Appendix J. Detailed information on glycaemic emergencies

J.1 Hypoglycaemia

Hypoglycaemia is a common complication of the management of type 1 diabetes. But the frequency of hypoglycaemia in type 2 diabetes is underestimated. Its clinical significance, especially in the elderly patient, is great. Hypoglycaemia can lead to falls, fractures, injuries, arrhythmias and, in severe cases, death. Symptoms may go unrecognised or may be mistaken for other conditions (eg transient ischaemic attack [TIA], vasovagal episodes).

Patients at risk of hypoglycaemia (apart from the elderly) include people who have:

- longstanding type 2 diabetes with cardiovascular disease (CVD)
- renal impairment and chronic kidney disease (CKD)
- monotherapy or combination therapy with insulin or long-acting sulphonylureas
- excessive alcohol intake
- beta-blocker therapy (rare), in particular vasodilatory agents (eg propranolol, atenolol)
- participated in unaccustomed or vigorous exercise.

The risk of hypoglycaemia with each sulphonylurea relates to the drugs' pharmacokinetic properties. Long-acting preparations are associated with higher risks of hypoglycaemia (eg glibenclamide [Daonil, Glimel]). Studies have shown significantly lower rates of hypoglycaemia associated with the use of gliclazide (Diamicron) compared with other sulphonylureas.

Although many newer therapies for type 2 diabetes do not cause hypoglycaemia when used as monotherapy, their use in combination with insulin or sulphonylureas increases the risk of hypoglycaemia. The use of insulin analogues may limit, but not eradicate, the risk of hypoglycaemia.

Symptoms of hypoglycaemia vary between persons. Patients often learn to recognise their unique symptoms. The onset of symptoms usually occurs with a blood glucose level (BGL) of <4.0 mmol/L. Common symptoms fall into two categories:

- Adrenergic symptoms – trembling or shaking, sweating, hunger, lightheadedness and numbness around the lips and fingers
- Neuroglycopaenic symptoms – lack of concentration, weakness, behavioural change, tearfulness/crying, irritability, headache and dizziness.

Severe hypoglycaemia occurs clinically when a patient develops a reduced conscious state and requires assistance from another person to manage an episode of hypoglycaemia. A BGL of <3.0 mmol/L puts the person at increased risk of severe hypogylcaemia.

Asymptomatic hypoglycaemia (or biochemical hypoglycaemia) occurs when a BGL is low (<3.9 mmol/L).

Impaired hypoglycaemia awareness is of particular concern and refers to the clinical situation where a patient loses the ability to detect the early symptoms of hypoglycaemia. This results from repeated episodes of mild hypoglycaemia or can arise with long duration of diabetes due to loss of adrenergic and glucagon response, with eventual loss of adrenergic and neuroglycopaenic symptoms. It can lead to confusion and marked behavioural change, which is not recognised by the patient and may progress to loss of consciousness.

The cause needs to be identified and the episode dealt with by reinforcing education, counselling the patient and perhaps changing treatment.

Management of an episode of hypoglycaemia

If a patient with diabetes is showing signs of potential hypoglycaemia, first make sure that the patient is safe (eg seated securely and not at risk of falling).

If possible, confirm that the symptoms are due to hypoglycaemia by performing a finger prick BGL.

If the person is awake, alert and can swallow, hypoglycaemia may be managed according to the **'Rule of 15'**.

If the patient is symptomatic, or if BGL is <4.0 mmol/L:

- provide **15 g** of quick-acting carbohydrate that is easy to consume (eg half a can of regular – non-diet – soft drink, half a glass of fruit juice, three teaspoons of sugar or honey, six or seven jellybeans, three glucose tablets)

- wait **15 minutes** and repeat blood glucose check – if the level is not rising, suggest eating another quick-acting carbohydrate from the above list
- provide some longer acting carbohydrate if the patient's next meal is more than **15 minutes** away (eg a sandwich; one glass of milk or soy milk; one piece of fruit; two or three pieces of dried apricots, figs or other dried fruit; one tub of natural low-fat yoghurt; six small dry biscuits and cheese)
- test glucose every one to two hours for the next four hours.

Patients and carers should be made aware of the use of an alternative 'Rule of 15'.

If the patient is symptomatic, but the blood glucose or capillary glucose cannot be performed to confirm that the episode is due to hypoglycaemia, treat the patient as if they have hypoglycaemia by administering 15 g of quick-acting carbohydrate. If there is no improvement after 15 minutes, the patient could have another cause for the episode and further medical assistance may be necessary.

If the patient cannot safely swallow 15 g of carbohydrate due to their reduced conscious state, consider the administration of 1 mg of glucagon intramuscularly or subcutaneously into the thigh, buttock or upper arm, if available. If not, further emergency medical assistance will be required.

If glucagon is administered, always review the monitored capillary glucose after 15 minutes to ensure effective management of the hypoglycaemia has occurred and the blood glucose remains ≥4 mmol/L. Test again one hour after severe hypoglycaemia to ensure stable glucose levels.

Post-hypoglycaemia – Re-assess the patient's circumstances, medication dosages, and dietary intake, as well as overall need for glucose monitoring after any severe hypoglycaemic episode with the patient and/or with their immediate family or support persons. Also ensure implications for driving competence (refer to Section 14.3 Driving and www.austroads.com.au/drivers-vehicles/assessing-fitness-to-drive), operation of machinery and other similar areas are discussed with the patient.

J.2 Hyperglycaemic emergencies

Severe hyperglycaemia has significant morbidity and mortality.

Hyperglycaemic emergencies should be preventable in people known to have diabetes, and their occurrence in this group signifies a major breakdown in medical management. Adequate early management of sick patients with diabetes will prevent the development of hyperglycaemic emergencies.

Diabetic ketoacidosis

Diabetic ketoacidosis (DKA) is a medical emergency requiring specialist care and should generally be managed in hospital. Whatever the setting, it is important that treatment commences as early as possible.

DKA, once thought to typify type 1 diabetes mellitus, can occur in patients with type 2 diabetes mellitus under stress (eg during surgery, trauma, infections, high dose steroids). The very young, older people and pregnant patients are also at greater risk of DKA. A type of ketoacidosis has now been identified (although rarely) with the use of sodium glucose co-transporter 2 (SGLT2) inhibitors alone or in combination with other glucose lowering medications. This type of diabetic ketosis is characterised by the absence of extreme hyperglycaemia and may lead to overlooked diagnoses. Refer to the Therapeutic Goods Administration (TGA) warning at www.tga.gov.au/alert/sodium-glucose-co-transporter-2-inhibitors-used-treat-type-2-diabetes

Pathophysiology

DKA occurs when there is an absolute deficiency of insulin. For DKA to occur in type 2 diabetes, there needs to be significantly impaired insulin secretion as a result of 'glucotoxicity', or a long duration of diabetes together with severe insulin resistance, typically as the result of severe infection or other stresses.

This results in:

- increasing hepatic glucose production causing hyperglycaemia
- increasing peripheral lipolysis releasing free fatty acids – these are converted to ketoacids by the liver resulting in a metabolic acidosis
- hyperglycaemia-induced osmotic diuresis leading to sodium, potassium and phosphate depletion
- dehydration causing pre-renal failure.

Assessment

The biochemical criteria for DKA are:

- hyperglycaemia, defined by a BGL >11 mmol/L*
- venous pH <7.3 or bicarbonate <15 mmol/L
- presence of blood ketones or urinary ketones (abnormal ketones is ≥0.5 mmol/L, severe ketosis is >3.0 mmol/L)

*Note the absence of hyperglycaemia may occur with ketosis with SGLT2 inhibitors

Blood ketone testing is preferred but urinalysis may be used for initial assessment if blood ketone testing is not available. Blood ketone testing equipment should be made available for medical practices and 'at risk' patient use.

When treating adult patients with DKA, the following must be considered and closely monitored:

- correction of fluid loss with intravenous fluids
- correction of hyperglycaemia and suppression of ketone production with insulin
- correction of electrolyte disturbances, particularly potassium loss
- resolution of acid–base balance
- treatment of concurrent infection/conditions (eg stroke, myocardial infarction, deep vein thrombosis), if present.

The main aim in treating DKA is to progressively normalise the blood pH and clear the body of excessive ketones – achieved by aggressive fluid replacement and insulin therapy. This also improves the blood glucose concentration. The hyperglycaemia corrects before the acidosis. Therefore, intravenous glucose is required to allow the insulin infusion to continue to suppress ketone production while acidosis resolves.[176]

Wherever possible the patient should be managed in a specialist medical unit. In rural and remote practice, this may not be possible. In this situation, it is advisable to contact the most appropriate diabetes resource person for advice while commencing treatment promptly.

Hyperosmolar hyperglycaemic state

Hyperosmolar hyperglycaemia usually occurs in type 2 diabetes most often in the elderly, or in those with newly diagnosed type 2 diabetes. It is characterised by severe hyperglycaemia (usually >25 mmol/L) , hyperosmolality, dehydration and a change in mental state with little or no ketoacidosis. It may present as hypovolaemic shock and coma in severe cases.[176] This is usually a result of illness or infection; however, it can also be due to poor patient compliance. Older patients are at higher risk of hyperosmolar hyperglycaemic state (HHS).

Pathophysiology

HHS develops because of relative rather than absolute insulin deficiency. Significant insulin deficiency causes hyperglycaemia due to increased hepatic gluconeogenesis. However, as absolute insulin deficiency is not present, peripheral lipolysis remains suppressed and the release of free fatty acids is low. Little substrate is available for the generation of ketoacids and a metabolic acidosis does not occur.

The hyperglycaemia results in an osmotic diuresis leading to pre-renal failure. Eventually, severe intravascular volume depletion occurs resulting in a further deterioration of renal function. Consequently, glomerular filtration diminishes, preventing the further excretion of glucose. With ongoing increasing hepatic glucose production, decreased peripheral glucose utilisation and reduced urinary glucose losses, severe hyperglycaemia results.

The depletion of the total body water leads to the hyperosmolality of body fluids reflected by the extreme hyperglycaemia and increased plasma sodium. This hyperosmolar state affects consciousness and may cause coma.

General outline for the management of HHS

Wherever possible, the patient with HHS should be managed in a specialist medical unit. It may present as hypovolaemic shock and coma in severe cases.[176] It is important to note that blood glucose meters do not register very high glucose levels, so access to a laboratory is necessary to monitor the correction of hyperglycaemia as well as to monitor sodium and potassium levels. Rapid correction of the hyperosmolar state is dangerous.

In remote rural practice, this may not be possible. In this situation it is advisable to contact the most appropriate diabetes resource person (specialist endocrinologist) for advice while promptly commencing treatment.