Recombinant factor VIIa to control bleeding following cardiac surgery in children

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Introduction: Various factors may be responsible for coagulation disturbances following surgery for congenital heart disease. When clinically significant bleeding occurs, therapy includes correction of coagulation function with the administration of blood products (cryoprecipitate, FFP, platelets) according to laboratory parameters. Despite its efficacy, problems exist with FFP including the transmission of infectious diseases, volume overload, anaphylactoid reactions, alterations in ionized calcium and decreases in mean arterial pressure. Following its efficacy in the hemophilia population, there is increasing clinical experience with recombinant factor VIIa (rFVIIa, NovoSeven®, NovoNordisk, Princeton, NJ) in other clinical scenarios. We present our experience with the use of rFVIIa to treat excessive blood loss following cardiopulmonary bypass (CPB) and cardiac surgery in pediatric patients.

Methods: This retrospective review was approved by the hospital's IRB. The patients were operated on during the January 2003 trip of Heart Care International to Santo Domingo, Dominican Republic. Chest tube output for the first 3 postoperative hours was evaluated and patients who demonstrated excessive blood loss ($\geq$ 4 mL/kg/hr) for 3 consecutive hours were administered rFVIIa as a single bolus dose of 90 mcg/kg. For a comparison group, chest tube output was recorded in 8 patients who did not have excessive blood loss and who did not receive rFVIIa. Following the dose of rFVIIa, chest tube output was evaluated for the next 3 hours. Demographic data included age, weight, gender, and underlying congenital cardiac defect. Data regarding the surgical procedure included CPB time and aortic cross clamp time. Chest tube output before and after rFVIIa was compared using a paired, two-tailed t-test. A non-paired, two-tailed t-test was used to compare demographic data (age, weight), CPB time, aortic cross clamp time, and chest tube output between the two groups. All data are presented as the mean $\pm$ SD with $p<0.05$ considered significant.

Results:

	rFVIIa patients	**Comparison patients**
number of patients	9	8
age (years)	9 ± 4	10 ± 3
weight (kgs)	29 ± 12	28 ± 11
surgical procedure (repair of):		
TOF*	6	5
VSD**	1	0
mitral valve	1	0
sinus venosus ASD***	1	0
primum ASD***	0	3
cardiopulmonary bypass time (min)	97 ± 55	113 ± 37
aortic cross clamp time (min)	68 ± 26	68 ± 23
first 3 hr chest tube output (mL/kg/hr)	5.8 ± 2.8	$1.6 \pm 0.9^{++}$
next 3 hr chest tube output (mL/kg/hr)	$2.0 \pm 1.3^{+++}$	$1.2 \pm 0.6^{\#}$

*TOF = tetralogy of Fallot, **VSD = ventricular septal defect, ***ASD = atrial septal defect
++ p=0.002 compared to first 3 hr of chest tube output of rFVIIa patients
+++p=0.0011 compared to first 3 hr of chest tube output prior to rFVIIa
#p=NS compared to chest tube output after rFVIIa

Discussion: rfviia administration resulted in a significant decrease in chest tube output following surgery for congenital heart disease in children. Chest tube output decreased to approximately one-third of its volume prior to the administration of rfviia. Given its potential therapeutic impact, rfviia warrants further investigation in the pediatric cardiac surgery population. These studies will also need to include an ongoing assessment for potential adverse effects related to this agent.