Observational case-control comparison of bivalirudin versus heparin anticoagulation for pediatric extracorporeal membrane oxygenation (ECMO)

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Introduction

- Although there are theoretical advantages of bivalirudin, the effectiveness and risk profile of bivalirudin compared to heparin (the traditional anticoagulant) for extracorporeal membrane oxygenation (ECMO), is currently unknown.
- An objective comparison of heparin and bivalirudin is necessary to inform further pediatric ECMO anticoagulation practice recommendations.

Methods

- Single center, retrospective observational case-control study of extracorporeal membrane oxygenation (ECMO) patients between January 1, 2010 and September 18, 2017.
- During the study period, an institutional practice change was implemented to allow the use of either heparin or bivalirudin-based anticoagulation for ECMO, which allowed a contemporaneous comparison of the two cohorts.
- Cases (those who received bivalirudin) were 1:2 matched to controls (those who received heparin) with matching by age (+/- 5 years), VV or VA, number of times sternum accessed (+/- 1), and central versus peripheral cannulation.
- The primary outcomes compared were mortality, clinically significant thromboembolic complications (stroke, mesenteric ischemia, pulmonary embolism, and massive circuit thrombosis), and allogeneic blood product use per 24 hours of ECMO.
- The secondary outcomes compared were blood loss, number of ECMO circuit interventions (oxygenator or pump exchange, thrombus extraction), frequency of anticoagulant dose adjustment, and overall cost .

Table 1:characteristics and outcomes of pediatric ECMO patients

Parameters	Bivalirudin group (n= 10)	Heparin group (n= 20)	P-value
Characteristics			
Age (years)	3.76(0.17-6.70)	3.03(0.15-6.20)	0.52
Gender, male, n (%)	5(50)	13(65)	0.43
BMI	14.8(12.6-17.3)	15.6(13.2-18.2)	0.81
APACHE Score	71.0(52.5-76.0)	53.5(45.2-66.2)	0.19
VA-ECMO, n (%)	8(80)	19(95)	0.20
Central cannulation, n (%)	8(80)	17(85)	0.73
Renal Replacement Therapy, n (%)	2(20)	4(20)	1.00
Invasive ventilation days (days)	38.1(7.0-95.7)	11.2(4.7-25.3)	0.04*
ECMO duration (hrs)	118.5(64.6-245.8)	116.6(59.1-201.0)	0.91
ICU length of stay (days)	46.3(20.0-104.2)	26.2(11.3-72.2)	0.46
hospital length of stay (days)	65.9(22.2-136.3)	36.3(16.8-74.3)	0.36
Admission type			
Elective, n (%)	3(30)	11(55)	
Emergency, n (%)	0(0)	3(15)	
Urgent, n (%)	6(60)	5(25)	
Newborn, n (%)	1(10)	1(5)	
Outcomes			
ICU Mortality, n (%)	2(22)$	8(40)	0.35
RBC transfusion (ml)			
RBC tx between ECMO hrs 0-24	77.5(0-365.7)	293.5(51.5-778.6)	0.12
RBC tx b/w ECMO hrs 0-24 per kg	7.0(0-37.9)	42.1(13.6-81.2)	0.09
RBC tx between ECMO hrs 25-72	259.5(22.5-382.5)	155.0(63.2-700.1)#	0.87
RBC tx b/w ECMO hrs 25-72 per kg	15.4(5.3-24.9)	32.2(14.1-63.6)#	0.29
Estimated blood loss (EBL), ml			
EBL between ECMO hrs 0-24	484.8(242.3-834.7)	612.7(237.8-1080.5)	0.47
EBL b/w ECMO hrs 0-24 per kg	39.6(20.1-93.9)	62.3(27.0-144.0)	0.32
EBL between ECMO hrs 25-72	524.3(351.9-1282.4)	281.4(180.5-1394.5)#	0.20
EBL b/w ECMO hrs 25-72 per kg	53.7(28.4-109.1)	40.8(11.5-148.7)#	0.76
Thromboembolic complications			
CVA (cerebral vascular accident), n (%)	0(0)	2(10)	0.30
PE (pulmonary embolism), n (%)	1(10)	0(0)	0.15
MI (myocardial infarction), n (%)	0	0	
Mesenteric ischemia, n (%)	0	0	
DVT (deep-vein thrombosis), n (%)	0(0)	1(5)	0.47
Thromboembolic events per ECMO days	0 (0-0)	0 (0-0)	0.84
Circuit interventions per 10 ECMO days	0(0-1.47)	0(0-1.43)	0.91

#, n=18; $, n=9; *, P<0.05

Results

- We identified 10 pediatric ECMO patients managed with bivalirudin and 20 matched controls managed with heparin. (Table 1.)
- The invasive ventilation days were significantly longer in the bivalirudin group than in heparin group.
- The bivalirudin and heparin groups had similar thrombotic complication rates, blood loss, red blood cell transfusion requirements, ECMO duration, ICU and hospital length of stay, required circuit interventions and ICU mortality.

Discussion and Conclusions

- Further comparison of frequency of anticoagulant dose adjustment and cost are forthcoming. Despite matching, the observational study design is susceptible to selection bias, so ultimately a randomized trial is required.
- This matched case-control comparison of bivalirudin versus heparin anticoagulation during pediatric ECMO demonstrated similar ECMO blood loss, transfusion requirements, ICU mortality, and ECMO circuit interventions.
- Markers of bleeding and thrombosis were similar in this single-center matched case-control comparison of heparin and bivalirudin for pediatric ECMO anticoagulation.

References

1. Weitz JI et al. J Clin Invest. 1990;86(2):385-391.
2. Ranucci M et al. Crit Care. 2011;15(6):R275.