Comparison of the Effectiveness and Safety of Low-Molecular Weight Heparin Versus Unfractionated Heparin Anticoagulation After Heart Valve Surgery

Claudia Bucci, PharmD[a,b,*], William H. Geerts, MD[c], Andrew Sinclair BScPhm[b], and Stephen E. Fremes, MD[d]

Although unfractionated heparin (UFH) is used routinely after heart valve surgery at many institutions, cardiovascular surgery patients have a particularly high risk for developing heparin-induced thrombocytopenia (HIT). The aim of this study was to compare the efficacy and safety of low-molecular-weight heparin (LMWH) or UFH after heart valve surgery by conducting a retrospective evaluation of consecutive cardiovascular surgery patients in whom the LMWH dalteparin (n = 100) was used as the postoperative anticoagulant. This group was compared to an earlier group of patients who received UFH (n = 103). The main outcomes included the efficacy of the anticoagulant regimens (determined by the incidence of valve thrombosis, arterial thromboembolic events, and venous thromboembolic events) and the safety (determined by major bleeding, HIT, thrombotic events in HIT-positive cases, and death). Overall, there were for fewer thrombotic events in the LMWH-treated group (4% vs 11%, p = 0.11). There was a higher rate of bleeding events in the UFH-treated group (10% vs 3%, p = 0.08). Six patients in the UFH-treated group developed HIT, 4 of whom had thrombotic events (HIT with thrombosis). In the LMWH-treated group, 3 patients developed HIT, 1 of whom had HIT with thrombosis. In conclusion, in this study, an LMWH regimen after heart valve surgery was effective and safe, with fewer thrombotic, bleeding, HIT, and HIT with thrombosis events. **(Am J Cardiol 2011;107:591–594)**

In the past, intravenous unfractionated heparin (UFH) was used routinely at our institution after heart valve replacement surgery to prevent thrombotic complications (Appendix A). LMWH is associated with a substantially lower rate of heparin-induced thrombocytopenia (HIT) and HIT with thrombosis than UFH and may be a safer alternative after heart valve surgery.[1] We replaced intravenous and subcutaneous UFH with subcutaneous low-molecular-weight heparin (LMWH) in prophylactic or therapeutic doses for early anticoagulation after heart valve replacement surgery (Appendix B). The objective of the study was to assess the efficacy and safety of anticoagulation with LMWH after heart valve surgery compared to UFH.

Methods

In March 2006, we implemented an "avoid-heparin policy" after cardiovascular surgery (Appendixes A and B). Intraoperative UFH was used in all cases. We conducted a retrospective evaluation of consecutive patients in whom the LMWH dalteparin was used, and we compared this group to an earlier group of patients who received UFH. This study was approved by the ethics review board of Sunnybrook Health Sciences Centre. The main outcome measures included the efficacy (determined by the incidence of valve thrombosis, arterial thromboembolic events, and venous thromboembolic events) and the safety (determined by major bleeding, HIT, thrombotic events in HIT-positive cases, and death) of the 2 anticoagulant regimens. All outcomes collected occurred during the operative hospital admission.

Confirmed HIT was defined by 1 of the following: positive serotonin release assay, positive HIT enzyme-linked immunosorbent assay plus high clinical probability for HIT

[a]Department of Pharmacy and [b]Faculty of Pharmacy, University of Toronto; and [c]Thromboembolism Program, Department of Medicine, and [d]Division of Cardiovascular Surgery, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada. Manuscript received July 15, 2010; revised manuscript received and accepted October 11, 2010.

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*Corresponding author: Tel: 416-480-6755; fax: 416-480-5887.
E-mail address: claudia.bucci@sunnybrook.ca (C. Bucci).

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Table 1
Baseline characteristics

Characteristic	Heparin (n = 103)	Dalteparin (n = 100)	p Value
Age (years)	65.1 ± 12.6 (31–87)	66.1 ± 12.1 (43–84)	0.57
Age >75 years	23 (22%)	24 (24%)	0.87
Men/women	72/31	67/33	0.76
Left ventricular function			0.65
1	57 (55%)	52 (52%)	
2	22 (21%)	28 (28%)	
3	16 (16%)	15 (15%)	
4	8 (8%)	5 (5%)	
Atrial fibrillation*	66 (64%)	68 (68%)	0.67
Renal dysfunction†	13 (13%)	16 (16%)	0.55
Valve replacement			0.63
Single	95 (92%)	90 (90%)	
Mechanical aortic	27	23	
Tissue aortic	21	19	
Mechanical mitral	17	21	
Tissue mitral	14	8	
Mitral annuloplasty	15	18	
Tricuspid repair	1	1	
Double	8 (8%)	10 (10%)	0.63
Coronary bypass	43 (42%)	32 (32%)	0.19
Length of surgery (hours)	4.9 ± 1.7 (2.3–10.2)	5.3 ± 1.9 (2.7–12.9)	0.09
Length of stay after surgery (days)	15.9 ± 9.9 (5–61)	16.1 ± 9.5 (6–64)	0.87

Data are expressed as mean ± SD (range) or as number (percentage).

* Includes transient and chronic episodes. Transient atrial fibrillation occurred in 49 and 43 patients in the heparin and LMWH groups, respectively (p = 0.57). Chronic atrial fibrillation was present preoperatively and/or was persistent after surgery and occurred in 17 and 25 patients in the heparin and LMWH groups, respectively (p = 0.17).

† Creatinine clearance <30 ml/min.

or strongly positive HIT enzyme-linked immunosorbent assay (optical density ≥1.0). HIT was ruled out in patients with negative results on HIT enzyme-linked immunosorbent assay or serotonin release assay.

Major bleeding was defined as any overt bleeding meeting ≥1 of the following criteria: proved fatal bleeding, intracranial hemorrhage (computed tomography or magnetic resonance imaging required), retroperitoneal bleeding (ultrasound, computed tomography, or magnetic resonance imaging required), bleeding requiring an intervention (pericardial bleeding requiring reoperation or catheter drainage of blood, pleural bleeding requiring thoracotomy or chest tube, gastrointestinal bleeding requiring surgery or endoscopic treatment, wound bleeding requiring reoperation), other life-threatening bleeding at a critical site, bleeding requiring transfusion of ≥2 U of red blood cells, or bleeding that resulted in chronic sequelae or prolongation of the hospital stay. Bleeding requiring pericardiocentesis, thoracentesis, or diagnostic endoscopy alone was not considered major. Nonmajor bleeding was defined as any of the following: epistaxis requiring nasal packing, airway bleeding, hematuria, hematemesis (but not just coffee grounds), or gastrointestinal bleeding (frank blood or melena stools) not requiring an intervention.

All analyses were done using InStat version 3 (GraphPad Software, San Diego, California). All statistical tests were 2 sided and used a p value of 0.05 as the threshold for statistical significance. Baseline discrete variables are presented as frequencies or percentages, while continuous variables are presented as mean ± SD or as median (interquartile range). The frequencies of the clinical end points were compared using a chi-square or Fisher's exact tests.

Results

The control group consisted of 103 consecutive patients treated with UFH after heart valve surgery from April 2004 to May 2006. These patients received only UFH in therapeutic (83%) or prophylactic (17%) doses. The control group patients were compared to 100 heart valve patients given therapeutic (73%) or prophylactic (27%) dalteparin postoperatively from March 2006 to August 2007.

The 2 groups were similar for a large number of demographic and clinical characteristics (Table 1). The mean age was approximately 65 years, and 68% of patients were men. Thrombotic and bleeding risk factors in the 2 groups were similar apart from greater postoperative aspirin use in the UFH patients (Table 2). Approximately 60% of the study population had ≥1 risk factor for thrombosis, and >80% of patients had ≥1 risk factor for bleeding.

Overall, there were fewer thrombotic events in the LMWH-treated group, although the difference was not statistically significant (4% vs 11%, p = 0.11; Table 3). In the UFH group, there were 11 thrombotic events (5 strokes, 1 valve thrombosis, 1 ischemic bowel, 2 transient global amnesia, 1 foot embolus, 1 kidney infarction). In the dalteparin group, there were 4 thrombotic events (3 strokes, 1 ischemic bowel). The thromboembolic events are listed in Table 4 . In the UFH-treated group, 4 thrombotic events occurred in