

Bivalirudin use in pediatrics

In patients with heparin induced thrombocytopenia, heparin resistance, or significant thrombosis while on therapeutic heparin, alternative anticoagulation management is desired, such as a direct thrombin inhibitor (DTI). Young children have lower concentration of anticoagulants such as antithrombin (AT), Protein C and S, especially during the neonatal period.

Bivalirudin has the shortest half-life among all DTI's with lower dependence on renal or liver function for removal (~80% enzymatic) which is a benefit in patients who have a high risk of bleeding, organ failure, or who may require an invasive procedure.

The dosing presented below is a guide to aid in the initiation of Bivalirudin infusion; however alterations may occur based on the clinical presentation of the patient. All other uses including for surgical procedures/intraoperative use, call Anticoagulation Service.

Bivalirudin initial dosing guide: *(Note this is not the package insert dose)*

- Range: 0.03-0.3 mg/kg/hour
 - *If deemed necessary by physician, bolus dose: 0.1-0.2 mg/kg*

Dose Adjustments:

- aPTT values 1-15 seconds outside of target → adjust by 0.02mg/kg/hr of the initial infusion rate
- aPTT values 16-30 seconds outside of target → adjust by 0.04mg/kg/hr of the initial infusion rate

Monitoring:

- Request aPTT 4 hours post starting the infusion. Target aPTT is 1.5-2.5 times baseline value or institutional mean value if baseline value is unknown
- In high bleeding risk patients, a Q2 hour aPTT x3 draws is suggested to evaluate response
- INR every day with (morning) aPTT
- CBC/Platelets/aPTT 4 hours post each rate adjustment and every morning while on DTI infusion
- Do not stop the DTI infusion simply because the INR increases (no warfarin); If the INR exceeds baseline INR by 0.5 with an aPTT that is not excessively elevated, call the pharmacy for further assessment.

References

1. Young G. Old and new antithrombotic drugs in neonates and infants. *Seminars in Fetal & Neonatal Medicine* 16(2011):349-354.
2. Young G, Tarantino MD, Wohrley J, Weber LC, Belvedere M, Nugent DJ. Pilot dose-finding and safety study of bivalirudin in infants <6 months of age with thrombosis. *J Thromb Haemost* 2007; 5: 1654–9.
3. Rayapudi S, Torres A, Deshpande GG, et al. Bivalirudin for anticoagulation in children. *Pediatr Blood Cancer* 2008;51:798-801.

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Bivalirudin use in extracorporeal life support (ECLS)

ECLS is an invasive, lifesaving intervention in patients with temporary and reversible cardiac and/or respiratory failure. Due to the conflict between the blood and nonbiologic surface of the circuit, patients require systemic anticoagulation to prevent thrombosis. Heparin is usually the standard; however bivalirudin may be desirable in select patients. Please call the Anticoagulation Service for assistance.

Bivalirudin has the shortest half-life among all DTI's with lower dependence on renal or liver function for removal (~80% enzymatic) which is a benefit in patients who have a high risk of bleeding, organ failure, or who may require an invasive procedure.

The dosing presented below is a guide to aid in the initiation of Bivalirudin infusion; however alterations may occur based on the clinical presentation of the patient. All other uses including for surgical procedures/intraoperative use, call Anticoagulation Service.

Bivalirudin initial dosing guide: (Note this is not the package insert dose)

- Range: 0.15-0.4 mg/kg/hour
 - *If deemed necessary by ECLS Attending Physician, bolus dose: 0.1-0.2 mg/kg*

Dose Adjustments:

- aPTT values 1-15 seconds outside of target → adjust by 0.02mg/kg/hr of the initial infusion rate
- aPTT values 16-30 seconds outside of target → adjust by 0.04mg/kg/hr of the initial infusion rate

Monitoring:

- aPTT goal to be determined by ELCS attending physician and documented in bivalirudin order. Target aPTT is 1.5-2.5 times baseline value (or the institutional mean if the baseline value is unknown) or unless otherwise specified.
- Request aPTT 4 hours post starting the infusion
- In high bleeding risk patients, a Q2 hour aPTT x3 draws is suggested to evaluate response
- If aPTT greater than goal, do NOT stop infusion, call HO
- INR every day with (morning) aPTT
- CBC/Platelets/aPTT 4 hours post each rate adjustment and every morning while on DTI
- Do not stop the DTI infusion simply because the INR increases (no warfarin); If the INR exceeds baseline INR by 0.5 with an aPTT that is not excessively elevated, call the pharmacy for further assessment.

References:

1. Nagle EL, Dager WE, DUBY JJ et al. Bivalirudin in pediatric patients maintained on extracorporeal life support. *Pediatr Crit Care Med* 2013;14:e-182-e188.
2. Ranucci et al. Bivalirudin-based versus conventional heparin anticoagulation for postcardiotomy extracorporeal membrane oxygenation. *Critical Care* 2011;15:R275.
3. Pieri M, Agracheva N, et al. Bivalirudin versus heparin as an anticoagulant during extracorporeal membrane oxygenation: a case-control study. *Journal of Cardiothoracic and Vascular Anesthesia*; 27;1; February 2013:pp 30-34.
4. Pappalardo F, Maj G, Scandroglio A, et al. Bioline heparin coated ECMO with bivalirudin anticoagulation in a patient with acute heparin-induced thrombocytopenia: the immune reaction appeared to continue unabated. *Perfusion* 2009;24:135-137.

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