

# HYPOGLYCAEMIA IN THE ELDERLY PATIENT

The older patient with diabetes is more prone to having hypoglycaemia, especially when glucose lowering drugs are used. Yet the International Diabetes Federation estimates that over half the population of people with diabetes do not know that they have it.

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The most recent prevalence of diabetes has been estimated at 8.3% around the world,<sup>1</sup> although prevalence in patients over the age of 65 years is likely to be significantly higher, ranging from 15% to over 20%.<sup>2,3</sup> It has been further estimated that in the care home population the prevalence of diabetes is over 25%.<sup>2</sup>

The International Diabetes Federation estimates that over half the population of people with diabetes do not know that they have it.<sup>1</sup> The World Health Organization criteria for diagnosing type 2 diabetes includes a fasting blood glucose of above 7mmol/L on one occasion if the patient has symptoms or two occasions if the patient is asymptomatic. In addition, in those with a post prandial or random blood glucose of greater than 11.1mmol/L or an HbA1c of greater than 48mmol/mol.

As someone ages, post prandial hyperglycaemia becomes a more prominent characteristic in people with type 2 diabetes. Thus, if a fasting blood glucose is used as the diagnostic criteria then diabetes may be missed. As the prevalence of diabetes increases the older figure of 90% of cases being type 2 diabetes is likely to be an underestimate. Having said this, there is now data to show that patients with type 1 diabetes are living longer.<sup>4</sup>

Over the past few years, a large number of new classes of agent have been launched to treat type 2 diabetes. They can be divided broadly into those medications that lower blood glucose, in particular insulin secretagogues, such as sulphonylureas, meglitinides and insulin or those drugs that prevent blood glucose from rising, such as metformin, acarbose, thiazolidinediones, DPP-4 inhibitors, GLP-1 analogues and SGLT-2 inhibitors.

The pharmacology of these drugs is quite important because drugs that stop blood glucose levels from rising are much less likely to be associated with hypoglycaemia than those drugs that lower blood glucose. Hypoglycaemia is defined as a lower than normal blood glucose level. Usually this is defined as less than 4mmol/L and in the UK

is either classified as either mild (if a patient is able to self-treat the episode or severe (if they require third party assistance).

The American Diabetes Association definition of hypoglycaemia is different, and they classify hypoglycaemia into five categories, as shown in Table 1.<sup>5</sup> Dearie et al have produced an excellent table of the symptoms that patients may experience, depending on how low their blood glucose levels drop. Initially, autonomic symptoms predominate, such as sweating, shaking, palpitations and hunger. Eventually neuroglycopenic symptoms begin to appear as cerebral glucose levels drop. These include drowsiness, confusion, speech disturbance and eventually coma, fits and death.<sup>6</sup>

## Hypoglycaemia is a cardiovascular risk

Acute hypoglycaemia is associated with a marked sympathetic response. This leads to a surge of counterregulatory hormones, in particular glucagon and adrenalin and to a lesser extent, growth hormone, vasopressin, noradrenalin and cortisol. This catecholamine release can cause hypokalaemia, which leads to an acute change in the QTc. This effect is augmented in patients with pre-existing abnormalities of the QT segment, such as those who have autonomic neuropathy or who are taking drugs that are known to affect QT interval. There are also a proportion of people who have a genetic predisposition to prolonged QT intervals.<sup>7</sup>

A recent study looking at ECG changes during hypoglycaemia in patients with type 2 diabetes showed an increase in incidence of arrhythmias, bradycardia, atrial and ventricular ectopics, especially during nocturnal hypoglycaemia.<sup>8</sup>

The haemodynamic changes following a hypoglycaemic episode are compensatory mechanisms to maintain cerebral perfusion and splanchnic perfusion to maintain gluconeogenesis. These haemodynamic changes lead to an increase in cardiac stress, in particular an increase in heart

**TABLE 1. AMERICAN DIABETES ASSOCIATION CLASSIFICATION OF HYPOGLYCAEMIA<sup>2</sup>**

<b>1. Severe hypoglycaemia</b>
An event requiring third party assistance to actively administer carbohydrate, glucagon or other corrective action
<b>2. Documented symptomatic hypoglycaemia</b>
A blood glucose recorded as $\leq 3.9$ mmol/L with accompanying symptoms typical of hypoglycaemia
<b>3. Asymptomatic hypoglycaemia</b>
A blood glucose recorded as $\leq 3.9$ mmol/L without accompanying symptoms of hypoglycaemia
<b>4. Probable symptomatic hypoglycaemia</b>
A situation where an individual experiences or displays symptoms of hypoglycaemia but where a blood glucose value is not determined
<b>5. Pseudo-hypoglycaemia</b>
A situation where an individual experiences or displays symptoms of hypoglycaemia but where a blood glucose value is $\geq 4.0$ mmol/L

rate and systolic blood pressure, a decrease in peripheral arterial resistance and a widening pulse pressure. Hypoglycaemia also leads to an increase in myocardial contractility and stroke volumes. In patients who have pre-existing ischaemic heart disease this increase in cardiac stress may have a significant impact, increasing the likelihood of myocardial damage. Furthermore hypoglycaemia has been shown to stimulate and increase levels of inflammatory cytokines, such as C-reactive protein, interleukin-1 and interleukin-6, tumour necrosis factor alpha and endothelin-1.<sup>9</sup> Together these result in endothelial injury and changes in the coagulation cascade, which increases the risk of subsequent cardiovascular events.

Hypoglycaemia also stimulates platelet aggregation and platelet activation.<sup>9,10</sup> Previous work looking at the effects of ageing on hormonal responses has shown that in healthy elderly men symptoms of hypoglycaemia start at lower blood glucose levels compared to men who are younger.

The elderly group were also prone to develop severe cognitive impairment during their hypoglycaemia than the younger age group and less likely to experience warning signs as blood glucose levels drop.<sup>11</sup> This is likely to be responsible for the risk of severe hypoglycaemia in older patients with diabetes treated with sulphonylureas and insulin.

In the ageing population it has been suggested that almost half of patients who have diabetes have several other long-term conditions at the

same time.<sup>12</sup> Not all of these comorbidities have the same effect on the patients as their diabetes but they can affect the ability of individuals to self-manage their own diabetes.<sup>13</sup>

Thus, in the ageing population one is less inclined to aggressively treat diabetes to prevent long-term complications, but rather to prevent the immediate harm that may be associated with either severe hypoglycaemia or hyperglycaemia.

Previous work suggests that cognitive dysfunction due to either Alzheimer's dementia or multi-infarct dementia is twice as likely to occur in people with diabetes.<sup>14</sup> Clearly, the inability to remember events makes tasks such as glucose monitoring, medication dose adjustment or even regular meals difficult to follow and hypoglycaemia is far more frequent in patients who have cognitive impairment.<sup>15</sup> In addition, as patients age they are less likely to become physically active.<sup>15</sup> The cause of this functional impairment is multi-factorial and includes interactions between co-existing medical conditions, peripheral neuropathy, visual and hearing difficulties and gait and balance problems. This leads to an increased risk of falls and fractures as well as mental health difficulties, all of which have negative consequences to self-care.<sup>16</sup>

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### Treatment goals in the elderly

A recent publication from North America classified patients into three health status categories, which were designed to consider glycaemic goals. The three categories were: those who were relatively healthy, those who had complex medical histories for who self care may be difficult, and those with a very significant comorbid illness and functional impairment, many of whom may have had limited life expectancy.

It was felt that glycaemic control was categorised, based on their HbA1c level, as tight (less than 53mmol/mol), moderate (53-74mmol/mol) and poor (greater than 75mmol/mol). These authors found that nearly two thirds of older adults with diabetes who had complex or intermediate health status were trying to attain tight glycaemic control; this is clearly potentially associated with harm from hypoglycaemia with no benefit in terms of prevention of long term micro and macrovascular disease in an elderly group.<sup>7</sup>



In addition, NICE guidelines suggest that the clinical team involve the individual with diabetes about individualising their HbA1c target. This could be less than 48mmol/mol in people who are otherwise very well, fit and active and who are able to recognise and treat their own hypoglycaemia. However, for many people this target would be unacceptably tough and indeed targets of 59 to 69mmol/mol may be more appropriate, depending on the cognitive and physical abilities of the patient. This is the range recommended by the European Diabetes Working Party for Older People.<sup>17</sup>

It would also be prudent to consider changing medication to ensure high risk individuals are not on glucose lowering medication but rather on medication that prevents blood glucose levels from rising.<sup>18</sup>

## Conclusion

In summary, the older patient with diabetes is more prone to having hypoglycaemia, especially when glucose lowering drugs are used. They may be less aware of symptoms of hypoglycaemia and have a higher number of co-existing comorbidities, which make management of hypoglycaemia more difficult. Hypoglycaemia itself is associated with higher morbidity, including cardiovascular risk, injury and hospital admission. It is therefore important to individualise glycaemic targets and educate patients regarding the common precipitants of hypoglycaemia and its appropriate management.

Conflict of interest: none declared

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## KEY POINTS

- The older patient with diabetes is more prone to having hypoglycaemia, especially when glucose lowering drugs are used
- Over the past few years a large number of new classes of agent have been launched to treat type 2 diabetes
- The elderly group were also prone to develop severe cognitive impairment during their hypoglycaemia than the younger age group and less likely to experience warning signs as blood glucose levels drop
- Previous work suggests that cognitive dysfunction due to either Alzheimer's dementia or multi-infarct dementia are twice as likely to occur in people with diabetes