



PAEDIATRIC ACUTE CARE GUIDELINE

Poisoning - Hypoglycaemic Agent

Scope (Staff):	All Emergency Department Clinicians
Scope (Area):	Emergency Department

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Poisoning - Hypoglycaemic Agent

This guideline is a general approach to hypoglycaemic agent poisoning. For specific details please contact **Poisons Information: 131126** or refer to the Toxicology Handbook.

Agents:

Sulfonylureas:

- Glibenclamide
- Gliclazide
- Glimepiride
- Glipizide

Biguanides:

- Metformin

Glitazones (thiazolidinediones):

- Pioglitazone
- Rosiglitazone

Background

- Oral hypoglycaemic agents are used for type II diabetes mellitus (non-insulin dependent diabetes)
- Sulfonylurea agents increase pancreatic insulin secretion and are the most important cause of hypoglycaemic toxicity
 - Modified-release preparations may delay onset of symptoms for up to 8-18 hours
- Metformin is a biguanide agent that acts by decreasing carbohydrate absorption from the gut, increasing glucose uptake in peripheral tissues in the presence of insulin, and reducing hepatic gluconeogenesis
- The thiazolidinedione agents act at a nuclear receptor to improve insulin sensitivity in adipose tissues, skeletal muscles and the liver. Minimal information is available regarding overdose.

Assessment

Risk Assessment

- The **sulfonylurea agents** may cause prolonged and profound life-threatening hypoglycaemia after accidental paediatric ingestion or deliberate self-poisoning
 - Large overdoses may require treatment for several days
 - A single tablet in a toddler has the potential to cause life-threatening hypoglycaemia.
 - The onset of hypoglycaemia may be delayed up to 18 hours after ingestion. Admission for a minimum of 12- 24 hours is indicated for blood glucose monitoring.
 - Discharge from hospital should only occur in the daylight hours.
- **Metformin** ingestion is not associated with hypoglycaemia in normal patients, but may cause life-threatening lactic acidosis in large overdoses or in the presence of renal or cardiac failure, or when there are co-ingestants which impair renal perfusion.
 - Haemodialysis resolves the acidosis as well as removing metformin from the blood
 - Nausea and vomiting may occur in smaller overdoses
 - Asymptomatic patients following accidental exposure to metformin do not require referral to hospital, decontamination or investigation
 - Children who have taken an unintentional ingestion of up to 1700 mg do not require hospital assessment

- There are very few reports of accidental **thiazolidinedione** ingestion or deliberate self-poisoning
 - There are no reports of hypoglycaemia and it is thought to be unlikely
 - A conservative approach, with 8 hours of blood sugar monitoring, is recommended until further data are available

Typical Clinical Course:

Sulfonylureas:

Autonomic and CNS manifestations of hypoglycaemia may include:

- Tachycardia
- Sweating
- Anxiety
- Drowsiness
- Altered mental status
- Coma
- Seizures

Metformin:

- Acute metformin overdose is usually asymptomatic
- Hypoglycaemia is uncommon and easily corrected with glucose

Lactic acidosis is usually delayed by several hours and may manifest as:

- Reduced level of consciousness
- Nausea, vomiting and diarrhoea
- Dyspnoea
- Tachycardia
- Hypotension
- Shock, coma and death

Investigations

Screening tests in deliberate self-poisoning:

- 12-lead ECG and paracetamol level

Specific investigations as indicated:

- Serial BSL
- UEC
- Insulin levels may have some application (if available) for **sulfonylurea** overdoses on the advice of toxicology services.
- VBG/ABG (including lactate) should be done in **metformin** overdoses to confirm lactic acidosis and to monitor progress in any unwell patient or following clinical deterioration.

Management

Resuscitation

Sulfonylurea:

- Obtain IV access and administer concentrated IV glucose solutions if the patient is hypoglycaemic
 - Children – 5ml/kg of 10% glucose IV bolus
- Maintain euglycaemia by continued administration of concentrated glucose solution until octreotide can be started
- BSL needs to be checked at least hourly until the patient is stable and on octreotide (refer to [Antidotes](#))
- **Note** that recurrent administration of concentrated glucose boluses stimulates endogenous insulin release and leads to rebound hypoglycaemia until octreotide is commenced

Metformin

- Attention to airway, breathing and circulation
- In the severely intoxicated patient, administration of sodium bicarbonate may be required to acutely manage acidosis and hyperkalaemia until haemodialysis can be performed

Decontamination

Activated charcoal (1g/kg up to 50g) should be administered to the following patients:

- The cooperative patient who presents within an hour post-ingestion (or four hours with modified release preparations)
- The cooperative patient who presents within 2 hours of deliberately self-poisoning with >10 g of metformin

- Any intubated patient once the airway is secure

Enhanced elimination

Sulfonylurea:

- Not clinically useful

Metformin:

- Haemodialysis rapidly corrects acidosis as well as removing metformin from the body, preventing further lactate production
- Indications:
 - Any unwell patient with lactic acidosis
 - Worsening lactic acidosis following acute overdose where signs of clinical instability are present or emerging

The requirement for haemodialysis may be prolonged for at least 15 hours

Antidote

Sulfonylurea:

- Octreotide is a long-acting synthetic analogue of somatostatin and is a specific antidote for the sulfonylurea agents by suppressing insulin release from pancreatic cells.
- **Dose:**
 - Children – 1 microgram/kg IV followed by 1 microgram/kg/hour continuous infusion
 - Adolescents or adults – 50 microgram IV bolus followed by 25 microgram/hour continuous infusion for at least 24 hours
- Once the octreotide infusion is running, it is likely that normoglycaemia will be achieved without glucose supplementation. If hypoglycaemia recurs, it should be corrected with glucose and the infusion rate of octreotide doubled.

Octreotide infusion may be ceased when all the following criteria have been met:

- 10% glucose infusion ceased at least 4 hours prior
- No symptoms of hypoglycaemia
- Bedside BSL > 2.5 mmol/L for more than 4 hours
- Daylight hours – octreotide should not to be ceased during evening or night-shift

Following cessation of octreotide, the BSL should be checked every hour

The patient can be medically cleared once:

- Normoglycaemia is maintained for 12 hours off octreotide and the patient is on a normal diet
- If available, a plasma insulin level in the normal range at 6 hours after cessation of the octreotide infusion

Management Summary for Sulfonylurea Overdose
<p>If patient has symptoms of hypoglycaemia or BSL < 2.5 mmol/L at any time:</p> <ul style="list-style-type: none"> • Give 5mL/kg of 10% glucose as bolus • Check serum insulin level • Commence 10% glucose infusion at 1-2 mL/kg/hour • Give octreotide 1 microgram/kg IV stat (maximum dose 50 micrograms) • Commence octreotide infusion 1 micrograms/kg/hour <ul style="list-style-type: none"> ◦ Dilute 250 micrograms of octreotide in 250 mL 5% glucose = 1 microgram/mL • Check bedside BSL hourly • Recheck formal serum BSL and serum insulin level (if available) one hour after commencing octreotide infusion • Admit to hospital High Dependency/PICU • The patient may commence normal diet
<p>If delayed admission and symptoms of hypoglycaemia occur again, or BSL < 2.5mmol/L, despite octreotide and 10% glucose infusions:</p> <ul style="list-style-type: none"> • Give 5mL/kg of 10% glucose as bolus • Increase 10% glucose infusion rate to 2-4 mL/kg/hour • Check bedside BSL hourly • Discuss with PICU for central line placement and commencement of 20% glucose infusion
<p>If BSL > 12 mmol/L cease 10% glucose infusion</p>

Metformin

- No antidote is available

Disposition**Patients who can usually be managed at home:**

- Asymptomatic patients following accidental metformin ingestion
- Children who acutely ingest less than 1700 mg of metformin

Patients who should be evaluated in hospital:

- All patients suspected of deliberate self-poisoning
- All patients potentially exposed to thiazolidinedione or sulfonylurea agents
- Children who have metformin overdoses of more than 1700mg, or more than 10 g in adult-sized children, mandate observation for at least 8 hours. Patients who remain well

with a normal bicarbonate at the end of that period may be medically cleared.

Patients who should be admitted:

- Patients with a BSL < 2.5mmol/L are to be admitted to High Dependency/PICU
- All patients potentially exposed to a sulfonylurea agent should be admitted for observation and monitoring of bedside BSL for a minimum of 18-24 hours
- Symptomatic patients with hypoglycaemia treated with IV glucose and octreotide
- Any patients post metformin overdose who presents with or develops lactic acidosis requiring critical care admission, monitoring and assessment for urgent haemodialysis

Nursing


- Baseline observations include heart rate, respiratory rate, oxygen saturation, blood pressure and neurological observations
- Minimum hourly observations should be recorded whilst in the emergency department
- Check bed-side blood glucose level at least every hour during first eight hours or until levels are stable
- Any significant changes should be reported immediately
- Careful fluid input and output monitoring
- Supportive care such as pressure area care, IDC, TED prophylaxis, diet as indicated

References

1. Murray L, Little M, Pascu O, Hoggett K. Toxicology Handbook 3rd Edition. Churchill Livingstone 2015
2. Chu J and Stolbach A. Sulfonylurea Agent Poisoning (2015) UpToDate. Accessed www.uptodate.com
3. Chu J and Stolbach A. Metformin Poisoning (2015) UpToDate. Accessed www.uptodate.com
4. ToxinZ Poisons Information online, 2013 National Poisons Centre, New Zealand

This document can be made available in alternative formats on request for a person with a disability.

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