Anticoagulation

Initiation of full anticoagulation with heparin

In patients with renal failure the use of unfractionated heparin is still recommended for full anticoagulation. The use of LMW heparins in fully anticoagulating doses is not recommended as their action is prolonged and may be potentiated by uraemic bleeding tendency.

- Give bolus of intravenous heparin 5,000 units (5ml of 1000 units/ml). For a major pulmonary embolus give 10,000 units (10ml of 1000u/ml); consider omitting bolus if bleeding risk high.
- Set up intravenous infusion of heparin at 1200 units/h (1.2ml/h of 1000u/ml)
- Check APTT ration after 6h. Therapeutic range is 2.0-3.0 (altered from 1.5-2.5 in Sep 2010).
- Keep heparin running but don't take sample from same arm or same central line
- Monitor platelet count on alternate days: stop heparin and review if bleeding or platelets <100.

Adjust heparin infusion rate as follows:		
APTT ratio	**Heparin infusion (1000 units/ml)<**	**Recheck APTT**
> 5.0	Stop for 1h, then decrease by 500 units/h	2h
4.1 – 5.0	Decrease by 300 units/h (0.3ml of 1,000u/ml per h)	6h
3.1 – 4.0	Decrease by 200 units/h (0.2ml/h)	6h
2.0 – 3.0	No change	within 24h*
1.5 – 1.9	Increase by 100 units/h (0.1ml)	6h
1.2 – 1.4	Increase by 200 units/h (0.2ml/h)	6h
< 1.2	Increase by 400 units/h (0.4ml/h)	6h

* Sooner if APTT has been unstable

- Checking APTT daily is the mandatory minimum frequency for all patients receiving intravenous heparin.
- Continue heparin until oral anticoagulant is established and the international normalised ratio (INR) is stable within the appropriate

therapeutic range.

Special circumstances

• Urgent reversal of anticoagulation: contact haematologist.

• Lupus anticoagulant may render APTT results meaningless, and require more complex assays.

• For further information on these or other issues please contact the consultant haematologist.

Warfarinisation

Schedule for induction of warfarin therapy

From Fennerty et al, Br Med J (1988) 297:1285-5

Day	INR (best taken 0900-1000)	Dose in mg (best given 1700-1800)
1	<1.4 This schedule is not applicable if INR is 1.4 or higher – give smaller loading dose	10
2	<1.8 1.8 >1.8	10 1 0.5
3	<2.0 2.0-2.1 2.2-2.3 2.4-2.5 2.6-2.7 2.8-2.9 3.0-3.1 3.2-3.3 3.4 3.5 3.6-4.0 >4.0	10 5 4.5 4 3.5 3 2.5 2 1.5 1 0.5 zero

Day	INR	Predicted maintenance dose (mg)
4	<1.4 1.4 1.5 1.6-1.7 1.8 1.9 2.0-2.1 2.2-2.3 2.4-2.6 2.7-3.0 3.1-3.5 3.6-4.0 4.1-4.5	>8 8 7.5 7 6.5 6 5.5 5 4.5 4 3.5 3 miss out next day's dose then give 2mg
4	>4.5	miss two doses then give 1mg

Alternatives to heparin

These may be used in patients with heparin-induced thrombocytopaenia (HIT) or sometimes in those at high risk of haemorrhage.

Epoprostenol (prostacyclin, Flolan®) is a potent vasodilator that inhibits platelet aggregation. A half-life of about 3 mins means that it must be given by continuous infusion but that its efffects wear off quickly. Hypotension, flushing, headache, nausea and vomiting, and other symptoms may occur.

The freeze-dried drug is diluted first with the accompanying diluent and then with saline to 2000 nanograms/ml. Infusion rate is 1-5ng/kg/min, gradually building up the dose over 30 mins before connecting to the machine. At tolerated doses it is usually found to be less effective than heparin at preventing clotting in extracorporeal circuits.

Danaparoid (Orgaran®) is a heparinoid. In the UK available on a named-patient

basis. Acts by blocking factor Xa. Has a prolonged action that is greater in renal failure because it is normally renally excreted; monitor Xa levels. Difficult to reverse. Side effects are similar to heparin. In HIT, cross-reactivity may occur in 10%. The following has been used during haemofiltration (an unlicensed indication):

- Bolus 2500U i.v., then a continuous infusion at 600U/h for 4h, then 400U/h for 4h, then 200-600U/h to maintain anti-Xa levels at 0.5-1.0U/ml.
- If patient is <55kg, bolus 2000U should be followed by 400U/h for 4h then 150-400U/h. Further instructions from renal pharmacist (or kept on renal HDU in Edinburgh).

Lepirudin is a recombinant hirudin (anti-thrombin). Activity can be monitored by APTT (aim for ratio 2.0-3.0 versus control) but this does not correlate precisely with plasma hirudin levels. Prolonged excretion in renal failure means that full anticoagulation is practically continuous for patients on alternate day dialysis, and there is no easy way of reversing the anticoagulation. Side effects related to anticoagulation but also fever, allergy, and injection site reactions. Use in haemodialysis is not surprisingly unlicensed but the following protocol has been used:

- 0.08-0.1 mg/kg for first dialysis as slow i.v. bolus follwed by 50% of this dose at subsequent dialyses.
  A hepatically metabolised hirudin with shorter half-life is in development.

Heparin-induced thromboctopaenia (HIT-II)

This is caused by platelet factor 4 antibodies, which can activate platelets. Existing tests often give positive results in patients who do not have the syndrome of:

- Low platelets
- Thrombotic events (venous and arterial)

In patients at highest risk, the acutely ill, there are usually alternative possible explanations for thrombocytopaenia. Because current alternatives to heparin may be hazardous in themselves, it is important to consider the balance of probabilities and risks.

Sometimes there may be acute, allergic-type reactions on dialysis, and there may

be eosinophilia.

Reference: The Heparins: all a nephrologist should know. NDT 20:2036-42 (2005) (Hetzel & Suker)

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