Emergency Management of Hypoglycaemia

Definition

- Hypoglycaemia is defined as blood glucose <3.0 mmol/L; however, below 2.5 mmol/L is considered pathological requiring investigation.[1]
- In hospitalised patients, any blood glucose ≤4.0 mmol/L should be treated if the patient is symptomatic.[2]
- The glucose level that is considered hypoglycaemic in children is still debated, particularly in neonates. Older literature suggests levels above 1.7 mmol/L are acceptable in this age group. The World Health Organization (WHO) defines hypoglycaemia in children as levels below 2.5 mmol/L. [3]

The diagnosis of hypoglycaemia rests on three criteria (Whipple's triad) of plasma hypoglycaemia, symptoms attributable to a low blood sugar level and resolution of symptoms with correction of the hypoglycaemia.

The annual prevalence of severe hypoglycaemia is around 30% in people with type 1 diabetes. [4] It is higher in those with risk factors - eg, strict glycaemic control, impaired awareness of hypoglycaemia and increasing duration of diabetes. It is also common during sleep - nocturnal hypoglycaemia.

Risk factors for hypoglycaemia

These include:[2]

- Tight glycaemic control.
- Malabsorption.
- Injection into lipohypertrophy sites.
- Alcohol.
- Insulin prescription error (notable in hospitalised patients).
- Long duration of diabetes.
- Renal dialysis.
- Drug interactions between hypoglycaemic agents - eg, quinine, selective serotonin reuptake inhibitors (SSRIs).
- Impaired renal function.
- Lack of anti-insulin hormone function - eg, Addison's disease, hypothyroidism.

Other risk factors particularly for children include:

- Fasting or long duration of poor or nil intake.
- Inborn errors of metabolism - eg, glycogen storage disorders.
- Insulinoma.
- Congenital or primary hyperinsulinism.
- Accidental ingestion of medications - eg, salicylate, sulfonylureas, iron supplements, paracetamol.
- Poorly controlled diabetes mellitus in pregnancy is a risk for neonatal hypoglycaemia.
- Sepsis is also a risk for neonatal hypoglycaemia.

Presenting features

Neurological manifestations include coma, convulsions, transient hemiparesis and stroke, while reduced consciousness and cognitive dysfunction may cause accidents and injuries. Cardiac events may be precipitated - eg, arrhythmias, myocardial ischaemia and cardiac failure.

Management in adults

Essentially, a quick-acting carbohydrate needs to be given, followed by a longer-acting carbohydrate.

**Initially**

- Glucose 10-20 g is given by mouth, either in liquid form or as granulated sugar (two teaspoons) or sugar lumps.
- GlucoGel® - formerly known as Hypostop® Gel - may be used.

Repeat capillary blood glucose after 10-15 minutes; if the patient is still hypoglycaemic then the above can be repeated (probably up to 1-3 times).[2]

**If hypoglycaemia causes unconsciousness, or the patient is unco-operative**
Intravenous administration of 75-80 ml 20% glucose or 150-160 ml of 10% glucose (the volume will be determined by the clinical scenario).\(^2\)
25 ml of 50% glucose concentration is viscous, making it more irritant and more difficult to administer intravenously. It is rarely used now.

Once the patient regains consciousness, oral glucose should be administered, as above.

**If the patient is at home, or intravenous (IV) access cannot be rapidly established**
- Glucagon 1 mg should be given by intramuscular (IM), or subcutaneous (SC) injection.\(^5\)
- This dose is used in insulin-induced hypoglycaemia (by SC, IM, or IV injection), in adults and in children over 8 years (or body weight over 25 kg). **NB**: 1 unit of glucagon = 1 mg of glucagon.

The patient must be admitted to hospital if hypoglycaemia is caused by an oral antidiabetic drug, because the hypoglycaemic effects of these drugs may persist for 12-24 hours and ongoing glucose infusion or other therapies such as octreotide (see under 'Hypoglycaemia which causes unconsciousness or fitting is an emergency', below) may be required.

**Glucagon**
Glucagon can have variable absorption, as it is given SC or IM. It has a relatively slow onset of action and relies on glycogen stores. Therefore, it may not be effective in cachectic patients, those with liver disease, and in young children. It is contra-indicated in insulinoma and phaeochromocytoma. It also causes more insulin to be released and creates the potential for secondary rebound hypoglycaemia.

Once the patient is more alert, longer-acting carbohydrate should be given - eg, toast, a normal meal. For inpatients, an infusion of 10% glucose may need to be considered - eg, 100 mL/hour.\(^2\) If the patient received glucagon then a larger portion of the longer-acting carbohydrate is needed. Also, they may need their regular insulin if it is due - although the dose may need to be reviewed.

**Prolonged hypoglycaemic coma**
This is usually caused by cerebral oedema and follows profound hypoglycaemia lasting more than five hours:
- Use IV mannitol and dexamethasone with constant glucose monitoring and IV glucose to keep serum level at 5-10 mmol/L until either consciousness has been restored or permanent brain damage is diagnosed.
- With overdoses of insulin or sulfonylurea, up to 80 g/hour glucose as 25-50% solution through a central line may be required.
Treatment of hypoglycaemia in children

Prompt treatment of hypoglycaemia in children, from any cause, is essential to prevent subsequent neurological damage. For risk factors - see above.

Initially

- Glucose 10-20 g is given by mouth either in liquid form (eg, milk 200 mL) or as granulated sugar (two teaspoons) or sugar lumps.
- If necessary, this may be repeated following 10-15 minutes.
- Further food is required to prevent recurrence of hypoglycaemia.

Children whose hypoglycaemia is caused by an oral antidiabetic drug should be transferred to hospital because the hypoglycaemic effects of these drugs may persist for 12-24 hours.

Hypoglycaemia which causes unconsciousness or fitting is an emergency

- In hypoglycaemia, if sugar cannot be given by mouth, glucagon can be given by injection. A child aged under 8 years or of body weight under 25 kg should be given 500 micrograms.
- Carbohydrates should be given as soon as possible to restore liver glycogen.
- Glucagon may be issued to parents or carers of insulin-treated children for emergency use in hypoglycaemic attacks.
- It is often advisable to prescribe on an 'if necessary' basis to hospitalised insulin-treated children, so that it may be given rapidly by the nurses during a hypoglycaemic emergency.
- If not effective in 10 minutes, IV glucose should be given.

Alternatively, 2-5 mL/kg of glucose IV infusion 10% (200-500 mg/kg of glucose) may be given IV into a large vein, through a large-gauge needle.

- This concentration is irritant, especially if extravasation occurs.
- Glucose IV infusion 50% is not recommended, as it is very viscous and hypertonic. \(^{[2]}\)

The patient should be monitored closely, particularly in the case of an overdose with a long-acting insulin because further administration of glucose may be required.

Octreotide appears to be a safe and effective treatment where glucose therapy is escalating in sulfonylurea overdose. Bolus doses of 1-2 micrograms/kg can be given every 6-8 hours or an infusion of 30 ng/kg/minute; however, the optimal dosing regime is debated and a toxicologist or endocrinologist should be consulted.

Glucagon is not effective in the treatment of hypoglycaemia due to fatty acid oxidation or glycogen storage disorders. Glucagon is not appropriate for chronic hypoglycaemia.

Neonatal hypoglycaemia

- Neonatal hypoglycaemia is treated with glucose IV infusion 10% given at a rate of 5 mL/kg/hour.
- An initial dose of 2.5 mL/kg over five minutes may be required if hypoglycaemia is severe enough to cause loss of consciousness, or fitting.
- Mid asymptomatic persistent hypoglycaemia may respond to a single dose of glucagon.
- The dose is 20 micrograms/kg.
- Glucagon has also been used in the short-term management of endogenous hyperinsulinism.

Prevention of hypoglycaemia is a crucial part of the management of diabetes mellitus and all cases should be followed up and reviewed.

Further reading & references

- Type 1 diabetes in adults: diagnosis and management; NICE Guidelines (August 2015, updated July 2016)
- Type 2 diabetes in adults: management; NICE Guidelines (December 2015, updated May 2017)
- The hospital management of hypoglycaemia in adults with diabetes mellitus; Joint British Diabetes Societies/Diabetes UK (Sept 2013)
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