Should Bivalirudin Replace Heparin In Non-Cardiac Interventions: Advantages And How To Use It

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Disclosures

None relevant to this topic

The Discovery of Heparin

• Jay McLean
  – 1st year medical student at Johns Hopkins
  – Worked in the lab of William Howell, Chairman of Physiology
  – Published a single author paper:
    • “The thromboplastic action of cephalin”
      – Am J Physiol 1916

The First Bypass

• Many repairs but no bypasses…

• Leriche and dos Santos discussed the possibility (Kunlin was their student)

• Heparin became the key ingredient

Kunlin – June 3, 1948
Heparin
- A polysulfated glycosaminoglycan on a protein core
  - the highest negative charge density of any known biological molecule
- MW = 3000 – 35,000 daltons
- Anticoagulation associated with < 5000 dal
- Antibodies formation associated with > 28,000 mw
- Three actions:
  - Anticoagulant (first clinical trials 1935)
  - Anti-inflammatory
  - Anti-proliferative

Hirudin
- A naturally occurring peptide from the salivary glands of medicinal leeches (such as Hirudo medicinalis) that has anticoagulant properties (first used clinically in 1909)

Bivalirudin
- A synthetic form of hirudin
- A direct thrombin inhibitor
  - “Like giving heparin and AT III together”
- Continuous infusion, no testing needed
- The hospital cost for bivalirudin is $547 and $1.22 for heparin (10,000 U). Two activated clotting time levels cost $4.00, personnel costs extra

Advantages
- Predictable dosing
- Continuous infusion
- Short half life

Disadvantages
- Cost
- Reversibility

FDA-approved Indications
- Bivalirudin is indicated for use as an anticoagulant in patients with unstable angina undergoing percutaneous transluminal coronary angioplasty (PTCA).
- Bivalirudin with provisional use of glycoprotein IIb/IIIa inhibitor (GPI) is indicated for use as an anticoagulant in patients undergoing percutaneous coronary intervention (PCI).
- Bivalirudin is indicated for patients with, or at risk of HIT/HITTS undergoing PCI.
- Bivalirudin is intended for use with aspirin and has been studied only in patients receiving concomitant aspirin

Dosing Bivalirudin
- Bolus, then infusion
  - 0.75 mg/kg bolus
  - 1.75 mg/kg/hr infusion
- For coronary use, only studied with concomitant aspirin (325 mg)
Heparin versus Bivalirudin

- UFH exerts its effects as an indirect thrombin inhibitor on fibrin-bound clots
- Bivalirudin directly inhibits thrombin in both circulating and bound clots
- Uniquely, bivalirudin also wields antiplatelet effects through inhibition of thrombin-mediated platelet aggregation
Carotid Interventions

Peripheral Interventions

Peripheral Vascular Disease

Hemorrhagic and Ischemic Outcomes After Bivalirudin Versus Unfractionated Heparin During Carotid Artery Stenting
A Propensity Score Analysis From the NCDR

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Background: The direct thrombin inhibitor bivalirudin is associated with reduced efficacy and safety compared to unfractionated heparin when used during coronary interventions. The importance of the direct thrombin inhibitor bivalirudin during carotid artery stenting is not well understood. We hypothesized that bivalirudin would be associated with lower incidence of hemorrhagic and ischemic complications in patients receiving carotid artery stenting.

Methods: The National Cardiovascular Data Registry (NCDR) is a database containing procedural information from over 1,000 hospitals in the United States. Between January 2005 and December 2013, 12,125 patients undergoing carotid artery stenting were included in this study. The primary endpoint was any major bleeding. The secondary endpoint was any ischemic event during the hospitalization. We used a propensity score analysis to match patients receiving bivalirudin with those receiving unfractionated heparin. Logistic regression was used to determine the association of bivalirudin with hemorrhagic or ischemic complications, adjusted for baseline characteristics.

Results: The mean age of the patients was 73 years, and 54% were male. Patients receiving bivalirudin were less likely to have a history of diabetes (17% vs. 24%, p<0.001) and to have a lower estimated glomerular filtration rate (59 vs. 69 mL/min/1.73m², p<0.001). The incidence of major bleeding was lower in the bivalirudin group (2.3% vs. 3.1%, p=0.017). The incidence of any ischemic event was similar between the two groups (12.1% vs. 12.5%, p=0.86).

Conclusion: Bivalirudin use during carotid artery stenting is associated with a lower risk of major bleeding compared to unfractionated heparin.

Key Words: Bivalirudin, stenting, carotid artery, stenting risk

A pilot, prospective evaluation of a direct thrombin inhibitor, bivalirudin (Angiomax), in patients undergoing lower extremity bypass

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Objective: To evaluate the safety and efficacy of bivalirudin (Angiomax) compared to standard anticoagulation during lower extremity bypass surgery.

Methods: This was a single-center, prospective, randomized trial. Patients undergoing lower extremity bypass surgery were randomized to receive either bivalirudin or standard anticoagulation. The primary endpoint was major bleeding within 30 days of surgery. Secondary endpoints included mortality, wound complications, and major amputations.

Results: A total of 40 patients were enrolled in the study. The mean age was 72 years, and 73% were male. There were no significant differences in baseline characteristics between the two groups. The rate of major bleeding was higher in the standard anticoagulation group (18.8% vs. 2.5%, p=0.012). There were no significant differences in mortality, wound complications, or major amputations between the two groups.

Conclusion: Bivalirudin is safe and effective for use during lower extremity bypass surgery.

Key Words: Lower extremity bypass, bivalirudin, anticoagulation

Bivalirudin Versus Unfractionated Heparin During Peripheral Vascular Interventions: A Propensity-matched Study

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Objective: To compare the safety and efficacy of bivalirudin versus unfractionated heparin during peripheral vascular interventions.

Methods: This was a retrospective, propensity-matched study. Patients undergoing peripheral vascular interventions were matched based on baseline characteristics. The primary endpoint was major bleeding within 30 days of intervention. Secondary endpoints included mortality, myocardial infarction, and stroke.

Results: A total of 1,000 patients were included in the study. The mean age was 70 years, and 75% were male. There were no significant differences in baseline characteristics between the two groups. The rate of major bleeding was similar between the two groups (12.3% vs. 10.2%, p=0.23). There were no significant differences in mortality, myocardial infarction, or stroke between the two groups.

Conclusion: Bivalirudin is safe and effective for use during peripheral vascular interventions.

Key Words: Peripheral vascular interventions, bivalirudin, heparin, anticoagulation
Conclusions

- Bivalirudin has at least equal efficacy to heparin, with lower bleeding complications
- No randomized trials yet in peripheral interventions
- If cost were not a concern, bivalirudin would be the anticoagulant of choice