

Paediatric Intensive Care Unit

Reversal of Heparin & Warfarin for PICU use

Staff relevant to:	PICU medical & nursing staff.
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1. Introduction

This guideline is for use within the UHL Paediatric Intensive Care Unit. The aim of this clinical guideline is to help health professionals to make informed decisions about the treatment of over-heparinisation or over-warfarinisation.

Objectives:

- To provide evidence-based recommendations for appropriate treatment
- To provide structured pathway for stabilization, timely escalation and transfer for patients needing critical care for over-heparinisation or over-warfarinisation.

This clinical guideline is based on available evidence in conjunction with clinical expertise and experience. The current guideline is not intended to take the place of clinicians' judgment and does not override the individual responsibility of healthcare professionals to make their own treatment decisions about care on a case-by-case basis using their clinical judgment, knowledge and expertise along with patient/family wishes. Users always are urged to seek out newer information that might impact the diagnostic and treatment recommendations contained within this guideline.

2. Reversal of heparin and warfarin guidance

2.1 Reversal of Unfractionated Heparin

Protamine sulphate is administered to reverse the excess of heparin; ACT and Protamine dose administered post cardiac surgery should be taken into consideration when deciding further doses; discuss with surgical/anaesthetic team.

Calculate the number of units of heparin given **in last 3 hours**. Max Protamine dose is 50mg (except for cardiopulmonary bypass); administer over 10 min with rate not exceeding 5mg/minute. Watch for hypersensitivity reaction – particularly if known fish allergy or previous Protamine administration.

Time since last Heparin dose	Protamine dose (mg)
< 30 min	1mg /100 units of Heparin received
30 – 60 min	0.75 mg / 100 units of Heparin received
60 – 120 min	0.5 mg / 100 units of Heparin received
> 120 min	0.25 mg / 100 units of Heparin received

2.2. Reversal of Low molecular weight heparin

Calculate the amount of LMWH given **in last 24hours**. Maximum dose of Protamine is 50mg. The half-life of Protamine is shorter compare to LMWH half-life; hence repeated doses might need to be administered.

Time from last LMWH dose	Dose of Protamine for each 100 units of Dalteparin
Less than 8 hours	1mg protamine per 100 units of Dalteparin
8 hours or more	0.5mg protamine per 100units of Dalteparin

2.3. Warfarin reversal if NO haemorrhage

Warfarin interferes with the synthesis of clotting factors II, VII, IX and X.

Over-anticoagulation should be managed according to the INR and the clinical situation as follows.

- Find out why the patient has gone out of control (e.g. confusion over dosing? addition of other drugs (often antibiotics)? unwell? sudden change in diet?)
- If the patient has a fingerpick INR value >4, it must be repeated on a venous sample, since the fingerpick values are unreliable at high levels.
- INR > 8 (venous sample):
 - The patient will need a clinical review and assessment to determine if reversal of anticoagulation is required. **Contact senior paediatric cardiologist** or haematologist on call.
 - If indicated **and agreed with senior cardiologist**, a very small dose of Vitamin K might be considered. **Do not administer vitamin K without discussion with senior cardiologist!** (intravenously or orally i.e. 15-30 micrograms/kg; there are no therapeutic guidelines for children – this dose is extrapolated from experience in adults in whom 1/10 to 1/20 of the

standard dose is enough. A very small dose of Vitamin K will partially reverse the INR without preventing ongoing anticoagulation.)

- 3) Repeat the INR (venous) 6 hours post treatment, and again the following day. An effect may be seen within 4 hours if given intravenously, but it may take longer to produce maximal reversal.

A full dose of Vitamin K (300 micrograms/kg) will completely reverse the anticoagulant effect and make Warfarin very difficult to reintroduce for up to 2 weeks – i.e. warfarin resistance. The dose chosen will depend upon the clinical circumstances. If venous access is very difficult the dose of vitamin K may be given orally. This route has a greater delay in producing reversal.

INTRAMUSCULAR INJECTIONS MUST NOT BE GIVEN to patients taking anticoagulant drugs because of the risk of intramuscular bleeding. GREAT CARE must be taken in measuring the very small volumes of vitamin K required for partial reversal.

2.4. Warfarin reversal if haemorrhage

Initial management will depend on the severity of the bleeding and the indication for anticoagulation.

- a) The patient will need a rapid clinical review and assessment to determine if reversal of anticoagulation is required.
- b) Discuss with senior doctors on call and contact paediatric cardiology/haematology team. Measures used to decrease the INR will vary with the clinical situation.

INR >3 with haemorrhage

Treatment options are blood product +/- partial or complete reversal with vitamin K:

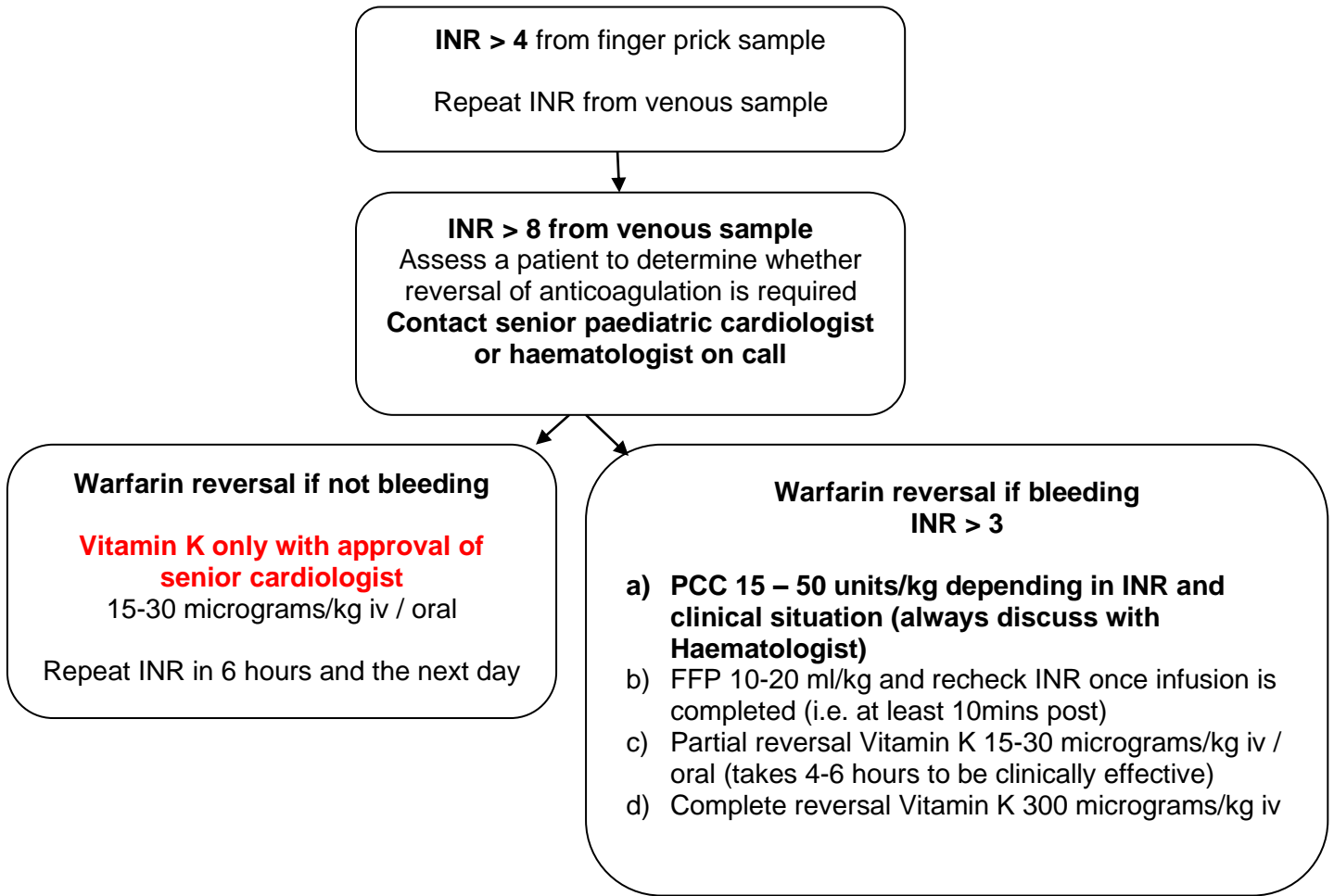
- 1) **Reversal with prothrombin complex concentrate – PCC is treatment of choice in emergency** - Octaplex or Beriplex; this should be discussed with a Haematology Consultant who will advise on the appropriate dose; usually 15 – 50 units/kg depending in INR and clinical situation. PCC is a plasma-derived pooled blood product containing factors II, VII, IX and X and will instantly correct the clotting, but the effect will dissipate with time unless Vit K is given in addition.
- 2) FFP may occasionally be a better option particularly in babies where PCC would be wasted. It will however not correct the INR completely. FFP 10-20 ml/kg and recheck INR once infusion is completed (i.e. at least 10mins post) The INR will not fully correct and as with PCC the longevity of the effect equates to the half-lives of the individual coagulation factors. Treatment for high INR will depend on the child's underlying diagnosis and clinical condition. Seek advice from Consultant Haematologist as necessary.
- 3) Partial reversal 15 – 30 micrograms/kg iv Vitamin K or complete reversal with iv vitamin K – 300 micrograms/kg (this may take 4-6 hours to be clinically effective)

Documented acute intracranial haemorrhage is almost always an indication for full reversal.

Patients with prosthetic heart valves are at risk if complete reversal is achieved; at the same time it is important to consider risk and benefit ratio bleeding vs leaving mechanical valve without anticoagulation.

Note that any source of bleeding in an anticoagulated patient needs investigating in its own right.

Reversal of warfarin flow chart:



3. Education and Training

Training and raising awareness are on-going processes. On-going awareness is promoted through the induction and continuous bedside teaching. Training is provided for medical staff during regular lunchtime teaching and other sessions, and at junior doctors’ induction training. Nursing education is supported by the Practice Development teams, and nursing educators.

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Review notes of patients who have required reversal of anti-coagulation therapy	Audit of patient notes	PICU Consultants	Annually	PICU CPM
Prescribing and/or administration errors of reversal agents (Protamine/Vitamin K)	Datix	Specialist Pharmacist	Six monthly	PICU CPM

5. Supporting References

None

6. Key Words

Over-warfarinisation, PCC, Heparin reversal, warfarin reversal, Protamine, vitamin K

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.

As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

Contact and review details	
Guideline Lead (Name and Title) S Wheeler – Senior Paediatric Pharmacist	Executive Lead Chief Medical Officer
Details of Changes made during review: Monitoring and Compliance section added	