

Recognising, managing and preventing hypoglycaemia

Debbie Hicks

Since the discovery of insulin by Banting and Best in 1922, there have been a number of important developments in the treatment of diabetes. However, it is well known that a common side effect of blood-glucose-lowering treatments, such as insulin and sulphonylureas, is hypoglycaemia. Studies investigating the prevalence of hypoglycaemia have provided some alarming results. In particular, the Diabetes Control and Complications Trial (1993) reported a three-fold increase in severe hypoglycaemia and coma in intensively treated people with diabetes versus conventionally treated people. This CPD module discusses the potential causes of hypoglycaemia and circumstances in which hypoglycaemia risk is increased. The article also provides the signs and symptoms, as well as treatment and prevention.

The global burden of diabetes is increasing. According to the latest figures by the International Diabetes Foundation (2012), more than 371 million people have diabetes worldwide and the prevalence of diabetes is increasing in every country. Furthermore, diabetes is predicted to become the seventh leading cause of death in the world by the year 2030 (World Health Organization, 2011) and it is the leading cause of blindness and kidney failure in developed countries. People with diabetes also have a greater risk of developing cardiovascular disease and this is a major cause of death in people with diabetes.

The discovery of insulin by Banting and Best in 1922 was a major breakthrough in the treatment of type 1 diabetes and insulin use means that people with type 1 diabetes are no longer likely to die as a result of diagnosis. Further developments in the treatment of diabetes include the development of oral hypoglycaemic agents in the 1950s, including biguanides and sulphonylureas as treatment for type 2 diabetes. However, it is now widely accepted that hypoglycaemia is a side effect of both insulin

and sulphonylureas rather than diabetes itself. This article is the first of two CPD modules on hypoglycaemia, which will explore many aspects of hypoglycaemia including recognition, treatment and prevention as well as the impact it has on the person with diabetes. The second article, which will be published in early 2014, will focus on the costs and complications of hypoglycaemia.

Background

Hypoglycaemia occurs when a person has a low level of blood glucose, usually <3.5 mmol/L. It can be termed as “mild” if it can be self-treated and “severe” if assistance is required from a third party (Diabetes Control and Complications Trial [DCCT], 1993). Hypoglycaemia is the most common side effect of insulin and sulphonylurea therapy.

People with diabetes tend to under-report hypoglycaemia because they or their carers do not recognise what is happening. They may also be reluctant to talk about hypoglycaemia due to the risk of increased restrictions to their way

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Article points

1. It is well known that blood glucose lowering therapies, such as insulin and sulphonylureas, can cause hypoglycaemia and studies have shown that prevalence of hypoglycaemia is high (Diabetes Control and Complications Trial, 1993).
2. Hypoglycaemia can be caused by: inappropriate insulin or sulphonylurea dosage; missing a meal; alcohol intake; taking part in physical activity without replacing lost glucose and increased sensitivity to insulin through weight loss or improved physical fitness.
3. It is crucial that people with diabetes who take either insulin or sulphonylureas receive the correct education to allow them to recognise and treat a hypoglycaemic episode and more importantly, prevent further hypoglycaemic episodes occurring.

Key words

- Hypoglycaemia
- Insulin
- Prevention
- Sulphonylureas

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1. The Diabetes Control and Complications Trial (DCCT, 1993) reported a three-fold increase in severe hypoglycaemia and coma in intensively treated people with diabetes versus conventionally treated people.
2. In the 2012 National Diabetes Inpatient Audit of 13 409 diabetes inpatients (Health and Social Care Information Centre, 2012), 20.4% had experienced mild hypoglycaemia (blood glucose of 3–4 mmol/L) and 10% had severe hypoglycaemia (blood glucose <3 mmol/L).
3. Hypoglycaemia can be caused by one factor or a combination of factors, such as inappropriate insulin or sulphonylurea dosage; missing a meal; alcohol intake; taking part in physical activity without replacing lost glucose and increased sensitivity to insulin through weight loss or improved physical fitness. Other factors are reduced renal function and lipohypertrophy.

of life, such as loss of their driving licence or job. This under-reporting means that the actual number of people with diabetes who experience hypoglycaemia is unknown (Bailey and Day, 2010).

Prevalence

Studies investigating the prevalence of hypoglycaemia have provided some alarming results. The DCCT (1993) reported a three-fold increase in severe hypoglycaemia and coma in intensively treated people with diabetes versus conventionally treated people. An intensively treated individual with type 1 diabetes can experience up to 10 episodes of symptomatic hypoglycaemia per week and severe temporarily disabling hypoglycaemia at least once a year. An estimated 2–4% of deaths of people with type 1 diabetes have been attributed to hypoglycaemia (DCCT, 1993). Hypoglycaemia is also relatively common in type 2 diabetes, with prevalence rates of 70–80% in clinical trials using insulin to achieve good metabolic control (UK Hypoglycaemia Study, 2007).

The UK Hypoglycaemia Study (2007) found that people with type 1 diabetes had an average of two self-treated episodes of hypoglycaemia per week while for those with type 2 diabetes, 39% on sulphonylureas had at least one episode each week. Furthermore, 51% of those who had been on insulin for less than 2 years had at least one episode each week and 60% of those taking insulin for more than 5 years had at least one episode each week.

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Figure 1 shows that just as many people taking sulphonylureas experienced severe hypoglycaemic episodes as those with type 2 diabetes taking insulin for less than two years (UK Hypoglycaemia Study, 2007). This study also showed that a person with type 2 diabetes who had been taking insulin for more than five years was just as likely to have a severe hypoglycaemic episode as someone with type 1 diabetes who had been on insulin for less than five years.

Causes of hypoglycaemia

Hypoglycaemia may be caused by a single factor or a combination of factors. The following list describes factors that can lead to a hypoglycaemic episode:

- Insulin or sulphonylurea doses are inappropriate, for example, the dose does not match the lifestyle of the individual. If the person with diabetes is active at one part of the day when the insulin or sulphonylurea is peaking, this could precipitate a hypoglycaemic episode.
- It is difficult to ensure the same amount of carbohydrate is taken at each meal every day. However, if the person with diabetes does not eat at a mealtime, either because they are distracted or during times of fasting, such as Ramadan, then the blood glucose levels will begin to fall and precipitate a hypoglycaemic episode.
- When alcohol is drunk in certain quantities the glucose production from the liver is decreased. If insulin or sulphonylureas are taken they will continue to reduce the blood glucose level. Often alcohol is taken in the evening so it is crucial that people are educated to have a bedtime snack when drinking over the advised level of daily alcohol consumption (two units for women and three units for men) to prevent a hypoglycaemic episode occurring during the night.
- When muscle is active it requires glucose for energy. If a person with diabetes is taking insulin or sulphonylureas they need to compensate for the activity by replacing the glucose, otherwise the glucose store will be depleted and hypoglycaemia will occur. Hypoglycaemia can occur during, 1–2 hours after, or up to 17 hours after exercise (Diedrich et al, 2002).
- Sensitivity to insulin is increased following weight loss or improved physical fitness so it may be necessary to decrease the insulin or sulphonylurea dose to prevent hypoglycaemia occurring. It would not be appropriate to increase the glucose intake as this could cause weight gain.
- As the renal function declines, the medication taken to control the blood glucose may need to be decreased to prevent hypoglycaemia. This is due to the delayed clearance of the medication which amplifies the glucose-lowering effect.
- Lipohypertrophy, or fatty lumps at injection

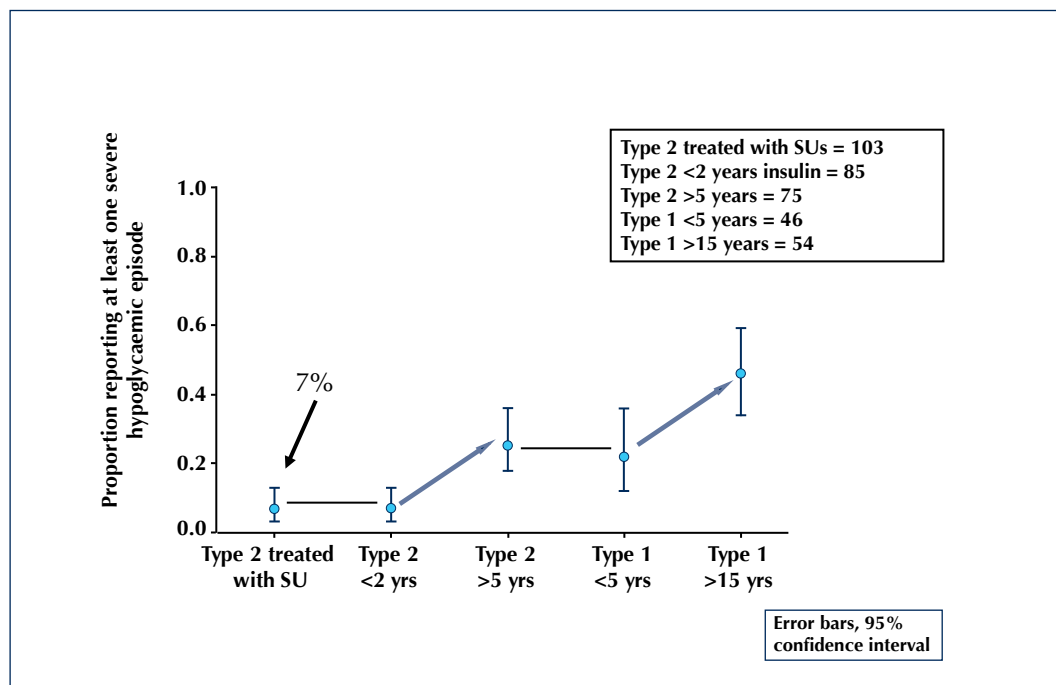


Figure 1. Results of the UK Hypoglycaemia Study (2007) showing occurrence of severe hypoglycaemia (reproduced with permission from Diabetologica).
 SU= sulphonylurea.

sites, caused mainly by poor site rotation and re-use of needles, can precipitate hypoglycaemia as the lipohypertrophic tissue does not allow the normal absorption of the insulin. If the insulin is absorbed too quickly then hypoglycaemia will follow. Hyperglycaemia is also possible if the insulin absorption is delayed (Vardar and Kizilci, 2007).

Factors that increase risk of hypoglycaemia

There are certain factors which may increase the risk of hypoglycaemia:

- If a person with diabetes taking insulin or sulphonylureas has had a severe hypoglycaemic event, there is evidence to suggest that they are at an increased risk of having a further severe event within the next 24 hours (DCCT, 1993).
- There is an increased risk of hypoglycaemia in a person who has had type 1 diabetes for a long time. This may be due to the recognition of the signs and symptoms diminishing over time.
- Longer duration of use of insulin therapy in type 2 diabetes may also contribute to the increased risk of hypoglycaemia; again, this may be due to the recognition of the signs and

symptoms diminishing over time.

- Strict glycaemic control over a period of time, such as during pregnancy, may also increase the incidence of hypoglycaemia as the blood glucose level has to fall much less before it enters into the hypoglycaemia range. The person with diabetes may not sense the small decrease in the blood glucose level and it is not until the blood glucose level drops further that symptoms may be experienced.
- Impaired awareness of hypoglycaemia develops when frequent episodes of hypoglycaemia lead to changes in how the body reacts to low blood glucose levels. The body stops releasing the hormone epinephrine and other stress hormones when blood glucose drops too low. The loss of the body's ability to release stress hormones after repeated episodes of hypoglycaemia is known as hypoglycaemia-associated autonomic failure.
- The risk of severe or fatal hypoglycaemia associated with the use of oral hypoglycaemic agents and insulin increases exponentially with age. Furthermore, older adults with comorbidities, those using multiple medications and those who are frequently hospitalised are at greater risk from hypoglycaemia. As most people

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1. Once plasma glucose concentrations fall below 3.8 mmol/L, a sequence of responses is activated including: the release of neuroendocrine hormones; stimulation of the autonomic nervous system; and production of adrenergic and neuroglycopenic symptoms to protect the brain and limit systematic effects of hypoglycaemia.
2. A person with mild hypoglycaemia can be treated with 15–20 g glucose. If the person does not feel better or if their blood glucose level is still less than 4 mmol/L after 5–10 minutes, treatment should be repeated.
3. In cases of severe hypoglycaemia the person affected will need someone else to treat them (DCCT, 1993), as they may not realise they are having a hypoglycaemic episode or may be unable to treat themselves.

with type 2 diabetes are over 60 years of age, it is important to appreciate the idiosyncratic and age-specific manifestations of hypoglycemic symptoms, for example, confusion, dizziness, weakness, which could be confused with signs of dementia.

- Nocturnal hypoglycaemia is not uncommon but can be missed as the individual is not woken by symptoms of low blood glucose, which can be due to the slow decrease in blood glucose. It is often the spouse or partner that is alerted to the hypoglycaemia due to the person with diabetes being restless or clammy (Allen and Frier, 2003).

Signs and symptoms

The brain depends on a continual supply of glucose and is vulnerable to any glucose deprivation. Unable to synthesise or store this primary source of energy, the brain is one of the first organs affected by lowered blood glucose levels. Once plasma glucose concentrations fall below the physiological range at a glycaemic threshold of <3.8 mmol/L, a sequence of responses is activated: the release of neuroendocrine hormones (also called counterregulatory or anti-insulin hormones); stimulation of the autonomic nervous system; and production of adrenergic and neuroglycopenic symptoms to protect the brain and limit systematic effects of hypoglycaemia. The normal physiological counterregulatory response to hypoglycaemia

consists of suppression of insulin release and secretion of glucagon (Cryer et al, 2003).

As the blood glucose begins to fall below normal levels, the adrenergic symptoms begin to be experienced (see *Box 1*). If treatment is not given, either because the person with diabetes is unaware of the falling blood glucose level or is unable to self-administer, then the symptoms will get worse and include further neuroglycopenic symptoms as the brain struggles to function properly. These symptoms are shown in *Box 1*.

Treatment of hypoglycaemia

In cases of mild hypoglycaemia, 15–20 g of glucose should be given; suitable treatments include:

- 100 mL of Lucozade™.
- 150 mL of non-diet fizzy drink.
- 200 mL of smooth orange juice.
- Five or six dextrose tablets.
- Four large jelly babies.
- Seven large jelly beans.
- Two tubes of glucose gel.

If the person does not feel better or if their blood glucose level is still less than 4 mmol/L after 5–10 minutes, treatment should be repeated. When the person starts to feel better and if they are not due to eat a meal, they should eat some starchy food, such as a sandwich or a banana, and be monitored afterwards.

In cases of severe hypoglycaemia the person affected will need someone else to treat them (DCCT, 1993), as they may not realise they are having a hypoglycaemic episode or may be unable to treat themselves. If the person is conscious and able to swallow safely, they should be given one of the suitable treatments listed above. Treatment should be repeated as required and the person should be accompanied until they have recovered. If the person is unconscious, they should be put in the recovery position (on their side with their head tilted back). Glucose treatment should not be put in their mouth. Glucagon can be injected if there is a trained person present. Otherwise, an ambulance should be called. The publication *Recognition, treatment and prevention of hypoglycaemia in the community* (TREND, 2011) provides a very helpful algorithm outlining the treatment pathway.

Box 1. Signs and symptoms of hypoglycaemia (Henderson et al, 2003).

Adrenergic

- Sweating
- Light-headedness
- Trembling/shaking
- Hunger
- Anxiety
- Palpitations
- Lip tingling
- Irritability
- Pallor

Neuroglycopenic

- Weak legs
- Drowsiness
- Poor concentration
- Blurred vision
- Headache
- Confusion
- Poor coordination
- Slurred speech
- Glazed eyes
- Aggressive behaviour
- Seizures
- Loss of consciousness

The NICE Quality Standards for diabetes in adults (NICE, 2011) recommend that people with diabetes receive an ongoing review of treatment to minimise hypoglycaemia. If they have experienced a hypoglycaemic episode requiring medical attention they should be referred to a specialist diabetes team.

Prevention

It is crucial that people with diabetes who take either insulin or sulphonylureas receive the correct education to allow them to recognise and treat a hypoglycaemic episode and, more importantly, prevent further hypoglycaemic episodes occurring.

Information should be provided to enable the person with diabetes to assess whether there is a potential risk of hypoglycaemia occurring and what steps are needed to prevent this. For example, if a person taking insulin decided they were going to take part in a prolonged period of exercise, such as a round of golf, they should be advised to check their blood glucose level prior to commencing the round but also to consume long-acting carbohydrate, such as a muesli bar, before starting, or extra carbohydrate at the previous meal to prevent the blood glucose level dropping. If the activity involves short bursts of exercise, such as a game of football, then the carbohydrate would need to be much quicker in action, such as glucose tablets or a glucose drink.

It is always advisable to check the blood glucose level after the extra activity and then 2 hours later as hypoglycaemia can often occur long after the activity has finished (Cryer, 2009). It is also important that anyone taking medication that can cause hypoglycaemia should carry an ID card that identifies the type of medication taken.

All healthcare professionals working with people with diabetes should complete the NHS Diabetes (now part of NHS Improving Quality) e-learning module "Safe management of hypoglycaemia". This module can be accessed at <http://bit.ly/Sw9JZN>. Other useful documents for healthcare professionals are *The hospital management of hypoglycaemia in adults with diabetes mellitus* (NHS Diabetes, 2010) and *Recognition, treatment and prevention of hypoglycaemia in the community* (TREND, 2011).

Summary

Hypoglycaemia is the cost associated with strict glycaemic control; it can cause significant morbidity and occasional mortality and can affect every aspect of daily living. Hypoglycaemia should be avoided at all costs in frail, elderly people, those people with established cardiovascular disease and people who are unable to recognise symptoms of hypoglycaemia. Every person with diabetes who takes either sulphonylureas or insulin therapy should be given the appropriate education to recognise, self treat and prevent hypoglycaemia. The second article will address the cost, complications and burden caused by hypoglycaemia. ■

"It is crucial that people with diabetes who take either insulin or sulphonylureas receive the correct education to allow them to recognise and treat a hypoglycaemic episode."

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Online CPD activity

Visit www.diabetesonthenet.com/cpd to record your answers and gain a certificate of participation

Participants should read the preceding article before answering the multiple choice questions below. There is ONE correct answer to each question. After submitting your answers online, you will be immediately notified of your score. A pass mark of 70% is required to obtain a certificate of successful participation; however, it is possible to take the test a maximum of three times. A short explanation of the correct answer is provided. Before accessing your certificate, you will be given the opportunity to evaluate the activity and reflect on the module, stating how you will use what you have learnt in practice. The CPD centre keeps a record of your CPD activities and provides the option to add items to an action plan, which will help you to collate evidence for your annual appraisal.

1. During the Diabetes Control and Complications Trial how many episodes of hypoglycaemia were noted per week in the intensively treated group?
Select ONE option only.

- A. 2
- B. 4
- C. 6
- D. 10

2. What percentage of deaths in people with type 1 diabetes are attributed to hypoglycaemia?
Select ONE option only.

- A. 1–2%
- B. 2–4%
- C. 5–7%
- D. 10%

3. Which of following can be causal factors of hypoglycaemia?
Select ONE option only.

- A. Unplanned physical activity
- B. Excess alcohol
- C. Lipohypertrophy
- D. All of the above

4. Which of the following describes four adrenergic symptoms of hypoglycaemia?
Select ONE option only.

- A. Pallor, palpitations, trembling and hunger
- B. Tingling of lips, confusion, pallor and anxiety

- C. Hunger, slurred speech, blurred vision and palpitations
- D. Sweating, trembling, drowsiness and pallor

5. Which of the following describes four neuroglycopenic symptoms of hypoglycaemia?
Select ONE option only.

- A. Confusion, hunger, slurred speech and drowsiness
- B. Coma, seizures, blurred vision and aggressiveness
- C. Anxiety, lack of concentration, pallor and poor coordination
- D. Drowsiness, confusion, palpitations and weak legs

6. What percentage of inpatients were recorded as having “mild hypoglycaemia” only in the 2012 National Diabetes Inpatient Audit report?
Select ONE option only.

- A. 16%
- B. 18%
- C. 19%
- D. 20%

7. What is the appropriate amount of glucose to be given for a mild hypoglycaemic episode?
Select ONE option only.

- A. 5 g
- B. 10–20 g
- C. 15–20 g
- D. 30 g

8. Which of the following contains the appropriate amount of glucose required to treat a hypoglycaemic episode?
Select ONE option only.

- A. Four jelly beans
- B. One tube of glucose gel
- C. 100 mL of Lucozade™
- D. 200 mL of diet lemonade

9. With regard to severe hypoglycaemia, which of the following statements is FALSE?
Select ONE option only.

- A. A person will always be aware if they are experiencing severe hypoglycaemia
- B. A third party will be needed in order to treat severe hypoglycaemia
- C. If the person is unconscious, they should not be given glucose treatment orally
- D. Glucagon can be injected if there is a trained person present

10. With regard to prevention of hypoglycaemia during physical activity, which of the following is TRUE?
Select ONE option only.

- A. Blood glucose should be checked before, immediately after and 2 hours after exercise
- B. For a prolonged period of physical activity, the person should eat long-acting carbohydrate
- C. For short bursts of activity, the person should consume faster-acting carbohydrates
- D. All of the above