World Journal for Pediatric and Congenital Heart Surgery
2017, Vol. 8(4) 475-479

DOI: 10.1177/2150135117713698
journals.sagepub.com/home/pch
SAGE

Experience Using Kaolin-Impregnated Sponge to Minimize Perioperative Bleeding in Norwood Operation

Takeshi Shinkawa, MD[1], Jessica Holloway, PA[1], Xinyu Tang, PhD[2], Jeffrey M. Gossett, MS[2], and Michiaki Imamura, MD, PhD[1]

Abstract

Purpose: A kaolin-impregnated hemostatic sponge (QuikClot) is reported to reduce intraoperative blood loss in trauma and noncardiac surgery. The purpose of this study was to assess if this sponge was effective for hemostasis during Norwood operation. **Description:** We conducted a retrospective review of patients undergoing Norwood operation in infancy between 2011 and 2016 at our institution. **Evaluation:** Of 31 identified Norwood operations, a kaolin-impregnated sponge was used intraoperatively in 15 (48%) patients. The preoperative profiles and cardiopulmonary bypass status were similar between the operations with or without kaolin-impregnated sponge. The comparison on each operative outcome between operations with or without kaolin-impregnated sponge showed that the intraoperative platelets, cryoprecipitate, and factor VII dosage were significantly less in the operations with kaolin-impregnated sponge (55 mL, 10 mL, 0 μg/kg vs 72 mL, 15 mL, 45 μg/kg; $P = .03$, .021, .019), as well as the incidence of perioperative bleeding complications (second cardiopulmonary bypass for hemostasis or postoperative mediastinal exploration, 0% vs 31%, $P = .043$). A logistic regression model showed that the nonuse of kaolin-impregnated sponge and longer aortic cross clamp time were associated with perioperative bleeding complication in univariable model ($P = .02$ and .005). **Conclusions:** Use of kaolin-impregnated hemostatic sponge was associated with reduced blood product use and perioperative bleeding complications in Norwood operation at a single institution.

Keywords

surgery, complications, morbidity, congenital heart disease (CHD), blood transfusion

Submitted February 16, 2017; Accepted May 8, 2017.

Introduction

Intraoperative and postoperative bleeding are the most serious complications in cardiovascular surgery. Inadequate intraoperative hemostasis require increased use of blood products or additional hemostatic agents and increased need for unplanned reinterventions, which results in higher mortality and morbidity.[1-3] The bleeding tendency seemed more evident in smaller children due to more hemodilution by the relatively larger cardiopulmonary bypass circuit compared to body size and less mature coagulation function.[4]

The kaolin-impregnated hemostatic sponge (QuikClot; Z-Medica, Wallingford, Connecticut) is a newly developed hemostatic agent employing an inorganic mineral (kaolin). Kaolin is an aluminum silicate mineral that accelerates the natural intrinsic clotting pathway in contact with blood by activating factor XII[5] and platelet-associated factor XI[6] and instigating the remainder of the coagulation cascade (Figure 1). Several reports in the literature indicate that the kaolin-impregnated sponge reduced blood loss in trauma,[7] interventional procedures, and noncardiac surgeries.[8-10]

To understand better the efficacy of this sponge, we retrospectively reviewed the outcomes of neonates and infants who had the Norwood operation at our institution. Major outcomes studied included blood products' usage and bleeding-related complications.

[1] Division of Pediatric and Congenital Cardiothoracic Surgery, Department of Pediatrics, Arkansas Children's Hospital, University of Arkansas for Medical Sciences, Little Rock, AR, USA
[2] Biostatistics Program, Department of Pediatrics, Arkansas Children's Hospital, University of Arkansas for Medical Sciences, Little Rock, AR, USA

Corresponding Author:
Takeshi Shinkawa, Pediatric Cardiothoracic Surgery, Arkansas Children's Hospital, 1 Children's Way, Slot 677, Little Rock, AR 72202, USA.
Email: tshinkawa@uams.edu

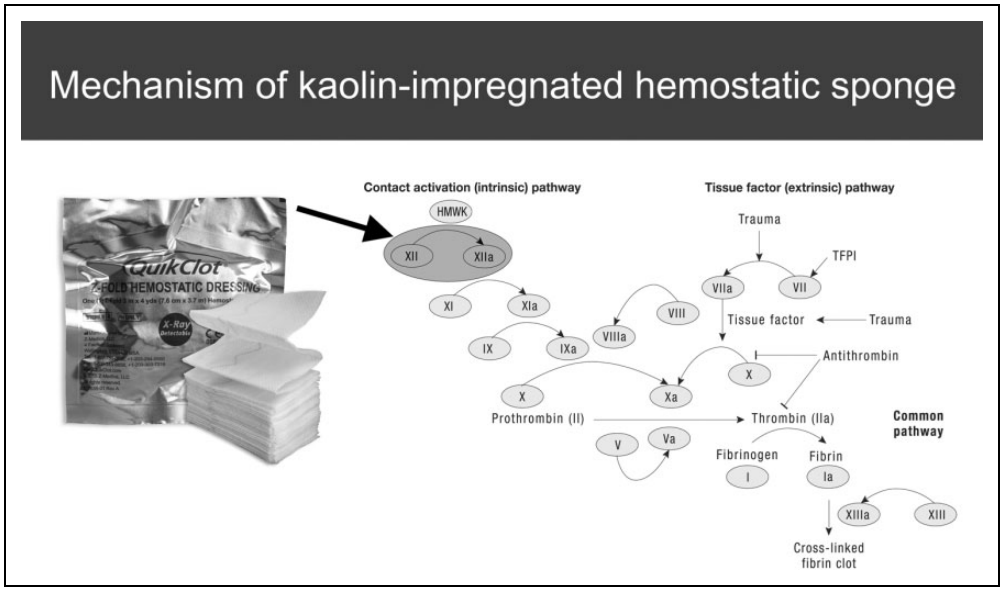

Figure 1. The mechanism of kaolin-impregnated hemostatic sponge. HWMK represents high-molecular-weight kininogen, and the kaolin activates the same process of accelerating the surface-mediated activation of factor XII on its negatively charged surface. Illustration used with permission of Z-Medica.

Materials and Methods

Study Design

All children less than 120 days old who had a Norwood operation by the Division of Pediatric and Congenital Cardiovascular Surgery at Arkansas Children's Hospital between January 2011 and June 2016 were included in this retrospective study. Patients of 120 days of age or older at the time of Norwood operation and who had postoperative extracorporeal membrane oxygenation support were excluded from this study.

This study was approved and monitored by the University of Arkansas for Medical Sciences' institutional review board, and the need for patient consent was waived due to the study's retrospective nature. Medical records were reviewed, and the following data were retrieved and analyzed: basic demographic data, anatomical information, surgical history, intraoperative data, and postoperative outcomes. Bleeding complication was defined as second cardiopulmonary bypass run for hemostasis or postoperative mediastinal exploration.

Statistical Analysis

All the data were analyzed using statistical software R v3.2.5 (R Foundation for Statistical Computing, Vienna, Austria). Descriptive statistics were expressed as median (first quartile, third quartile) for continuous variables and count (percentage) for categorical variables. The distributions of continuous variables were compared between the operations with or without kaolin-impregnated hemostatic sponge using the Mann-Whitney *U* tests, while the proportions of the categorical variables were compared using the Fisher's exact tests. A logistic regression model with Firth's penalized likelihood approach was fitted for bleeding complication as a function of each risk factor to assess the univariable association between outcome and each risk factor. Due to a relatively small sample size, risk factors with a univariable *P*-value of less than .1 were selected to be included in the multivariable model. A multivariable model was fitted for bleeding complication as a function of kaolin-impregnated hemostatic sponge use, body weight, and aortic cross clamp time. *P*-values $\leq$.05 were considered to indicate statistical significance.

Results

Patient Characteristics and Operative Interventions

For the study period (January 2011 to June 2016), 31 Norwood operations were identified (9 operations with extracorporeal membrane oxygenation supports and 5 operations at more than 120 days of age were excluded from the total of 45 operations). Preoperative diagnoses included hypoplastic left heart syndrome (27), interrupted aortic arch and single ventricle (3), and transposition of great arteries and hypoplastic right ventricle (1). Nine patients had previously undergone bilateral pulmonary artery banding or hybrid stage I procedure.

All patients had the Norwood operation including aortic arch reconstruction with homograft patch augmentation, Damus-Kaye-Stansel anastomosis, atrial septectomy, and pulmonary artery blood supply (right ventricle to pulmonary artery conduit in 25 and systemic to pulmonary artery shunt in 6 operations) via median sternotomy under cardiopulmonary bypass. No comprehensive stage II procedures were included in this cohort, and all nine patients with prior bilateral pulmonary artery banding or hybrid stage I procedure underwent a delayed Norwood operation. The cardiopulmonary bypass circuit had a Capiox FX05 oxygenator (Terumo Cardiovascular Systems Corp, Ann Arbor, Michigan) and a prime volume of

Table 1. Preoperative Profiles and Operative Details.[a]

Variables	All Operations, n = 31	Operations Without Kaolin-Impregnated Sponge, n = 16	Operations With Kaolin-Impregnated Sponge, n = 15	*P* Value
Gender, male	19 (61%)	11 (69%)	8 (53%)	.47
Age, day	9 (7, 32)	12 (9, 24)	7 (6, 32)	.07
Weight, kg	3.2 (3, 3.7)	3.2 (3, 3.7)	3.1 (3, 3.4)	.5
Genetic disorder	5 (38%)	2 (33%)	3 (43%)	.99
Previous surgery	9 (29%)	5 (31%)	4 (27%)	.99
Cardiopulmonary bypass time, minutes	152 (142, 167)	156 (143, 181)	150 (140. 160)	.28
Aortic cross clamp time, minutes	46 (42, 54)	42 (34, 47)	53 (46, 54)	.004
Regional cerebral perfusion time, minutes	43 (34, 50)	36 (28, 43)	50 (42, 52)	.013
Right ventricle to pulmonary artery conduit as pulmonary blood flow source	25 (81%)	11 (69%)	14 (93%)	.17

[a]Variables were expressed as median (first quartile, third quartile) for continuous variables and as count (percentage) for categorical variables.

approximately 350 mL and was primed with 1 unit of packed blood cells and 1 unit of fresh frozen plasma. During cardiopulmonary bypass, the hematocrit was maintained at approximately 35% with appropriate venous oxygen saturation. During aortic arch reconstruction, regional cerebral perfusion technique was preferably used with deep hypothermia to 18°C by the alpha-stat technique, and a brief period of circulatory arrest was applied in 16 operations as necessary. After cessation of cardiopulmonary bypass, modified ultrafiltration was performed for 15 minutes with the target hematocrit at the end of ultrafiltration of higher than 40%. After modified ultrafiltration, protamine was given to reverse the heparin effect. The bleeding before protamine and the circuit blood were recycled with an intraoperative cell salvage machine (Fresenius Continuous AutoTransfusion System Plus; Terumo Cardiovascular Systems Corp, Ann Arbor, Michigan). Packed red blood cells, platelet concentrate, cryoprecipitate, and factor VII were given as necessary by discussion between the surgeon and the anesthesiologist to achieve adequate hemostasis.

After protamine, the kaolin-impregnated sponge was preferably used as packing material in 15 (48%) patients, since mid-2013 by both surgeons. The kaolin-impregnated sponge was exclusively used around the reconstructed aortic arch and Damus-Kaye-Stansel anastomosis and left in situ until delayed chest closure if necessary. There was no event of heart structure compression by kaolin-impregnated sponge. Preoperative profiles and operative details were comparable between the operations with or without kaolin-impregnated sponge, and the significant differences were longer aortic cross clamp time and longer regional cerebral perfusion time in the operations with kaolin-impregnated sponge. Table 1 summarizes the preoperative profiles and operative details of the patients.

Operative Outcomes

The median dosages of the intraoperative packed red blood cells, platelet concentrate, and cryoprecipitate were 262, 60, and 10 mL, respectively. Factor VII was given in ten (32%) operations.

Two patients required an additional cardiopulmonary bypass run to obtain adequate hemostasis; one of these patients also required emergent mediastinal exploration. Five patients required emergent mediastinal exploration in the first 48 hours following Norwood operation; four of these patients had postoperative bleeding and the fifth patient had supraventricular tachycardia. Together, five patients (16%) had bleeding complications (second cardiopulmonary bypass for hemostasis or mediastinal exploration in the first 48 hours). All patients received delayed chest closure at a median of 4 days (2, 6 days) after Norwood operation and had postoperative mechanical ventilation for a median of 8 days (7, 13 days). All but one patient were discharged home with median hospital stay of 62 days (48, 86 days).

Factor VII was used less frequently in the operations with kaolin-impregnated sponge (13% vs 50%; $P = .029$), and the use of intraoperative platelets, cryoprecipitate, and factor VII was significantly lower in the operations with kaolin-impregnated sponge compared to those without (55mL, 10 mL, and 0 μg/kg vs 72 mL, 15 mL, and 45 μg/kg; $P = .03$, .021, and .019), respectively. The incidence of bleeding complications was significantly lower in the operations with kaolin-impregnated sponge (0% vs 31%; $P = .043$). The intubation time was significantly shorter in the operations with kaolin-impregnated sponge (eight vs ten days; $P = .049$). However, the postoperative mortality rate and hospital stay length were not significantly different between the operations with or without kaolin-impregnated sponge (6.7% and 65 days vs 0% and 60 days; $P = .48$ and .94), respectively. There were no thromboembolic events except in one surgery; in this sole operation, a central line–related right atrium thrombus occurred when kaolin-impregnated sponge was not used. Table 2 provides the details of operative outcomes.

Logistic Regression Model

A logistic regression model with Firth's penalized likelihood approach showed that the nonuse of kaolin-impregnated sponge and longer aortic cross clamp time were associated with perioperative bleeding complication in univariable model

Table 2. Operative Outcomes.[a]

Variables	All Operations (n = 31)	Operations Without Kaolin-Impregnated Sponge (n = 16)	Operations With Kaolin-Impregnated Sponge (n = 15)	*P* Value
Post-bypass packed red blood cell volume, mL	262 (168, 284)	268 (238, 295)	252 (0, 276)	.093
Platelet volume, mL	60 (50, 80)	72 (60, 86)	55 (42, 74)	.03
Cryoprecipitate volume, mL	10 (10, 20)	15 (10, 20)	10 (10, 10)	.021
Factor VII use	10 (32%)	8 (50%)	2 (13%)	.029
Factor VII, μg/kg	0 (0, 90)	45 (0, 180)	0 (0, N/A)	.019
Bleeding complication	5 (16%)	5 (31%)	0 (0%)	.043
Open chest time, days	4 (2, 6)	5 (4, 8)	3 (2, 5)	.09
Thromboembolic event	1 (3.2%)	1 (6.3%)	0 (0%)	.99
Intubation time, day	8 (7, 13)	10 (8, 18)	8 (7, 9)	.049
Hospital stay, day	62 (48, 86)	60 (49, 83)	65 (46, 114)	.94
Early mortality	1 (3.2%)	0 (0%)	1 (6.7%)	.48

Abbreviation: N/A, not applicable.
[a]Variables were expressed as median (first quartile, third quartile) for continuous variables and as count (percentage) for categorical variables.

Table 3. Firth Logistic Regression Models.

		Univariable Analysis		Multivariable Analysis	
Predictor	Comparison	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Kaolin-impregnated hemostatic sponge	Yes versus No	0.067 (0.0005-0.69)	.02	0.11 (0.0007-1.93)	.13
Age	1 day	1.00 (0.95-1.03)	.94		
Weight	1 kg	0.12 (0.006-1.11)	.063	0.071 (0.0005-0.84)	.034
Surgeon	M.I. versus T.S.	1.12 (0.08-163)	.94		
Pulmonary artery blood flow source	RVPA versus shunt	0.28 (0.04-2.09)	.20		
Cardiopulmonary bypass time	1 minute	1.03 (0.99-1.07)	.13		
Aortic cross clamp time	1 minute	0.87 (0.75-0.96)	.005	0.91 (0.77-1.01)	.079

Abbreviations: CI, confidence interval; OR, odds ratio; RVPA, right ventricle to pulmonary artery conduit.

($P = .02$ and .005) and that only smaller body weight was significantly associated with perioperative bleeding complication in multivariable model ($P = .034$; Table 3).

Comment

We introduced a newly developed kaolin-impregnated hemostatic sponge (QuikClot) as post-bypass packing material to our congenital cardiac surgeries with the hope of reducing perioperative bleeding. This retrospective study was conducted only for the Norwood operation in order to have a meaningful comparison in a similar patient population who underwent uniform operation. This study was the first report regarding kaolin-impregnated sponge usage after operations with cardiopulmonary bypass, and it was unique in that the outcomes were assessed by the secondary outcomes from bleeding (intraoperative blood products usage and bleeding complications) due to the difficulty in measuring the actual blood loss. The study outcomes are promising in that we had significant reduction in the use of intraoperative blood products and the rate of bleeding complications with kaolin-impregnated sponge. A logistic regression model showed that nonuse of kaolin-impregnated sponge was associated with bleeding complication in univariable model. However, we did not observe the improvement in early mortality or hospital stay, possibly due to the small sample size.

Clinically, we currently use this sponge for the majority of our congenital cardiac operations, and we observe that use of this sponge is associated with reduced perioperative bleeding complications in all patients including those with extracorporeal membrane oxygenation support. However, we are extremely careful not to have kaolin-contaminated blood entering the patient's blood stream or cardiopulmonary bypass circuit through the pump sucker or intraoperative cell salvage machine because this strong hemostatic mineral may cause thromboembolism, clots in bypass circuit, or acute shunt thrombosis.

The limitations of this study were its retrospective nature and small sample size. The results from the logistic regression model should be interpreted with caution.

In conclusion, use of the new kaolin-impregnated hemostatic sponge (QuikClot) was associated with reduced blood product use and perioperative bleeding complications with the Norwood operation at a single institution. Further analysis will be necessary to confirm the effectiveness of this sponge in larger cohort.

Authors' Note

The authors had full control of the design of the study, methods used, outcome parameters and results, analysis of data, and production of the written report.

Acknowledgments

The authors would like to thank John Gregan at the Arkansas Children's Research Institute for assistance with preparation of this manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Moulton MJ, Creswell LL, Mackey ME, Cox JL, Rosenbloom M. Reexploration for bleeding is a risk factor for adverse outcomes after cardiac operations. *J Thorac Cardiovasc Surg*. 1996;111(5): 1037-1046.
2. Unsworth-White MJ, Herriot A, Valencia O, et al. Resternotomy for bleeding after cardiac operation: a marker for increased morbidity and mortality. *Ann Thorac Surg*. 1995;59(3): 664-667.
3. Agarwal HS, Bennett JE, Churchwell KB, et al. Recombinant factor seven therapy for postoperative bleeding in neonatal and pediatric cardiac surgery. *Ann Thorac Surg*. 2007;84(1): 161-168.
4. Romlin BS, Söderlund F, Wåhlander H, Nilsson B, Baghaei F, Jeppsson A. Platelet count and function in paediatric cardiac surgery: a prospective observational study. *Br J Anaesth*. 2014; 113(5): 847-854.
5. Griffin JH. Role of surface in surface-dependent activation of Hageman factor (blood coagulation factor XII). *Proc Natl Acad Sci U S A*. 1978;75(4): 1998-2002.
6. Walsh PN. The effects of collagen and kaolin on the intrinsic coagulant activity of platelets. evidence for an alternative pathway in intrinsic coagulation not requiring factor XII. *Br J Haematol*. 1972;22(4): 393-405.
7. Travers S, Lefort H, Ramdani E, et al. Hemostatic dressings in civil prehospital practice: 30 uses of QuikClot Combat Gauze. *Eur J Emerg Med*. 2016;23(5): 391-394.
8. Trabattoni D, Gatto P, Bartorelli A. A new kaolin-based hemostatic bandage use after coronary diagnostic and interventional procedures. *Int J Cardiol*. 2012;156(1): 53-54.
9. Derkay CS, Baydoun HA, Stone L. Intraoperative use of QuikClot during adenotonsillectomy: a prospective pediatric trial. *Ann Otol Rhinol Laryngol*. 2015;124(5): 384-391.
10. Abbott EM, Nandyala SV, Schwend RM. Does a kaolin-impregnated hemostatic dressing reduce intraoperative blood loss and blood transfusions in pediatric spinal deformity surgery? *Spine (Phila Pa 1976)*. 2014;39(19): E1174-E1180.