

# Hypoglycaemia

Hypoglycaemia occurs when blood glucose drops below normal levels. Severe hypoglycaemia is defined as an episode in which the mental state of the patient is so disturbed that they are unable to self-treat. For elderly people who live alone this can be very dangerous as they have no one to help recognise the hypoglycaemic symptoms and act accordingly.

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**H**ypoglycaemia in older patients with type-2 diabetes is a substantial problem that impacts on mortality, morbidity and quality of life. Yet there remains a general lack of awareness of hypoglycaemia among diabetic patients, with many unable to identify the symptoms.

A recent online survey of 100 patients with type 2 diabetes found that half of the respondents did not know the correct meaning of hypoglycaemia. In the survey, 10% said they thought hypoglycaemia meant high blood sugar level, 6% that it meant high or low blood sugar level and 6% thought it meant a coma. Indeed, 14% of respondents claimed never to have heard the term hypoglycaemia. Perhaps most worryingly, the survey found that 49% of patients who had suffered hypoglycaemic-like symptoms had not reported them to their GP or practice nurse.<sup>1</sup>

## Scale of the problem

It is difficult to estimate the scale of the problem precisely because so few patients report hypoglycaemia to medical staff. One study found that only 15% of patients who experienced a mild or moderate event reported it to their doctor at their next scheduled visit. And only 2.5% of patients experiencing a severe event reported making an additional visit to their GP.<sup>2</sup> One reason is that patients may not want to admit hypoglycaemic events for fear of being unable to manage their condition.

A thorough review of the current literature on hypoglycaemia in type-2 diabetes was carried out in 2008.<sup>3</sup> It concluded that the primary cause of hypoglycaemia in type-2 diabetes is diabetes

medication; in particular those which raise insulin levels independently of blood glucose, such as sulphonylureas and exogenous insulin.

Patients taking insulin have the highest rates of self-reported severe hypoglycaemia—25% in patients who have been taking insulin for more than five years. Sulphonylureas are associated with lower rates of severe hypoglycaemia but because of the large numbers of patients taking sulphonylureas in the UK it is estimated that over 5,000 patients will experience a severe hypoglycaemic event caused by their sulphonylurea therapy, which needs emergency intervention.<sup>4</sup> A study by the UK Hypoglycaemia Study Group found that severe hypoglycaemic rates were similar in patients taking sulphonylureas to those who were on insulin for less than two years.<sup>4</sup>

## Risk factors

A number of risk factors have been identified that precipitate episodes of severe hypoglycaemia.<sup>3</sup> The risk of hypoglycaemia is increased in older patients, those who have had diabetes for a long time, patients with a lesser insulin reserve and perhaps in the drive for strict glycaemic control. The most common behavioural factor is missed or irregular meals. Other lifestyle factors include alcohol, exercise and incorrect use of glucose-lowering medication. The time of day is also important—just before the evening meal is when plasma glucose levels are at the lowest level and the risk of hypoglycaemia highest.

The UK Prospective Diabetes Study Group found that intensive blood glucose control by either sulphonylureas or insulin substantially decreases the risk of microvascular

complications, but not macrovascular disease. All intensive treatment, whether with sulphonylureas or insulin, led to more hypoglycaemic episodes than with conventional treatment.<sup>5</sup> The study found that 86% of intensively treated and 73% of conventionally treated patients had at least one severe hypoglycaemia episode over 10 years.

The current NICE guidance aims for strict glycaemic control with challenging HbA1c targets of <6.5%.<sup>6</sup> However, the guidelines do state that patients should be encouraged to set their own target and one higher than 6.5 may be appropriate if side effects from hypoglycaemic episodes impair the patient's quality of life.

### Elderly are more vulnerable

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Severe hypoglycaemia can have serious consequences, particularly in the elderly. In a prospective study of people over 80 years with well controlled type-2 diabetes, a quarter of hospital admissions associated with diabetes were due to severe hypoglycaemia.<sup>7</sup> In cases of severe hypoglycaemia induced by sulphonylurea monotherapy, the overall mortality rate has been estimated at approximately 9%.<sup>8</sup>

Severe hypoglycaemia is defined as an episode in which the mental state of the patient is so disturbed that they are unable to self-treat. For elderly people who live alone this can be very dangerous as they have no one to help recognise the hypoglycaemic symptoms and act accordingly.

A Canadian study found that type-2 patients are more anxious after a severe hypoglycaemic episode than type 1 patients.<sup>2</sup> The study of 202 type 1 and 133 insulin treated type-2 diabetic patients found that following a mild or moderate hypoglycaemic episode 38% of type-1 diabetes patients reported an increased fear of future hypoglycaemia compared to 30% of type-2 patients. But after a severe hypoglycaemic episode 84% of type-2 reported greater fear of future hypoglycaemia compared to 63% of type-1 diabetes patients.

Another study shows that older men are prone to more severe cognitive impairment during hypoglycaemia than younger men and are less likely to experience prior warning symptoms if blood glucose falls. The authors conclude that this effect of normal ageing may contribute to the risk of severe hypoglycaemia in older diabetic patients treated with sulphonylureas and insulin.<sup>9</sup>

### Cost implications

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Type-2 diabetes is a major health problem in England and the cost to the NHS is estimated to be in excess of £1.3 billion. The number of people diagnosed with type-2 diabetes has been increasing rapidly in recent years and it is estimated that by 2025 over 4 million people will be diagnosed with diabetes.<sup>3</sup> As well as the impact on the patient, hypoglycaemia has considerable cost implications—each hospital admission for severe hypoglycaemia costs around £1000.<sup>10</sup>

### Treatment options

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Diabetes is a progressive disease with a gradual decline in insulin secretion over time. Diet and exercise are the first choice of treatment but most patients will require oral glucose lowering drugs and ultimately insulin. NICE recommends metformin as first line treatment with sulphonylurea usually added second line if blood glucose levels remain poor or deteriorate (HbA1c >6.5%).

However, the most recent guidance from NICE<sup>11</sup> covering the newer drugs emphasise that patients should be treated according to their individual profile and needs. It states that where patients are at significant risk of hypoglycaemia or its consequences, such as older people, people in certain jobs for example those working with heavy machinery, or people living alone, then glitazones (thiazolidinediones) or gliptins (DPP-4 inhibitors) should be used in preference to sulphonylureas.

The guidelines also state that patients should be switched from human NPH insulin to a once daily long acting insulin analogue (insulin detemir, insulin glargine) if the patient's lifestyle is restricted by recurrent symptomatic hypoglycaemia episodes.

### Concordance with treatment

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Mild symptomatic hypoglycaemia is not thought to have any serious clinical effects. Nevertheless, people with diabetes are frightened of hypoglycaemia and even mild episodes may be enough to inhibit concordance with therapy. The evidence suggests that adherence to treatment in general is a bigger problem in the elderly. One study concluded that age is a major factor affecting adherence to medication for hypertension in a general practice population.<sup>12</sup>

A large retrospective cohort study found that in the community only one in three patients with type-2 diabetes had adequate adherence to oral hypoglycaemic drugs.<sup>13</sup> The study included 2,920 patients who had been prescribed oral hypoglycaemic drugs for at least 12 months. Of these adequate adherence, defined as over 90%, was found in 31% of those prescribed sulphonylureas alone and in 34% of those prescribed metformin alone.

The study found a significant linear trend between poorer adherence and the greater the number of daily tablets taken. The authors concluded: "One tablet per day administration was associated with greater adherence than multiple tablets. Poor adherence is a major obstacle to the benefit of complex drug regimens in the treatment of type 2 diabetes."

## Conclusion

Because type-2 diabetes is a progressive disease the number of tablets taken tends to increase with age. In the online survey nearly 40% of patients took between four and nine tablets per day. The survey also found that 84% of respondents would consider a medication switch if they could reduce the number of tablets taken. Some 43% had never had their medication changed, even though 35% had been diagnosed with type-2 diabetes for between five and 10 years and 13% of more than 10 years.

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