Discussion

In recent years, the number of patients meeting the criteria for implantation of an ICD has increased dramatically. A number of creative implantation methods have been reported, but each is faced with its own set of potential complications.¹⁻³ These complications range from postpericardiotomy syndrome⁴ to lead or patch trauma and failure.⁵

There are a number of advantages to this implantation, the first of which is that the patient avoids a median sternotomy, and the second of which is that no subcutaneous array is required, therefore eliminating the possibility of array failure.

This case is evidence that a minimally invasive approach to pediatric ICD implantation can be successful. In a patient determined to be too small for traditional transvenous implantation or with a lack of venous access, this method of ICD implantation should be considered.

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Argatroban anticoagulation for renal replacement therapy in patients with heparin-induced thrombocytopenia after cardiovascular surgery

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Heparin-induced thrombocytopenia (HIT) is a severe thrombogenic disease requiring the use of alternative anticoagulants. Argatroban is a synthetic monovalent direct thrombin inhibitor indicated for prophylaxis and treatment of thrombosis in patients with HIT. Renal failure requiring renal replacement therapy (RRT) is a frequent complication in patients in whom HIT develops after cardiovascular surgery. The hepatic metabolism and relative short elimination half-life of 45 minutes render argatroban an interesting option for anticoagulation during RRT. However, there are scant data on dosing, pharmacokinetics, safety, and efficacy of argatroban in this indication. We report our initial experience with argatroban anti-

coagulation for continuous veno-venous hemofiltration (CVVH) and intermittent hemodialysis (IHD) in 10 patients diagnosed with HIT after cardiovascular surgery in whom acute renal failure developed necessitating RRT.

Patients and Methods

After approval by the local ethics committee and having obtained informed consent, we analyzed the data of 10 patients. In accordance with the study protocol, data were collected for a maximum of 30 days during RRT. Clinical follow-up of patient outcome was performed for 3 months after initiation of RRT with argatroban. All patients had thrombocytopenia after surgery or presented persistent thrombocytopenia postoperatively. In all patients the diagnosis of HIT was confirmed in an antibody assay (Particle Gel Immune Assay; DiaMed, Cressier sur Morat, Switzerland) and in the heparin-induced platelet aggregation assay. The decision to perform CVVH (Ultraflux AV 600S; polysulfone high flux hemodialyzer, Fresenius Medical Care AG, Bad Homburg, Germany) or IHD (Polyflux 140 H; polyamix high flux hemodialyzer, Gambro, Hechingen, Germany) was based on stability of hemodynamics and mobility of the patient. In general, RRT was started with CVVH and changed to IHD after hemodynamics were stable and patient mobility increased. Only in 1 patient was RRT initiated with IHD. Target activated partial thromboplastin time (aPTT) (Roche Diagnostics, Mannheim, Germany, normal value 20-22 seconds) during RRT was 50 to 80 seconds and 40 to 60 seconds in periods without CVVH or IHD. Before the start of RRT, argatroban administration was started with a continuous infusion of $1 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ for 1 hour. Thereafter, the aPTT was

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TABLE 1. Argatroban dose and aPTT during and between CVVH and IHD

	During CVVH (n = 9)	Between CVVH procedures (n = 9)	Before IHD (n = 6)	During IHD (n = 6)	After IHD (n = 6)	Between IHD procedures (n = 6)
No. of procedures	73			29		
Argatroban ($\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$)	0.13 ± 0.21	0.29 ± 0.31	0.07 ± 0.11	0.06 ± 0.11	0.07 ± 0.12	0.20 ± 0.20
aPTT	64.4 ± 12.9	64.8 ± 17.3	53.4 ± 10.6	58.4 ± 9.8	54.0 ± 16.0	57.3 ± 16.2

aPTT, Activated partial thromboplastin time; CVVH, continuous veno-venous hemodialysis; IHD, intermittent hemodialysis.

measured and RRT started. During the procedures, argatroban infusion rates were adjusted to target values in increments of $0.25 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ depending on the results of coagulation tests.

Results

There were 7 male and 3 female patients. The mean age was 58.8 ± 11.0 years. Surgery performed was implantation of a ventricular assist device in 2 patients, heart transplantations in 3, lung transplantation in 1, pulmonary artery thrombectomy in 1, replacement of a thoracoabdominal aortic aneurysm in 1, and coronary artery bypass grafting in 2. No bleeding events attributed to problems of anticoagulation were observed. Five patients died during the observation period. Data for argatroban dosing and aPTT values are presented in Table 1. The total duration of the 73 CVVH procedures was 2252 hours with a mean of 30.8 ± 27.1 hours. The total duration of the 29 IHD procedures was 160 hours with a mean of 3.9 ± 1.0 hours. No filter system had to be exchanged during IHD as a result of premature filter thrombosis.

Discussion

This is the first investigation providing a dosing regimen for the use of argatroban during RRT in patients with HIT after cardiovascular surgery. Our data provide convincing evidence that in these patients the current protocol provides safe and effective anticoagulation for CVVH and IHD. The data obtained suggest the following:

1. In view of the good patency of filters of approximately 30 hours and the low rate of bleeding complications, prolongation of the aPTT to the 3- to 4-fold appears to be safe and effective for argatroban anticoagulation for both CVVH and IHD in this patient population.
2. In a previous investigation, we¹ demonstrated that argatroban dosing in patients after cardiovascular surgery is considerably lower than in medical patients and that the anticoagulant effect of the drug is immediately achieved by continuous infusion so that no bolus administration is necessary. In line with these observations, in our patients the mean argatroban infusion rate during RRT of 0.06 to $0.12 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ was considerably lower than the median infusion rate of $1.7 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ in medical patients. Moreover, a starting infusion rate of $1 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ for

1 hour provided reliable anticoagulation for the initiation of RRT, so that no bolus administration was necessary.²

3. In contrast to observations with the other direct thrombin inhibitors, bivalirudin and lepirudin, and in line with previous observations, the fact that argatroban dosing during and after CVVH and IHD was almost comparable with dosing during intervals without RRT suggests only minor elimination of the drug via the filter system.³⁻⁵ However, elimination of argatroban appears to be slightly more pronounced during CVVH.

On the basis of these observations, we conclude that dosing of argatroban according to the protocol outlined here provides reliable, safe, and effective anticoagulation during CVVH and IHD in patients with HIT after cardiovascular surgery. Inasmuch as the argatroban elimination half-life of 45 minutes is relatively short, elimination is independent of renal function and, as we observed, extracorporeal elimination during both CVVH and IHD is clinically insignificant, so that no dose adjustment is necessary during RRT, argatroban anticoagulation appears to be an excellent option in this indication. However, further detailed studies are needed to confirm this assumption.

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