Hypoglycaemia

Definition / Supporting Information

Most UK authorities would use a blood glucose concentration of < 2.6 mmol/L with or without associated signs and symptoms as a definition of clinically significant hypoglycaemia. In contrast, in children with diabetes a blood glucose level < 4.0 mmol/L would be described as a 'hypo' in routine clinical practice.

This information relates to children not known to have diabetes mellitus; however, the same principles for correction of hypoglycaemia apply.

Keywords / also known as: reduced glucose levels, low blood sugar

Essential History

Ask about:

- Previous hypoglycaemic episodes / known diabetes mellitus
- Possibility of drug (close family member with diabetes mellitus) or alcohol ingestion (see Drug Overdose and Poisoning)
  - Consider accidental or deliberate harm or neglect (see Child maltreatment: when to suspect maltreatment in under 18s [NICE clinical guideline 89])
- Intercurrent infection
- History of other affected family members or occurrence of unexplained infant deaths among close relatives or consanguinity
- Temporal relationship of symptoms to food intake
  - After the ingestion of protein
    - Hereditary defects of amino acid and organic acid metabolism
  - After ingestion of lactose (eg, milk products)
    - Galactosaemia
  - After sucrose / sugar ingestion
    - Hereditary fructose intolerance (HFI)
    - May be associated with avoidance of sweets
  - Fasting hypoglycaemia is characteristic of ketotic hypoglycaemia, hormonal deficiencies, hyperinsulinism, hepatic glycogen storage disease (GSD), and fructose diphosphatase deficiency.
- Duration of maximal fasting when well
- Early morning symptoms

‘Red Flag’ Symptoms and Signs

Ask about:

- Pallor
- Sweating
- Limpness
- Inattention
- Staring
- Listlessness
- Abdominal pain
- Vomiting
- Ataxia
- Headache
- Confusion
- Altered behaviour (see Psychotic behavior)
- Stupor
- Coma
- Convulsions

Look for:

- Evidence of sepsis / septic shock
  - Source of infection
  - Tachycardia
  - Evidence of poor perfusion / prolonged capillary refill time > 2 seconds
- Jaundice / ascites / hepatomegaly
  - Inborn errors of metabolism
- In-coordination of eye movements
- Strabismus
- Excessive irritability
- Motor in-coordination
- Short stature
- Dysmorphism (see Congenital Malformations)
  - Especially midline facial defects
- Evidence of delayed development

Differential Diagnosis / Conditions

Sepsis

- See Antibiotics for the prevention and treatment of early-onset neonatal infection [NICE clinical guideline CG149] and Management of bacterial meningitis

and meningococcal septicaemia in children and young people younger than 16 years in primary and secondary care [NICE clinical guideline CG102].

Diabetes mellitus

- See Diabetes (type 1 and type 2) in children and young people: diagnosis and management [NICE guideline NG18]

Hyperinsulinism

- Congenital hyperinsulinism of infancy (CHI)
  - The most common cause of persistent or recurrent hypoglycaemia in the first year of life
  - Transient hyperinsulinism associated with diabetic mothers, perinatal asphyxia, and intrauterine growth restriction
  - Persistent hyperinsulinism
    - Associated with diffuse or focal beta-cell dysfunction
    - May have an underlying genetic abnormality, although 50% have no recognised cause.
  - Beckwith–Wiedemann syndrome (omphalocele, macroglossia, and gigantism)
    - Hypoglycaemia occurs in many affected infants and resolves at several months of age
    - Some have hemihypertrophy
    - Increased incidence of adrenal, liver, and kidney (Wilms') tumours
  - HIHA (hyperinsulinism hyperammonaemia)

Inborn errors of metabolism

- Hepatic glycogen storage disease (GSD)
  - Glucose-6-phosphatase deficiency types Ia and Ib
    - Growth retardation (see Faltering Growth)
    - Cherubic facies
    - Protuberant abdomen
    - Large smooth liver (see hepatomegaly)
    - Enlarged kidneys
    - Fasting hypoglycaemia of only a few hours' duration
    - Ketosis, lactic acidaemia, hyperlipidaemia, hyperuricaemia
    - Bleeding diathesis
    - In type Ib, also neutropenia and increased frequency of infections
    - Death may result if hypoglycaemia and lactic acidaemia are not treated adequately and promptly with intravenous glucose and sodium bicarbonate.

- Galactosaemia
  - In a lactose-fed infant, characterised by:
    - Faltering growth
    - Jaundice
    - Vomiting
    - Susceptibility to infection
    - Hepatomegaly
    - Oedema
    - Ascites
    - Tendency to bleed
    - Cataracts
    - Proteinuria
    - Aminoaciduria
    - Galactosuria
    - Intellectual disability (variable)
    - Progressive liver failure
    - Death
  - Symptomatic hypoglycaemia is not a common finding
- Hereditary fructose intolerance (HFI; after fructose ingestion)
  - Aversion to sweets
    - Episodes of symptoms after ingesting fructose-containing items
  - Recurrent vomiting
  - Haemorrhage
  - Jaundice / hepatomegaly / abnormal liver function / hepatic failure
  - Faltering growth
  - Fructosuria
- Fructose-1,6-diphosphatase deficiency
  - Fasting hypoglycaemia
  - Lactic acidosis, ketosis
  - Hyperuricaemia
  - Hepatomegaly
  - Vomiting precipitates attacks
  - Life threatening in neonates and young children
- Disorders of amino acid and organic acid metabolism
  - Symptoms usually begin in neonatal period, but they may occur later.
- Fatty acid oxidation defects: hypoketotic hypoglycaemia
  - Acute life-threatening event
  - Sudden death
  - Rhabomyolysis
  - Encephalopathy even in absence of hypoglycaemia

Hormone deficiencies

- Hypopituitarism
  - Severe hypoglycaemia during the first few days of life
  - Occasionally, hypoglycaemia first appearing later in infancy or childhood
  - Septo-optic dysplasia (optic nerve hypoplasia and absence of the septum pellucidum) is present in some.
    - It may be accompanied by nystagmus.
  - Some male patients have a small penis (microphallus) or genitalia.
  - Older children with hypopituitarism may be short and relatively overweight for their height.
- Adrenal gland disorders
  - Destruction
    - Autoimmune
    - Infection
    - Haemorrhage
    - Adrenoleukodystrophy
  - Congenital adrenal hyperplasia/hypoplasia
  - ACTH deficiency
    - Hypopituitarism
    - Withdrawal from glucocorticoid therapy
  - ACTH resistance

Ketotic hypoglycaemia (‘accelerated starvation’)

- This is a diagnosis of exclusion
  - The pathogenesis is not understood
- Most common cause of hypoglycaemia after 1 year of age
- Children with low birth weight, poor weight gain, and male sex are at increased risk
- Combination of ketonuria, hypoglycaemia, and central nervous system symptoms
  - Unresponsiveness
  - Pallor
  - Vomiting
  - Coma and convulsions (see Seizures)
- Symptoms occurring in association with episodes of gastroenteritis or an upper respiratory tract infection or with prolonged fast, typical of ketotic hypoglycaemia
- Onset is between 18 months and 5 years of age, with peak incidence at 2 years.
  - Episode frequency tends to reduce with age
    - Rare after 7–8 years of age

Investigations

To be undertaken by non-specialist practitioners (eg, General Practitioner (GP) Team):

- Blood glucose level
  - May be approximated quickly by a finger prick and using a visual test strip or glucose meter
  - Can be confirmed later by appropriate chemical laboratory test

To be undertaken by specialist practitioners (eg, Emergency Department / General Paediatric / Neonatal / Paediatric Endocrinology / Paediatric Metabolic Team(s)) if not already done:

- Blood glucose level
  - May be approximated quickly at bedside by using a visual test strip or glucose meter
  - Diagnostic blood sample is generally taken before correcting blood glucose level
- Blood cultures / C-reactive protein:
  - If sepsis suspected
- Insulin / C-peptide
  - Hyperinsulinism associated with increased glucose requirement to correct and maintain normal blood glucose levels
- Growth hormone (GH) and cortisol
  - Low blood values of either in the presence of hypoglycaemia raise suspicion of deficiencies of these hormones and need for further studies.
- Lactic acid
- Venous blood gas analysis
- Ammonia
- Amino acids
- Acylcarnitine profile
- Plasma levels of β-hydroxybutyrate and free fatty acids
  - Both low in hyperinsulinism
  - Abnormal (increased) ratio of free fatty acids
    - β-hydroxybutyrate suggests disorder of fat oxidation.
- Capillary blood or urinary ketones (helpful in establishing diagnosis of ketotic hypoglycaemia)
  - Urine should be tested further for presence of amino acids and organic acids
- Glucose tolerance tests for GSD-I, GSD-III, GSD-FAMILY, FDPase, HFI
- Magnetic resonance imaging of the brain:
  - If hypopituitarism or GH deficiency is suspected.

Treatment Approach

To be undertaken by non-specialist practitioners (eg, GP Team):

- Correct hypoglycaemia (see Diabetes (type 1 and type 2) in children and young people: diagnosis and management [NICE guideline NG18, section 1.2])
    - For fully conscious patients, the first line of treatment should be the consumption of rapidly absorbed simple carbohydrate (eg, 10–20 g carbohydrate given by mouth).
        - Carbohydrate given in liquid form may be taken more easily
        - Frequent small volumes may be preferable, especially if the patient is vomiting.
        - This should raise blood glucose levels within 5–15 minutes
    - As symptoms improve or normoglycaemia is restored, additional complex long-acting carbohydrate (eg, pasta, basmati or easy cook rice, grainy breads, new potatoes, sweet potato and yam, porridge oats, natural muesli) should be given orally to maintain blood glucose levels unless a snack or meal is imminent.
- In patients with a reduced level of consciousness:
    - Intramuscular glucagon or concentrated oral glucose solution (eg, dextrose 40% gel, 'Glucogel') may be used.
    - Children and young people over 8 years old (or body weight more than 25 kg) should be given 1 mg glucagon.
    - Children under 8 years old (or body weight less than 25 kg) should be given 500 micrograms of glucagon.
    - Blood glucose levels should respond within 10 minutes.

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        - This should raise blood glucose levels within 5–15 minutes.
        - Frequent small volumes may be preferable, especially if the patient is vomiting.
        - Carbohydrate given in liquid form may be taken more easily.
    - As symptoms improve or normoglycaemia is restored, additional complex long-acting carbohydrate should be given orally to maintain blood glucose levels unless a snack or meal is imminent.

- In patients with a reduced level of consciousness:
  - Administer 2–5 mL/kg (200–500 mg/kg body weight) of 10% glucose intravenously.
    - This should raise blood glucose levels within 10 minutes.
  - Give intravenous fluids containing appropriate electrolytes and glucose at a rate sufficient to maintain plasma or serum glucose levels above 4 mmol/L.
  - Monitor blood glucose levels initially every 30–60 minutes at the bedside until stable, then every 2–4 hours.
    - Rate of glucose administered should be adjusted accordingly.
  - As symptoms improve or normoglycaemia is restored, in children and young people who are sufficiently awake, additional complex long-acting carbohydrate should be given orally to maintain blood glucose levels.
  - Overcorrection with subsequent hyperglycaemia may complicate fluid management by causing an osmotic diuresis.
- Treat sepsis
  - Broad-spectrum antibiotic cover (see Neonatal infection (early onset): antibiotics for prevention and treatment [NICE clinical guideline CG149] and Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management [NICE clinical guideline CG102])
- For further management of diabetes mellitus, see Diabetes (type 1 and type 2) in children and young people: diagnosis and management [NICE guideline NG18]

Specific Treatment

To be undertaken by specialist practitioners (eg, General Paediatric / Paediatric Endocrinology / Paediatric Metabolic Team(s)) if not already done:

- Hyperinsulinism
  - Diazoxide (in combination with chlorothiazide)
    - Normal glucose level is restored, use of the drug is continued, and the patient is assessed periodically until 5–7 years of age.
    - Clinical improvement may occur with increasing age, while abnormalities of glucose regulation may remain.
    - Hyperinsulinism caused by ABCC8 / KCNJ11 mutations may not respond to diazoxide.
    - If hypoglycaemia persists or recurs despite diazoxide therapy, octreotide should be considered.
    - Tachyphylaxis with octreotide is a problem with long-term use.
  - Surgery
    - Focal disease can be identified by ^{18}F-fluoro-L-DOPA positron emission tomography (PET) scanning, and limited pancreatic resection is curative.

        - For diffuse pancreatic disease unresponsive to medical therapy a 95% pancreatectomy is most commonly undertaken, but some children remain hypoglycaemic.
- Disorders of hepatic glycogen release / storage
    - Advise continuous nocturnal glucose-containing gastric feeds
    - Advise frequent feeds during the day, at least every 3–4 hours
    - Daily oral administration of uncooked cornstarch suspension is beneficial in older children but less so in infants.
- Galactosaemia
    - Stop galactose-containing feed immediately while awaiting awaiting results of erythrocyte enzyme studies and referral
    - Long-term management consists of avoidance of lactose- and galactose-containing foods.
- HFI
    - Reverse acute episodes of hypoglycaemia by intravenous administration of glucose
    - Long-term treatment consists of:
        - Strict elimination of dietary fructose
        - Elimination of fructose in cough syrups and other drugs
- FDPase deficiency
    - Treatment of acute attacks
        - Correction of hypoglycaemia and acidosis by intravenous infusion of glucose and sodium bicarbonate
    - Long-term management
        - Emphasises avoidance of fasting and provision of a fructose-free, high-carbohydrate diet
- Ketotic hypoglycaemia
    - Reverse acute hypoglycaemic attacks by buccal ‘Glucogel’ or intravenous administration of glucose
    - A liberal carbohydrate diet, including a bedtime snack, should be followed.
    - Avoid prolonged overnight fasting
        - Parents should use an ‘emergency regime’ providing regular carbohydrate-containing fluids and monitor capillary blood glucose levels during illness or periods of fasting.
        - If emergency feed is not tolerated, advise to attend emergency department for intravenous glucose

When to Refer

Refer to specialist practitioners (eg, Emergency Department / General Paediatric / Paediatric Endocrinology / Paediatric Metabolic Team(s)) for consideration of hospital admission if:

- Documented hypoglycaemia not caused by insulin therapy

Refer all metabolic conditions to a Metabolic Specialist Centre

'Safety Netting' Advice

- Patients with hypoglycaemia should have an emergency treatment plan and alert parents or carers before crises occur. They need regular review by their medical team.

Patient / Carer Information

**Please note: whilst these resources have been developed to a high standard they may not be specific to children.*

- Diabetes and Hypoglycemia (Web page), Diabetes.co.uk
- Dealing with hypoglycaemia (low blood sugar) (Web page), Patient
- Hypoglycaemia (low blood sugar) (Web page), the NHS website

Resources

National Clinical Guidance

Child maltreatment: when to suspect maltreatment in under 18s (Web page), NICE clinical guideline CG89, National Institute for Health and Care Excellence

Diabetes (type 1 and type 2) in children and young people: diagnosis and management (Web page), NICE guideline NG18, National Institute for Health and Care Excellence

Epilepsies: diagnosis and management (Web page), NICE clinical guideline CG137, National Institute for Health and Care Excellence

Meningitis (bacterial) and meningococcal septicaemia in under 16s: recognition, diagnosis and management (Web page), NICE clinical guideline CG102, National Institute for Health and Care Excellence

Neonatal infection (early onset): antibiotics for prevention and treatment (Web page), NICE clinical guideline CG149, National Institute for Health and Care Excellence

Suggested Resources

**Please note: these resources include links to external websites. These resources may not have national accreditation and therefore PCO UK cannot guarantee the accuracy of the content.*

Emergency guidelines (Web page), British Inherited Metabolic Diseases Group

Glucagon for hypoglycaemia (Web page), Medicines for Children

Hypoglycaemia: treatment summary (Web page), BNFc

Protocols for treating convulsive status epilepticus in adults and children (Web page), NICE guideline CG137, National Institute for Health and Care Excellence

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