

ANTICOAGULATION - COMMENCEMENT OF HAEMODIALYSIS

Summary

- *Aim: To prevent clotting of the extracorporeal circuit during haemodialysis*
- *If there are no contraindications, heparin can be used.*
- *In the first three sessions of dialysis:*
 - *Give 500 units heparin loading*
 - *Use heparin infusion rate of 500 units/hour until last hour.*
 - *Monitor response such as monitoring venous chamber and dialyser for clotting.*
- *After the first three sessions of dialysis it may be necessary to increase the dose to a routine level.*
- *Standard St George practice: 1,000 units loading and 1,000 units per hour infusion, turning off for the last hour for the AV fistula patients and heparin on until the end of treatment for the vascath patients.*
- *Before increasing loading dose or infusion rate ensure there are no other technical causes for clotting in the circuit such as blood flow, needle position, inadequate priming etc (see page 3)*
- *Coagulation profile should be checked if heparinised during dialysis on the same day as a surgical procedure.*
- *Low dose heparinisation (loading dose of 500 units of heparin and heparin infusion rate of 500 unit/hr) required where there is increased bleeding risk:*
 - *Active bleeding stopped more than three days but less than seven days*
 - *Surgery, biopsy or trauma more than three days but less than seven days before*
 - *Elective surgery less than four hours post dialysis*
 - *Pericarditis*

Background

Fischer 2007 indicates that the turbulence and shear caused by haemodialysis activates platelets directly, while contact of blood with artificial surfaces induces

profound activation of plasmatic coagulation. Hypercoagulability is also caused by uremic toxins, systemic inflammation and endothelial damage.

Clotting on artificial surfaces is thought to mainly occur via the intrinsic pathway while the extracorporeal blood purification procedures also activate the extrinsic pathway of coagulation (Fischer, 2007).

Agents interfering with the plasmatic clotting cascade are used for routine anticoagulation during extracorporeal blood purification (Davenport, 2011b; European Best Practice Guidelines, 2002; Fischer, 2007). Anticoagulants differ in their targets within the clotting cascade or their inhibitory potency. Heparin is not dialysed in haemodialysis. Where there is bleeding caused by over heparinization, 1mg of protamine is required to neutralise 100 International Units heparin ("MIMS Online," 2012; UK Renal Pharmacy Group, 2010)refer to protamine protocol.

Unfractionated Heparin (UFH)

Heparinization during haemodialysis requires an initial loading dose followed by a maintenance dose given via constant infusion into the arterial line via an infusion pump (European Best Practice Guidelines, 2002; Fischer, 2007). Aim to prolong the APTT to 150% of the pre dialysis value is recommended (European Best Practice Guidelines, 2002). Individualized dosing schedules can reduce bleeding complications. The half life of UFH is extended with kidney failure to between 30 and 120 minutes, but considerable variation is reported between patients and even drug batches (Davenport, 2011a, 2011b).

Monitoring UFH

Measurement of the activated partial thromboplastin time (APTT); or bedside testing using the activated coagulation time (ACT). Aim for ACT 140-180 seconds (180% of baseline) or a systemic aPTTr of 1.5-2.5 (Davenport, 2011b), or in patients with increased risk of bleeding aim for an ACT 120 seconds (140% of baseline) or a systemic aPTTr of 1.5-2.0 (Davenport, 2011a). Once haemodialysis is terminated, the ACT should have reduced to 140% of baseline or aPTTr <1.5 with the heparin infusion being ceased 20-60 minutes before the end of dialysis (Davenport, 2011a).

Heparin Administration during haemodialysis

St George Hospital Renal Department Guideline: INTERNAL ONLY

Larger volumes and more dilute concentrations of UFH are used in haemodialysis to compensate for adsorption to plastic surfaces such as the extracorporeal circuit. How UFH is administered is dependent on the patient's risk of haemorrhage. Patients with no risk of haemorrhage are administered a bolus dose of UFH followed by an infusion (or series of boluses) (Davenport, 2011a). Davenport 2011a p.S47, reports that "most centres pragmatically adjust dosages according to visual inspection of the dialyser header and venous air detector chamber, and determine the time to stop the heparin infusion by monitoring the time taken for needle puncture sites to stop bleeding at the end of the haemodialysis session". Ceasing the heparin infusion occurs between 20 and 60 minutes prior to the scheduled end of each haemodialysis session.

If the patient is at risk of haemorrhage, the UFH dose is reduced. If the dialyzer or venous air detector develops a thrombus, an additional bolus dose of UFH at approximately 50% of the original loading dose is suggested (Davenport, 2011a).

Loading dose 1500-2000 International Units (reduced if patient is <50kg and increased if >90kg), maintenance dose 1000-1500 International Units (reduced if patient is <50kg and increased if >90kg) (Davenport, 2011a, p. S44).

Caution

Because haemodialysis patients are systematically anticoagulated for at least 4 hours, an APTT must be checked before surgical procedures post dialysis (Fischer, 2007).

Complications

Cutaneous hypersensitivity (pruritis), skin necrosis (rare), development of thrombocytopenia is a rare but life threatening complication (European Best Practice Guidelines, 2002). Increased bleeding risk, worsening of osteoporosis and lipid status (Fischer, 2007).

Technical errors that can potentially result in clotting within the extracorporeal circuit (Davenport 2011)

1. **Dialyzer priming:** Failure to remove air in dialyzer or failure to adequately prime the heparin infusion line.
2. **Heparin bolus:** Failure to administer initial bolus, or time to short from loading dose to systemic anticoagulation (Davenport recommends bolus dose diluted to 10mL and injected into the venous limb of the circuit 2-3 minutes before connecting the patient)
3. **Heparin infusion:** Rate set too low. Concentration too high. Delayed start of heparin infusion. Failure to release clamp on heparin line.
4. **Inadequate flow:** Needle position. Excessive recirculation (needle position or venous obstruction). Secondary to multiple machine alarms and interrupted blood flows.

From the Literature

Table 1:(Copied from: Davenport, 2011b, 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 0.8mg/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 aPTTr <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 dialyate, hypocalcemia, hypomagnesemia, citrate toxicity, metabolic alkalosis or acidosis
Citrate dialyate	None	0.8 mmol/l in dialyate	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 70kg 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.

ANTICOAGULATION - LOW DOSE HEPARINSATION

Indications

1. Active bleeding stopped more than three days but less than seven days
2. Surgery, biopsy or trauma more than three days but less than seven days before
3. Elective surgery less than four hours post dialysis
4. Pericarditis
5. Increased bleeding risk

Method

- Use 50% of heparin dose known to be optimal for the patient.
- Otherwise give a loading dose of 500 units of heparin and start heparin infusion rate of 500 unit/hr. [250-500 International Units/hr (European Best Practice Guidelines, 2002)]
- Heparin regime requires ceasing 1 hour before the end of treatment when using a fistula for treatment.

References

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