant p-value indicates that at least one procedure group mean is different from others.

After conducting a linear regression models, there was a high association with PRBC/kg given with surgery time and Vitagel™ treatment (Table 4). The longer the surgery the more PRBC was given (p-value of 0.001). Cranioplasties using Vitagel™ also had decreased PRBC/kg given during surgery (p-value of 0.003). Vitagel™ use was associated with a decrease in PRBC of 15.6 ml/kg. (Table 4)

Table 4

Adjusted and unadjusted results of linear regression models to predict PRBC per kilogram of body mass.

Predictor	Comparison (High vs Low)		Adjusted effects (95% CI)	P value	Unadjusted "crude" effects (95% CI)	P value
	Low	High				
Surgery duration (min)	140	332	13.5 (5.7 to 21.2)	0.001	17.3 (9.2 to 25.4)	<0.001
Colloid	0	100	3.7 (0.4 to 7.0)	0.03	4.3 (0.5 to 8.1)	0.03
Vitagel treatment	Control	Vitagel	-15.6 (-24.4 to -6.9)	<0.001	-15.4 (-25.3 to -5.4)	0.003

DISCUSSION:

In our institution, there was a significant decrease in the intraoperative blood transfusion (ml/kg) in our patients where Vitagel™ was applied compared to those patients that did have the mixture applied at surgical closure. However, there could be other compounding factors that could be involved. Vitagel™ is applied near the end of the operative procedure after the major blood loss have occurred so it is difficult to say that this product alone could have prevented blood transfusion. No other anesthesia changes were made between the Vitagel™ and control group. Meticulous surgical technique could be a factor in reducing the blood transfusion. Theoretically, the affects of Vitagel™ should be evident in reduction of postoperative blood loss and need for additional blood product

transfusions. There was a decrease in blood loss at 48 hour after surgery from 410ml in the control group to 241ml in the Vitagel™ group (p-value of .08). (Table 1). The difference between the 6 hour post operative and 24 hour post operative blood loss was not as significant. Of course, this value is based on the assumption that the measurement of the blood collected from the drain was recorded accurately. The majority of the patients did not receive blood transfusion postoperatively.

When comparing the different types of cranioplasty surgery, sagittal cranioplasty was the quickest in surgical time (mean of 151 minutes) and the least in blood transfusion (196 ml or 25 ml/kg). (Table 3) These were also the youngest and smallest patients with a mean of 7.6 months and 7.8 kilograms. Of the total cases, about half (47%) were sagittal cranioplasty overall, and between both groups. (Table 2) Unicoronal and bilateral coronal cranioplasty were the longest surgery time at a mean of 350 minutes. The linear regression models in Table 4 showed that the longer the surgery duration the more PRBC per kg were given to the patient. This is not too surprising that longer surgeries tend to bleed more. We didn't find a strong association between giving colloid versus crystalloid to the amount of PRBC/kg that was given.

Overall there was a mean of 256 ml of PRBC (29.2 ml/kg) transfused for cranioplasty surgery in this institution. The average blood loss estimated by the anesthesiologist was 292 ml (34 ml/kg). (Table 1) In reviewing other literature, Stricker et al. reviewed 159 patients with cranioplasty and found the average PRBC transfused was 51 ml/kg.(5) Van Uitert et al. reviewed 44 patients and the mean transfused PRBC was 38 ml/kg with blood loss averaging 55 ml/kg (6). Kearney et al. retrospectively reviewed 76 cranioplasty patients and found blood loss ranging from 20 ml/kg for sagittal to 40 ml/kg for metopic repairs. (7). Kang et al. looked at 43 cranioplasty patients and the blood loss was between 21 percent to 30 percent of total blood volume.(2) Our blood loss was comparable to Kearney's experience. Only healthy nonsyndromic patients were used in this study and fresh frozen plasma (FFP), platelets, or cryoprecipitate were not given intraoperatively for any of the surgery.

Determining blood loss is usually very difficult to estimate for the anesthesiologist during cranioplasty surgery. Much of the blood lost is on the surgical drapes and surrounding surgical field. Intravascular volume losses may be difficult to access due to the speed and large amount of

blood loss in these infants even with appropriate perioperative monitoring. The typical time of rapid blood loss is during scalp dissection and raising of the periosteum, but constant oozing occurs throughout the procedure.(8) It is important to have good communication between the neurosurgeon and anesthesiologist for accurate assessment of blood loss. The smaller the patient in age and weight, the higher the percentage of blood loss in proportion to circulating blood volume. This may be due to the larger head surface area to the body in infants. Hughes et al. found a higher rate of allogenic blood transfusion with patients with smaller kilogram weight. (8) The optimal age for patients to undergo craniostomy is also complex. It should be done before the skull deformity is too large from growth and ossification of the dura, however it is better to do it after the physiologic nadir of hemoglobin which is around 6 months of age.(6) The average age for craniostomy surgery in our institution was over 10.3 months for primary craniostomy repair.

There are ways to lower the amount of blood transfusion in pediatric patients undergoing surgery. Perioperatively, iron supplementation and erythropoietin can be given to increase the hematocrit in patients that are anemic.(8) In infants it is difficult to have autologous transfusion due to their lower blood volume and feasibility. Intraoperatively, there are techniques that surgeons can employ like adrenaline infiltration or using other products like Vitagel™. Meticulous surgical technique is also an important factor in controlling blood loss in these patients.

Anesthesia techniques for blood conservation include cell salvage, acute normovolemic hemodilution, hypervolemic hemodilution, controlled hypotension, antifibrinolytics, and applying a transfusion strategy.(8) Many of these techniques used on older and larger children are limited in infants and neonates undergoing craniostomy repair as a consequence of their smaller blood volume and need to maintain cerebral perfusion pressure. (8) There are many complications for massive blood transfusion including coagulation disorders, transfusion reactions, electrolyte abnormalities, or overtransfusion. Stricker et al. found using FFP more readily to limit coagulation disorders instead of albumin was effective in reducing post-operative coagulation complications.(5) In our institution, we did not use FFP in our uncomplicated primary cranioplasty and albumin is readily given to the patients. Antifibrinolytics are not used in our institution at this point. There is still debate on its

effectiveness even though there are studies, which showed decreased blood loss and transfusion. (8) One study by Haas et al. showed a decrease blood transfusion for pediatric craniostomosis repairs by utilizing ROTEM® for management of blood product transfusions. (9) In our institution, we do not have a standardized blood transfusion protocol. Some anesthesiologists empirically give blood as soon as the incision is made, while others start blood after the hematocrit drops below 30%. Most of the pediatric cranioplasty repairs are done with an arterial line and two-three large bore intravenous lines, while central line placement is per the discretion of the anesthesiologist. One major goal in our hospital is to develop a comprehensive blood transfusion protocol for craniostomosis surgery, minimizing the number of blood unit exposures for these small patients, but avoiding overtransfusion.

There are limitations for this retrospective study. The information that we may be looking for may not be available when searching in a chart. Laboratory values would have also provided objective evidence for determining the effectiveness of our transfusions but it was not collected in this study. There was no standardization of the procedure or technique, which is a limitation of a retrospective study. It is important to develop a blood transfusion strategy to limit the amount of blood transfusion. Vitagel™ is a product which shows promise in reducing blood transfusion in cranioplasty

surgery.

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