High Dose Insulin Euglycaemic Therapy (HIET) for Calcium Channel Antagonist and Beta-Receptor Antagonist Poisoning Procedure

TARGET AUDIENCE and SETTING

Medical officers, registered nurses and enrolled nurses.

PURPOSE

This procedure is applicable to adults and adolescents (over 16 years) with known or suspected calcium-channel antagonist (in particular: verapamil or diltiazem poisoning) or beta-receptor antagonist poisoning with significant hypotension, within the emergency department or intensive care unit.

PRECAUTIONS/CONTRAINDICATIONS

This procedure is to be undertaken in consultation with Monash Health Toxicology Service.

High-dose insulin euglycaemic therapy (HIET) for poisoning requires large doses of insulin – it is not possible to draw this volume up with an insulin safety syringe. This procedure is the only exception to the standard preparation and administration of this high-risk medicine.

HIET forms a part of the management of calcium channel antagonist and beta-receptor antagonist poisoning – this is usually in conjunction with other inotropic and pressor agents as advised by the toxicologist.

Hypoglycaemia and hypokalaemia, if present, MUST be corrected prior to initiating HIET.

HIET may be associated with hypoglycaemia. This is prevented by co-administration of intravenous glucose infusion. Blood sugar concentration is monitored closely (see monitoring).

Insulin infusion may result in hypokalaemia as a result of increased intracellular movement of potassium rather than increased loss of potassium from the body (see monitoring).

Contraindication:

Hypersensitivity to human insulin.

EQUIPMENT

- Neutral, soluble, short-acting human insulin (e.g. Actrapid®) 100 units per mL, 3 mL cartridge
- Glucose 50% for intravenous infusion (25 g in 50 mL vial)
- 1 mL, 5 mL and 50 mL syringes
- Glucose 10% for intravenous infusion 500 mL bag
- Syringe pump driver for insulin infusion and glucose infusion

STANDARD REQUIREMENTS

When undertaking any clinical interaction with a patient, staff are expected to:

- Perform routine hand hygiene. Refer to the Hand Hygiene Procedure.
- Introduce themselves to the Patient and Carer/ Family if in attendance.
- Check patient identification. Refer to the Patient Identification Procedure.
- Obtain consent as per the Consent to Medical Treatment Procedure.
- Keep the patient/carer informed and involve them in decision making.
- Document interaction in the electronic medical record or health record using black pen; including date, time, signature and designation.

PROCEDURE

1. Discuss the treatment of complex or haemodynamically unstable poisoning cases with a consultant toxicologist and intensive care team.
2. Explain the procedure and reassure the patient.
3. Perform an urgent bed-side echocardiogram or other assessment of cardiac output (e.g. Pulse Contour Cardiac Output monitoring (PiCCO)) to assess the degree of myocardial impairment in severe poisoning. This will indicate whether inotropic agents and/or vasopressors are required to treat hypotension in individual poisoning cases. HIET has a mild coronary and peripheral vasodilatory effect.
4. Aim to provide glucose supplementation initially with 10% intravenous glucose through peripheral intravenous line. However, if hypoglycaemia is a continuing problem 50% glucose administration may be required. Central venous access is required for 50% glucose administration – insert a central venous catheter if necessary. Refer to the CVC central venous catheter (Adult) insertion procedure.
5. **Administer glucose loading dose:**
   - 5.1. Draw up 25 grams of glucose (50 mL of 50% glucose) into a 50 mL syringe
   - 5.2. Administer IV over 5-10 minutes.
6. **Administer insulin loading dose:**
   - 6.1. Draw up loading dose: 1 unit per kilogram.
   - 6.2. Administer intravenously (IV) over 5 minutes.
7. **Commence insulin infusion:**
   - 7.1. Using a 5 mL syringe, draw up 500 units (5 mL) of short acting insulin and add this to a 50 mL syringe.
   - 7.2. Draw up 45 mL of glucose 5% IV solution.
   - 7.3. Add the 45 mL of glucose 5% IV solution to the 50 mL syringe containing insulin and mix gently to make a solution of insulin 500 units in 50 mL glucose 5% (10 units per mL).
   - 7.4. Infuse initially at 1 unit per kg per hour IV using a syringe pump.
   - 7.5. The response of blood pressure to insulin infusion may be delayed - 30 minutes.
   - 7.6. **If systolic blood pressure remains less than 90 mmHg after 30 minutes, increase insulin infusion rate further by 1 unit per kg per hour, every 15-30 minutes, up to a maximum of 5 units per kg per hour.** (Up to 10 units/kg/hour has been used in some case reports without adverse effects)
   - 7.7. Prepare a new insulin infusion syringe every 12 hours.

8. **Administer glucose infusion (to prevent hypoglycaemia):**
   - 8.1. Commence glucose infusion 10% at 100 mL/hr.
   - 8.2. Titrate to blood sugar concentration (BSL) > 5.0 mmol/L.
   - 8.3. If more than 200 mL/hr of 10% glucose is required to maintain BSL > 5.0 mmol/L change to 50% glucose through central line.
   - 8.4. Draw up 50 mL of 50% glucose solution into a 50 mL syringe. (NOTE: 40 mL/hr 50% glucose = 200 mL/hr of 10% glucose). Administer 50% glucose IV via syringe pump.
   - 8.5. If blood sugar concentration is less than 5.0 mmol/L, increase the glucose infusion rate in increments of 5mL per hour increments, until it is more than 5.5 mmol/L.
   - 8.6. If the blood sugar concentration is greater than 11 mmol/L, decrease the glucose infusion rate by increments of 5 mL per hour until the concentration falls below 11 mmol/L.

9. **Monitoring:**
   - 9.1. Continuous invasive arterial blood pressure monitoring (via an arterial line) to measure haemodynamic response to treatment is indicated.
   - 9.2. Monitor blood pressure and blood sugar concentration every 30 to 60 minutes for the duration of high-dose insulin therapy.
   - 9.3. Monitor serum potassium concentration every 60 minutes until it is stable, then every two-hours thereafter. Insulin infusion will result in hypokalaemia. Intravenous potassium supplementation is indicated if serum potassium is <3.0 mmol/L. Refer Potassium Adult Medication Profile. However, hypokalaemia is NOT due to reduced body load of potassium. As a result, aim to keep serum [K+] in low normal range (3.0-3.5 mmo/L)
   - 9.4. Check serum magnesium concentration 12-hourly during the insulin infusion, as high-dose insulin may result in hypomagnesaemia.

10. Ensure other supportive treatments, vasopressors, and other inotropic therapies are optimised. If there is a failure of haemodynamic response to maximal therapies consider V-A ECMO therapy.

11. Refer patient to Intensive Care Unit if not done earlier.

12. **Cessation of insulin infusion:**
   - 12.1. Drug toxicity may last for several hours to days, particularly with sustained-release calcium channel antagonist poisoning.
   - 12.2. Reduction in and cessation of insulin infusion will vary from patient to patient.
   - 12.3. Decision to cease insulin is made in conjunction with intensive care consultant and clinical toxicology medical staff.

KEYWORDS

Calcium channel blocker, calcium channel blocker, verapamil, diltiazem, overdose, toxicity, insulin, high-dose, euglycaemic

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