Fibrinogen Concentrate Versus Cryoprecipitate in Restoring Hemostasis in Infants after Cardiopulmonary Bypass

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INTRODUCTION

After cardiac surgery with cardiopulmonary bypass (CPB), infants often develop acute acquired hypofibrinogenemia that contributes to impaired fibrin formation and inadequate clot formation. Cryoprecipitate is currently the standard of care to supplement fibrinogen. However, fibrinogen concentrate (FC) (Riastap®, CSL Behring, Kankakee, IL), an FDA approved form of purified fibrinogen, has several advantages over cryoprecipitate: 1) smaller volume; 2) accurate dosing; 3) immediate availability; 4) lower risk of infectious transmission; 5) lower risk of allergic and immunologic reactions. In this study, we compared the use of FC to cryoprecipitate as part of our post-bypass transfusion algorithm in infants after cardiac surgery.

METHODS

After IRB approval and parental consent, we prospectively randomized infants (greater than 32 weeks gestational age and with no personal or family history of thrombosis) to receive either 2 units of cryoprecipitate or FC. We targeted a post-transfusion fibrinogen level of 300 mg/dL as part of our post-bypass hemostasis algorithm. Clauss fibrinogen levels, thromboelastograms (TEG) and TEG functional fibrinogen (TEG-FF) were drawn at four time points: before CPB (baseline), on CPB, post-transfusion, and on arrival to the ICU. We compared fibrinogen levels and TEG-FF parameters (MA-FF and FLEV) between the two groups.

Table 1. Patient baseline characteristics

	All Patients (n=18)	Cryoprecipitate (n=9)	Fibrinogen Concentrate (n=9)
Age, median (IQR), mo	4.0 (3-4.75)	4.0 (3-5)	4.0 (3-4)
Weight, median (IQR), kg	5.5 (4.1-6.5)	5.2 (3.9-6.5)	6.1 (5.4-6.5)
Male, No. (%)	12 (72%)	6 (66%)	7 (78%)
Single Ventricle (yes)	4 (22%)	1 (11%)	3 (33%)
Cardiac Procedure			
VSD Closure	3 (16%)	0 (0%)	3 (33%)
CAVC	5 (28%)	4 (44%)	1 (11%)
TOF	4 (22%)	3 (33%)	1 (11%)
Arterial Switch	1 (6%)	1 (11%)	0 (0%)
Glenn	3 (16%)	1 (11%)	2 (22%)
BT shunt/PA plasty	1 (6%)	0 (0%)	1 (11%)
TAPVR	1(6%)	0 (0%)	1 (11%)
CPB Time, median (IQR), min	134 (108-137)	121 (114-134)	134 (106-138)

Table 2. Laboratory values for fibrinogen levels, FLEV, MA-FF at four different time points in patients who received cryoprecipitate or fibrinogen concentrate. (Cryoprecipitate and Fibrinogen Concentrate values compared using Mann-Whitney test; p <0.05 is considered significant).

Time point	All Patients (n=18)	Cryoprecipitate (n=9)	Fibrinogen Concentrate (n=9)	P values
Baseline				
Fibrinogen (mg/dL)	240 (199-264)	254 (217-280)	222 (181.0-245)	0.158
FLEV (mg/dL)	411.5 (364.1-480.0)	452.6 (397.8-512.8)	405.1 (361.3-421.5)	0.353
MA-FF (mm)	22.5 (20.0-26.3)	24.8 (21.8-28.1)	22.2 (19.8-23.1)	0.353
On bypass				
Fibrinogen (mg/dL)	109 (100-121)	120 (105-128)	101 (90-117)	0.133
FLEV (mg/dL)	181.6 (158.5-209.4)	189.9 (159.5-270.1)	173.4 (158.2-204.4)	0.402
MA-FF (mm)	9.95 (6.5-11.5)	10.4 (6.7-14.8)	9.5 (6.1-11.2)	0.331
Post transfusion				
Fibrinogen (mg/dL)	302 (269-323)	269 (194-325)	303 (298-311)	0.500
FLEV (mg/dL)	421.5 (346.7-441.6)	361.3 (306.6-423.4)	438.0 (379.6-483.6)	0.353
MA-FF (mm)	23.1 (19-24.2)	19.8 (16.8-23.2)	24 (20.8-26.5)	0.353
CICU				
Fibrinogen (mg/dL)	301 (287-339)	296 (232-345)	302 (297-321)	0.508
FLEV (mg/dL)	457.2 (367.7-487.2)	447 (354.0-476.3)	461.7 (379.6-490.6)	0.378
MA-FF (mm)	25.1 (20.1-26.7)	24.5 (19.4-26.1)	25.3 (20.8-26.9)	0.378

Figure 1. Median and interquartile ranges of fibrinogen levels at pre-determined time points for patients receiving either cryoprecipitate or fibrinogen concentrate after bypass. (BL = baseline; OB = on bypass; PT = post transfusion; ICU = intensive care unit; FC = Fibrinogen concentrate patients; Cryo = cryprecipitate patients). Post transfusion Fibrinogen levels in the FC group had significantly less variance from the target transfusion goal of 300mg/dL (P<0.001).

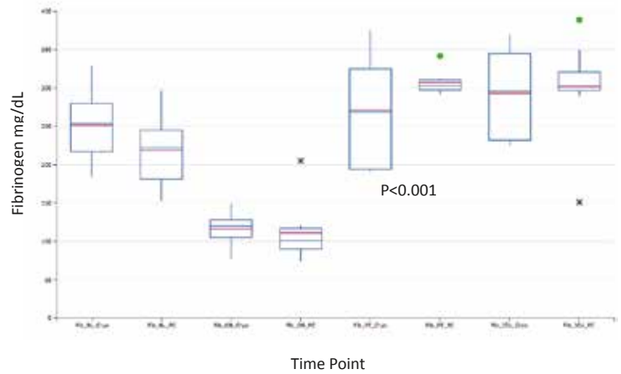
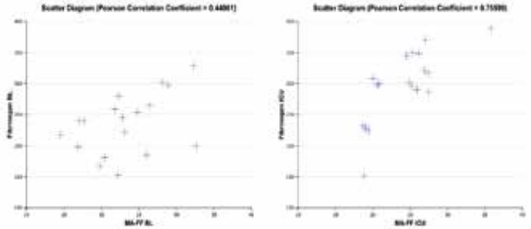


Figure 2. Correlation between Clausss Fibrinogen level and Functional Fibrinogen in infants and neonates demonstrate little correlation of neonatal fibrinogen with MA-FF, but correlation increases after transfusion of adult fibrinogen.



Time Point	Pearson Correlation Coefficient
Baseline	0.441
On Bypass	0.453
Post Transfusion	0.631
CICU	0.756

RESULTS

Nine patients received cryoprecipitate (median age 4.0 months (IQR 3-5); range: 1-10 months) and nine received FC (median age 4.0 months (IQR 3-4); range: 0-9 months) (Table 1). There was no significant difference between the two groups in fibrinogen, FLEV, or MA-FF values immediately post-transfusion or in the ICU (Table 2; Figure 1). However, the FC group more precisely achieved the targeted fibrinogen level (300 mg/dL), with significantly less variability compared to the cryoprecipitate group (p <0.001). Pre-CPB fibrinogen values did not correlate with FLEV in either arm (Pearson Correlation Coefficient R =0.441). However, after transfusion of adult fibrinogen, both the cryoprecipitate and FC groups demonstrated correlation between Clauss fibrinogen and FLEV values (Pearson Correlation Coefficient R = 0.756,) Figure 2.

DISCUSSION

Given the safety concerns associated with blood product administration, we compared FC to cryoprecipitate as part of our post-bypass transfusion algorithm in achieving a targeted fibrinogen level and clot strength using TEG-FF. Administration of FC achieved a targeted fibrinogen level more precisely than cryoprecipitate. Patients in both groups achieved similar MA-FF and FLEV values, suggesting no difference in functional fibrinogen between sources of fibrinogen. In conclusion, our data suggests that FC is an effective alternative to cryoprecipitate for achieving adequate fibrinogen levels and clot strength in infants undergoing cardiac surgery with CPB.

REFERENCES

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