ORGARAN (DANAPAROID SODIUM)

Summary

- Alternative anticoagulant for patients with a history of HITS.
- Patients on Orgaran with a vascath access for haemodialysis must also have Orgaran instilled into the vascath lock post dialysis.
- Platelets must be monitored.
- There is no antidote to danaparoid.
- Must be ordered on the medication chart and given as per hospital medication administration protocol.
- Bolus 3000units Orgaran intravenously into arterial port in haemodialysis circuit at commencement of haemodialysis (dose reduction required if patient weight is <55kg).

Cross References

Medication Handling in NSW Public Hospitals PD_2007 077

Vascath – Instillation of Anticoagulant / Antibiotic Lock CHN_CLIN_023

Indications

Orgaran is a heparinoid of low molecular weight and is used during haemodialysis as an alternative anticoagulation for patients who have a history of heparin induced thrombocytopenia syndrome (HITS) (Fischer, 2007; Keeling et al., 2006).

The patient receiving Orgaran must also have an antibiotic and Orgaran lock instilled into their vascath (refer to: Vascath – Instillation of Anticoagulant / Antibiotic Lock CHN_CLIN_023).

Not interchangeable with low molecular weight heparin ("MIMS Online," 2012).

Contraindications

Severe hypertension, severe gastric or duodenal ulcer, acute bacterial endocarditis, diabetic retinopathy, uncontrollable haemorrhagic bleeding state, hypersensitivity to sulfite ("MIMS Online," 2012).

Interaction with: Aspirin, other drugs affecting platelets, coagulation; ulcerogenic drugs eg corticosteroids (use with caution); prothrombin time, Thrombotest (within 5 hrs) ("MIMS Online," 2012).

Procedure:

- Orgaran must be ordered on a medication chart.
- Caution in patients allergic to sulfite.
- Follow the hospital medication protocol for drug administration.
- Bolus 3000units Orgaran intravenously into arterial port in haemodialysis circuit at commencement of haemodialysis.
- Watch for signs of fibrin deposits and clot formation within the extracorporeal circuit after danaparoid is administered and notify the medical team if this occurs.

Note: There is no antidote to danaparoid.

Monitoring

In monitoring of haemodialysis patients who have commenced danaproid therapy, attention should focus on platelet count. Anti-Xa activity has to be measured (European Best Practice Guidelines, 2002; Fischer, 2007), APTT is not useful. The half life of the anti-Xa activity of danaproid is 25 hr in patients without renal failure and is prolonged in uraemia (Fischer, 2007). Orgaran may potentially induce thrombocytopenia, therefore the platelet count should be monitored at regular intervals ("MIMS Online," 2012).

Expected pre dialysis ranges for anti-Xa levels from (UK Renal Pharmacy Group, 2010):

- *If plasma anti-Xa levels are <0.3 U/ml, then third and subsequent dialysis dose should be 3000 units (patients weighting <55kg use 2000 units)*
- *If plasma anti-Xa levels are 0.3-0.35 U/ml, then third and subsequent dialysis dose should be 2500 units (patients weighting <55kg use 1500 units)*

- *If plasma anti-Xa levels are 0.35-0.4 U/ml, then third and subsequent dialysis dose should be 2000 units (patients weighting <55kg use 1500 units)*
- *If plasma anti-Xa levels are >0.4 U/ml, then then do not give any danaparoid before dialysis (If fibrin threads form in the bubble chamber, then the patient may be given 1500 units IV bolus irrespective of patient's weight)*
- *During dialysis the plasma anti-Xa level should be between 0.5-0.8 U/ml.*
- *If no anti-Xa monitoring is available then the first 4 dialysis sessions should have pre dialysis IV bolus of 3750, 3750, 3000 and 2500 units respectively, then 2500 units thereafter. Take a blood sample prior to the 4th and 7th dialysis to ensure there is no accumulation (UK Renal Pharmacy Group, 2010) pp 205-206.*

Note: There is no antidote to danaparoid.

From the Literature

Table 1: From (Keeling, et al., 2006, p. 265)

Table III. Regimens for danaparoid and lepirudin for alternate day haemodialysis in patients who have previously had HIT (Fischer, 2004).

	IV Bolus	Monitoring
Danaparoid	3750 (2500) U* before first and second dialyses; 3000 U before third dialysis; then according to predialysis anti-Xa level <0·3 3000 (2000) U 0·3–0·35 2500 (1500) U 0·35–0·4 2000 (1500) U >0·4 0 U	Anti-Xa 0·5–0·8 U/ml
Lepirudin	80–150 µg/kg before dialysis	APTT 2·0–2·5

*For danaparoid use doses in parentheses for patients <55 kg.

Table 2: (Copied from: Davenport, 2011, p. 501)

Table 1 | Anticoagulation options for standard 4 h hemodialysis session*

Agent	Loading dose	Maintenance dose	Monitoring	Major issues and complications
Unfractionated heparin	1,000–1,500 IU	1,000 IU/h	aPTTr 2.0–2.5 ACT +80%	Bleeding, HIT type 2, allergic reactions
Low-molecular-weight heparins‡	Enoxaparin 0.8 mg/kg Tinzaparin 2,500–3,500 IU	None	Anti-Xa 0.4–0.6 IU/ml	Bleeding, HIT type 2, allergic reactions
Argatroban	250 µg/kg or ≤20 mg	2 µg/kg per min 6–15 mg/h	aPTTr 2.0–2.5	Increased effect in patients with liver disease (reduced dose is required), prolongs INR
Lepirudin	0.2–0.5 mg/kg 5–30 mg	None	Hirudin 0.5–0.8 µg/ml aPTTr 1.5–2.0	Prolonged half-life ensure aPPTr <1.5 pre-HD, irreversible effect, antihirudin antibodies
Danaparoid	3,750 IU (2,500 IU if <55 kg)	None	Pre-HD anti-Xa <0.20 IU/l	Prolonged half-life, can accumulate; reduce dose with subsequent HD to 3,000 IU (2,000 IU if <55 kg)
Fondaparinux	2.5 mg	None	Pre-HD anti-Xa <0.20 IU/l	Prolonged half-life, can accumulate
Citrate infusion	None	Adjusted to blood flow 300 ml/min ~50–60 mmol/h	Postdialyzer ionized calcium 0.2–0.3 mmol/l ACT pre/postdialyzer Systemic calcium	Requires specialist dialyzate, hypocalcemia, hypomagnesemia, citrate toxicity, metabolic alkalosis or acidosis
Citrate dialyzate	None	0.8 mmol/l in dialyzate	None	Hypomagnesemia, possible risk of circuit clotting
Prostacyclin	None	5–10 ng/kg per min	None	Hypotension
Nafamostat mesilate	5 mg/kg 10–40 mg	0.2–0.8 mg/kg per h 20–40 mg/h	aPTTr 1.5–2.0	Allergic reactions

*Options for a 70 kg patient with no increased risk of hemorrhage. ‡Tinzaparin and enoxaparin have been chosen as examples of low-molecular-weight heparins as they are at opposite ends of the spectrum in terms of half-lives and relative activity against thrombin and activated factor X. Abbreviations: ACT, activated clotting time as % of baseline; anti-Xa, anti-factor Xa activity; aPTTr, activated partial thromboplastin time ratio; HD, hemodialysis; HIT, heparin-induced thrombocytopenia; INR, international normalized ratio; IU, international unit.

References

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