Drug Guideline

Guideline Title  Protamine Sulphate
Summary: Protamine is a basic protein which combines with heparin to form a stable, inactive complex. It is used to counteract the anticoagulant effect of heparin before surgery; after renal dialysis; after open heart surgery; if excessive bleeding occurs; and when an overdose has inadvertently been given

Approved by: ICU Medical Director

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Next Review Date: July 2018

Replaces Existing Guideline: Protamine Sulphate_2011

Previous Review Dates: 2011, 2005

Background Information:

1. Introduction contains:
The risk addressed by this policy:

Patient Safety

The Aims / Expected Outcome of this policy:

Protamine Sulphate should be administered safely and without any adverse side effects

Related Standards or Legislation

NSQHS Standard 1 Governance
National Standard 4 Medication Safety

Related Policies

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2. Policy Statement:
   - All care provided within Liverpool Hospital will be in accordance with infection prevention/control, manual handling and minimisation and management of aggression guidelines.
- Medications are to be prescribed and signed by a medical officer unless required during an emergency.
- Medications are to be given at the time prescribed and are to be signed by the administering registered nurse.
- Parenteral medication prescriptions and the drug are to be checked with a second registered nurse prior to administration.
- Infection Control guidelines are to be followed.
- All drugs administered during an emergency (under the direction of a medical officer) are to be documented during the event, then prescribed and signed following the event.
- Adverse drug reactions are to be documented and reported to a medical officer.
- Medication errors are to be reported using the hospital electronic IIMS reporting system.
- Guidelines are for adult patients unless otherwise stated.

3. Principles / Guidelines

Actions
Combines with heparin to form a stable inactive complex, reversing its anticoagulant effect

Indications
- To counteract the anticoagulant effect of heparin before surgery; after renal dialysis; after open heart surgery
- An overdose of heparin has inadvertently been given

Contraindications
- Fish allergy—increases risk of allergy.

Precautions
- If the protamine dose is too high, it acts as an anticoagulant.
- Rapid IV injection has caused severe hypotension and anaphylactoid reactions.
- Patients who have previously received protamine are at risk of allergic reactions, including patients who have previously undergone procedures e.g. coronary angioplasty or cardiopulmonary bypass and diabetics who have been treated with protamine insulin.
- Patients allergic to fish and men, who have had a vasectomy or are infertile, may have antibodies to protamine and be at an increased risk of allergic reactions.

Pregnancy Implications
Animal reproduction studies have not been conducted. In general, medications used as antidotes should take into consideration the health and prognosis of the mother; antidotes should be administered to pregnant women if there is a clear indication for use and should not be withheld because of fears of teratogenicity. Protamine sulfate may be used during delivery to reduce the risk of bleeding following maternal use of heparin or low molecular weight heparin

Interactions
There are no known significant interactions.

Adverse Effects
- Common (>1%)
  - sensation of warmth, flushing, nausea, vomiting, tiredness
- Infrequent (0.1–1%)
  - hypotension, bradycardia, dyspnoea (especially if given rapidly), allergy (below), rebound bleeding with excessive doses
- **Allergy**
  - Urticaria and severe hypersensitivity reactions including cardiovascular collapse, bronchospasm and death have occurred.

- **Adverse reactions include**
  - bradycardia
  - pulmonary hypertension
  - dyspnoea
  - transient flushing and a feeling of warmth

**Presentation**

- Solution for injection (clear, colourless, sterile, pyrogen free), 10 mg/mL, 5 mL (glass ampoules)

**Administration Guidelines**

**Heparin anticoagulation reversal:**
- 1mg protamine for every 100 unit’s heparin given.
- Administer 100mg in 100mL of either sterile glucose or sterile 0.9% sodium chloride over 1 hour for heparin anticoagulation reversal.
- In a situation where rapid reversal is necessary a slow IV injection over 10 mins is acceptable.

**Post op cardiothoracic surgery:**
- 1 to 2 milligrams of protamine sulfate is administered intravenously for each 100 units of heparin given post bypass
- Administer 100mg in 100mL of either sterile glucose or sterile 0.9% sodium chloride over 15 to 30 minutes post-routine cardiopulmonary bypass cardiac-surgical patients.
- Repeat or adjusted doses of protamine are determined by the cardiothoracic (CT) surgical specialist or CT team, anaesthetist and/or ICU team.
- Protamine is not given to off-pump cardiopulmonary bypass surgery.

**Heparin overdose:**
- Administer 50mg in 100mL glucose or sterile 0.9% sodium chloride over 1 hour.
- The dose of protamine should be controlled by APTT measurement and clinical evidence of bleeding.
- Protamine sulphate injection may be administered by slow intravenous injection over a period of 10 minutes.
- The dose is dependent on the amount of heparin that has to be neutralised, the initial dose and timeframe.
- Protamine sulfate 1 mg will usually neutralise heparin 100 units.
- Heparin is continuously excreted, thus dosage is to be reduced if more than 15 minutes have elapsed since the heparin injection.
- In gross excess, protamine itself acts as an anticoagulant.
- Always seek specialist haematologist advice before administering protamine as in most cases careful monitoring is the best treatment of a heparin overdose.
- Further treatment is guided by monitoring the APTT every 20–30 minutes after protamine administration.

**Dalteparin or enoxaparin (Low molecular weight heparin: LMWH)**
- Though protamine neutralises the anti-factor IIa activity of LMWH, it only partially neutralises the anti-factor Xa effect, which can persist for about 24 hours.
- In a patient who is either bleeding or at high risk of major haemorrhage, seek specialist haematologist advice before considering protamine.
Dalteparin

- Administer 1 milligram (mg) of protamine sulfate for every 100 units of dalteparin. If the APTT (measured 2 to 4 hours after the first infusion) remains prolonged, a second infusion of 0.5 mg protamine sulfate per 100 units of dalteparin may be administered. It is important to note that even with additional doses of protamine sulfate; the APTT may remain more prolonged than it would following the administration of conventional heparin. The maximum neutralization of the anti-Factor Xa activity is about 60% to 75%

Enoxaparin

- Administer 1 milligram (mg) of protamine sulfate for every 1 mg of enoxaparin administered in the previous 8 hours. If more than 8 hours has elapsed since the last dose of enoxaparin was administered, or if the APTT (measured 2 to 4 hours after the first infusion) remains prolonged, a second infusion of 0.5 mg of protamine sulfate per 1 mg of enoxaparin may be administered. If more than 12 hours has elapsed since enoxaparin administration, protamine sulfate administration may not be necessary. It is important to note that even with additional doses of protamine sulfate; the APTT may remain more prolonged than it would following administration of conventional heparin. The maximum neutralization of the anti-Factor Xa activity is about 60%

4. Performance Measures
All incidents are documented using the hospital electronic reporting system: IIMS and managed appropriately by the NUM and staff as directed.

6. References / Links

1. Mims online. Accessed 2015 CIAP. Protamine Sulphate

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