Managing hypoglycemia

It is safer and more effective to prevent hypoglycemia than to treat it after hypoglycemia occurs.[8] Counsel patients who are at high-risk for hypoglycemia on how to prevent low blood glucose.[3]

Hypoglycemia is defined by[3]

1. The development of neurogenic or neuroglycopenic symptoms (see Hypoglycemia symptoms)
2. A low blood glucose level (<4.0 mmol/L for people with diabetes treated with insulin or an insulin secretagogue), and
3. The presence of symptoms that resolve following the intake of carbohydrates

Hypoglycemia symptoms[3]

Neurogenic (autonomic)

- Trembling
- Palpitations
- Sweating*
- Anxiety
- Hunger
- Nausea
- Tingling

Neuroglycopenic

- Difficulty concentrating
- Confusion
- Weakness
- Drowsiness
- Vision changes
- Difficulty speaking
- Headache*
- Dizziness
- Disturbed sleep*
- Abnormal dreams*

*Symptoms of nocturnal hypoglycemia

Reducing hypoglycemia risk	
Education	• Review hypoglycemia risk factors at each visit if possible (see Risk factors for severe hypoglycemia)[3] • Counsel patients, families and caregivers on risk factors and how to prevent, recognize and treat hypoglycemia (see Hypoglycemia low blood sugar in adults[i]) • Review the injection technique to reduce lipohypertrophy risk (lipohypertrophy increases severe hypoglycemia risk by 2.7 fold;[59] see Type 2 diabetes: insulin therapy > Safe insulin injection techniques and pen needle use) • Connect high-risk patients to a Certified Diabetes Educator, Diabetes Education Program/Centre or collaborative support (e.g., registered nurse, nurse practitioner, pharmacist, dietitian, see Local services for patients living with type 2 diabetes[ii])[3]
Monitor	• Support patients to self-monitor blood glucose more often • Consider a flash or continuous glucose monitoring system[3] • If readings are < 4.0mmol/L, test the glucose monitoring system accuracy using a fingerprick • For nocturnal hypoglycemia: advise patients to monitor their blood glucose levels periodically at the peak action time of their overnight insulin (use a glucose monitor that gives alerts based on blood glucose levels, e.g., DexCom® 6, FreeStyle Libre® 2 or FreeStyle Libre® combined with NightRider BluCon®)[3]
Reassess targets	• Reassess whether targets are appropriate for the patient • If patient has hypoglycemia unawareness or pseudohypoglycemia, may consider less stringent glycemic targets with avoidance of hypoglycemia signs or symptoms for up to 3 months[3]
Adjust medication	• Consider using medication (see Type 2 diabetes: non-insulin pharmacotherapy)[7] and insulin (e.g., long-acting insulin) with a lower risk of hypoglycemia[3] • Stop sulfonylureas when prandial (bolus) insulin is added to basal insulin[2] • Consider reducing basal insulin dose by 10-20% if adding another non-insulin agent (e.g., GLP1-RA, SGLT2i)[60] • Adjust insulin regimen or ratio[61]

Risk factors for severe hypoglycemia

Patient risk factors

- Advancing age and frailty[3,62]
- Female gender[63]
- Low A1C (<6.0%)[3]
- Hypoglycemia unawareness[3**]
- Prior episode of severe hypoglycemia[3]
- Long duration of diabetes (insulin insufficiency)[62]
- Neuropathy[3]
- Renal impairment (for eGFR <30, consider adjusting insulin dose and timing to minimize insulin stacking)[3, 62]
- Cognitive impairment[3]
- Poor health literacy[3]
- Food insecurity or erratic eating patterns[3, 62]

**Hypoglycemia unawareness occurs when the threshold for the development of neurogenic warning symptoms is close to, or lower than, the threshold for the neuroglycopenic symptoms, such that the first sign of hypoglycemia is confusion or loss of consciousness. Frequent hypoglycemia can lead to hypoglycemia unawareness by decreasing normal responses to hypoglycemia. Hypoglycemia unawareness can be improved or reversed by strictly avoiding hypoglycemia for up to 3 months.[3]

Managing hypoglycemia (continued)

Medication risk factors

- Use of insulin[64]
- Long-term use of insulin therapy[3]
- Basal insulin component too high[64]
- Prandial (bolus) insulin doses not adjusted for physical activity, carbohydrate intake or skipped meals[62]
- Not adjusting medications after weight loss or withdrawal of medications that raise blood glucose (e.g., corticosteroids)[62]
- Insulin mistakes (e.g., administering prandial (bolus) insulin at bedtime on an empty stomach instead of basal insulin)
- Insulin stacking (e.g., injecting insulin correction within 3 hours of a previous correction)
- Overbasalization (e.g., titration of basal insulin beyond an appropriate dose in an attempt to achieve glycemic targets)[55]
- Lipohypertrophy[59]
- Drugs that cause or mask symptoms of hypoglycemia (e.g., anti-hyperglycemics, beta blockers, ACE inhibitors, ethanol, fluoroquinolones, salicylates)[65]

Range of hypoglycemia severity[3]

Mild

Neurogenic symptoms may be present. The individual is able to self-treat. Blood glucose is typically <4.0 mmol/L.

Moderate

Both neurogenic and neuroglycopenic symptoms are present. The individual is able to self-treat. Blood glucose is typically <4.0 mmol/L.

Severe

Patient requires the assistance of another person to treat hypoglycemia. Unconsciousness may occur. Blood glucose is typically <2.8 mmol/L.

Treating hypoglycemia[3]

- Hypoglycemia treatment aims to promptly increase low blood glucose to a safe level to eliminate the risk of injury and relieve symptoms
- Avoid over-treatment, which can result in rebound hyperglycemia and weight gain

Mild-moderate hypoglycemia

1. Oral ingestion of 15g carbohydrate (glucose or sucrose tablets/solution preferred*)[3]
2. Re-test blood glucose in 15 minutes. If the blood glucose level remains at <4.0 mmol/L, re-treat with another 15g carbohydrate[3]
3. Once the hypoglycemia is reversed, eat the usual meal/snack that is due at that time of day. If a meal is >1 hour away, eat a snack with 15g carbohydrate and a protein source[3]

Examples of 15g of carbohydrate:[2]

- 4 glucose/sucrose tablets (most tablets are 4g each)
- 15mL (1 tbsp) of sugar dissolved in water
- 3 packets of sugar from fast food/restaurants
- 5 cubes of sugar
- 150 mL (2/3 cup) of juice or regular soft drink
- 6 Life Savers® (each is 2.5g of carbohydrate)
- 15 mL (1 tbsp) of honey

Severe hypoglycemia

Conscious patient:

1. Oral ingestion of 20g carbohydrate (glucose tablets or equivalent preferred*)[3]
2. Re-test blood glucose in 15 minutes. If the blood glucose level remains at <4.0 mmol/L, re-treat with another 15g carbohydrate[3]

Unconscious patient:

- With no intravenous access
  1. Caregiver or support person should administer 1mg of glucagon subcutaneously or intramuscularly, or 3mg intranasally (see Glucagon as treatment for severe hypoglycemia)[3,66]
  2. Caregiver or support person should call for emergency services and notify the care team as soon as possible[3]
- With intravenous access
  1. Caregiver or support person should administer 10-25g (20–50 mL of D50W) glucose intravenously over 1-3 minutes[3]
  2. Caregiver or support person should call for emergency services and notify the care team as soon as possible[3]

Once the hypoglycemia is reversed, patient should eat the usual meal/snack that is due at that time of day. If a meal is >1 hour away, eat a snack with 15g carbohydrate and a protein source[3]

*People taking an alpha glucosidase inhibitor (acarbose) must use glucose (dextrose) tablets or, if unavailable, milk or honey to treat hypoglycemia.[3]

Troubleshooting hypoglycemia when A1C is above target:

- Treat the low blood glucose first
- Identify reasons for low blood glucose (e.g., skipped meal, exercise, too much insulin, sulfonylurea)
- Review with the patient how to properly treat low blood glucose (some patients may take too much carbohydrate causing hyperglycemia)

Glucagon as treatment for severe hypoglycemia

- Glucagon should be prescribed to patients who experienceor are at high risk of experiencing severe hypoglycemia (e.g., those on long-term use of insulin who produce little to no insulin on their own, those at risk of insulin mistakes)
- Glucagon is to be administered by a caregiver or support person (1mg subcutaneously/intramuscularly or 3mg intranasally) to a patient experiencing a severe hypoglycemic reaction when impaired consciousness precludes oral carbohydrates[3,66]
- Intranasal and intramuscular/subcutaneous glucagon are similarly effective. Some studies however, demonstrate that intramuscular/subcutaneous glucagon may be slightly more effective.[67,68] Intranasal glucagon may be preferred due to ease of use, and intramuscular/subcutaneous glucagon may be preferred due to lower cost.[69]

Agent	Comments	Coverage (ODB[28], NIHB[29])	Dosage forms[28]	Usual dose	Drug cost for usual dose[28]

Intranasal glucagon (Baqsimi®)[66]	• Time to treatment response:
	  • Mean: 16.2 mins[68]
	  • Median: 10 (range 5-25) mins[68]
	• Time required to administer: 1 min[69]
	• Inhalation is not required by the patient[68]
	• Advantages:
	  • Preferred due to ease of use[69]
	  • Higher rate of administration success[68]
	  • No refrigeration required[66]
	• Disadvantages:
	  • Administration-related oronasopharyngeal and eye side effects (e.g., nasal discomfort, nasal congestion, nasal itching, sneezing, increased lacrimation, upper respiratory tract irritation)[68]
	  • Other side effects: nausea, vomiting, headache, fatigue[68,69]
		ODB ✓
		LU 625[91]
		NIHB x
			3mg prefilled device	3mg IN[66]	T: $165

Intramuscular/ subcutaneous glucagon (GlucaGen®, GlucaGen HypoKit®)[70,71]	• Time to treatment response:
	  • Mean: 12.2 mins[68]
	  • Median: 10 (range 10-20) mins[68]
	• Time required to administer: 1.3-5 mins[69]
	• Advantages:
	  • Less oronasopharyngeal and eye symptoms[68]
	  • No refrigeration required for GlucaGen HypoKit® (can be kept up to 18 months at room temperature) or generic IM/ SC glucagon (stored at room temperature)[70,71]
	• Disadvantages:
	  • Refrigeration required for GlucaGen® [70,71]
	  • Administration-related side effects (e.g., injection site pain and irritation)[68]
	  • Other side effects: nausea, vomiting, vertigo[68,69]
		ODB ✓
		NIHB ✓
			1mg vial (HypoKit® includes vial and prefilled syringe with diluent)	1mg IM/ SC[70,71]	G: $122
					T: $124

IN = intranasal, **IM** = Intramuscular, **G** = generic, **mg** = milligram, **SC** = subcutaneous, **T** = trade

Patient resources

[i] Diabetes Canada Hypoglycemia low blood sugar in adults

[ii] Centre for Effective Practice local services for patients living with type 2 diabetes

References

See Type 2 Diabetes: Insulin Therapy tool

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