The Challenges and Opportunities of Managing Diabetes in Long-Term Care

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The Challenges and Opportunities of Managing Diabetes in Long-Term Care

DIABETES AND PRE-DIABETES

Type 2 diabetes is a chronic metabolic disease that chiefly manifests as hyperglycemia that is the result of both insulin resistance and deficient insulin secretion.1 Hyperglycemia that does not qualify as diabetes is referred to as pre-diabetes and increases an individual's risk of developing type 2 diabetes; both diabetes and pre-diabetes increase the risk of heart disease and stroke.1 Diabetes has several potentially serious complications,2 and managing the disease and its complications requires constant vigilance on the part of patients and caregivers. Such vigilance is especially important when caring for elderly patients—especially those residing in long-term care (LTC) facilities—who may have multiple comorbidities along with functional and cognitive impairment. The care of these individuals necessitates a different approach to disease management than is appropriate for the general population.

This supplement will briefly discuss the prevalence and costs of diabetes and pre-diabetes before providing an overview of the epidemiology, pathophysiology, and complications of diabetes in the elderly population and focusing on the relationship between diabetes and cardiovascular disease (CVD). The body of this supplement will deal with the management and treatment of diabetes in the elderly LTC population, including the most recent guidelines established by the American Geriatric Society, the American Diabetes Association (ADA), and the American Medical Directors Association (AMDA). Finally, both established and newer pharmacotherapeutic options for the treatment of diabetes will be discussed.

Before examining the prevalence and cost of diabetes and pre-diabetes, it is important for healthcare practitioners to be familiar with the diagnostic criteria for them. The ADA has established criteria for determining whether a patient has diabetes or pre-diabetes; the criteria for a diagnosis of diabetes are listed in Table 1.1-4 The criteria set forth by the World Health Organization (WHO), although similar to the ADA's with regard to fasting glucose and oral glucose tolerance, differ with regard to intermediate hyperglycemia.4 According to the ADA, the criteria for pre-diabetes are impaired fasting glucose (IFG), which is a fasting plasma glucose (FPG) of 100 mg/dL to 125 mg/dL, and/or impaired glucose tolerance (IGT), which is a 2-hour plasma glucose [e, the result of an oral glucose tolerance test (OGTT)] of 140 mg/dL to 199 mg/dL.1 In contrast, the WHO criteria for IFG remain a fasting plasma glucose of 110 mg/dL to 125 mg/dL. The decision to retain these criteria was based on the concern that lowering them to include those with a reading between 100 and 109 mg/dL would increase the prevalence of IFG and significantly impact both individuals and healthcare systems.1

Prevalence

The Centers for Disease Control and Prevention (CDC) projected that, in the United States in 2005, 20.8 million people—roughly 7% of the US population—had diabetes. (The CDC estimated that there were 14.6 million diagnosed and 6.2 million undiagnosed cases.)1 In 2005, 20.9% of the total population of adults aged 60 years or older had diabetes, compared to only 9.6% of those aged 20 years or older (Figure 1).1 In 2005, the ADA estimated that the number of diagnosed cases of diabetes would not reach 14.5 million until 2010.1 This number has already been exceeded, and it is clear that the prevalence of diabetes is increasing from year to year at a rate much faster than anticipated. The global diabetic population is expected to reach 366 million people by 2030, more than doubling the current worldwide prevalence.1

The incidence of pre-diabetes is also high. According to the Third National Health and Nutrition Examination Survey from 1988–1994 (NHANES III), 15.6% of Americans aged 40 to 74 years had IGT and 9.7% had IFG.6 The CDC states that from 1999 to 2002, 26% of Americans aged 20 years or older had IFG and, although IGT was not measured for this study, 54 million Americans had pre-diabetes in 2002.1 It should be noted that the prevalence of diabetes and pre-diabetes increases with age.2 The elderly have an increased risk of several chronic diseases, including diabetes and CVD.1,3-4 As such, diabetes in the elderly requires constant vigilance on the part of patients and caregivers. Such vigilance is especially important when caring for elderly patients—especially those residing in long-term care (LTC) facilities—who may have multiple comorbidities along with functional and cognitive impairment. The care of these individuals necessitates a different approach to disease management than is appropriate for the general population.

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The Challenges and Opportunities of Increasing Incidence of Diabetes

Increasing incidence of diabetes is linked, at least statistically, to the increasing prevalence of obesity. According to the National Center for Health Statistics, more than 60 million Americans aged 20 years and older are obese, and the percentage of obese children, adolescents, and young adults (i.e., those aged 19 years or younger) has tripled since 1980. Among Americans, the prevalence of diabetes varies by race. Using several sources, the CDC compiled statistics on the prevalence of diabetes among various races in 2005 (see Figure 2). In a study by the Agency for Healthcare Research and Quality, it was found that the highest prevalence and incidence of diabetes were seen among minorities, and the prevalence of diabetes was found to be increasing most rapidly among Hispanics and Asians. Also, the elderly of several racial groups (e.g., Native Americans, Hispanics, blacks, and Micronesians) are disproportionately affected by diabetes. From 1980 through 2004, the age-adjusted prevalence of diabetes was found to be higher among black individuals than among non-Hispanic white individuals, and highest among black women.

Diabetes in the Elderly

The elderly population of the United States—those aged 65 years and older—is expected to account for almost 20% of the US population by 2020. Of the 15.6 million residents of LTC facilities in 1996, 91% were age 65 or older. A 1987 survey by the Agency for Health Care Policy and Research found that, in the United States, those over age 55 with diabetes were twice as likely as nondiabetic persons to reside in nursing care facilities. Diabetes is common in LTC facilities; according to a 2002 study, about 26% of nursing facility residents had diabetes at admission. On average, these residents were younger at admission than residents without diabetes; moreover, 69% also have hypertension and 30% experience depression. Elderly diabetic residents of LTC facilities are more likely to be treated with diet, are less obese, are less likely to be treated with insulin, and have a higher incidence of macrovascular and microvascular complications and skin infections than their community-dwelling peers. Also, compared to nursing facility residents without diabetes, those with diabetes have a greater incidence of comorbidities, need more assistance with activities of daily living, and take more medications as part of their healthcare regimen.

Epidemiology

According to Selvin and colleagues, NHANES 1999–2002 found that 15.3% of the elderly population—approximately 7.8 million people—had diagnosed diabetes and 6.9% had undiagnosed diabetes. About 66.6% of those individuals with diagnosed diabetes were diagnosed when they were aged 40 to 64. Individuals diagnosed during middle age were found to have statistically significantly higher levels of HbA1c than those diagnosed after age 64 (FPG of 172.4 mg/dL vs. 152.2 mg/dL, P=0.001).

Managing Diabetes in Long-Term Care

Elderly diabetes patients exhibit postprandial hyperglycemia more often than the rest of the diabetic population; for example, a 2001 study showed that among the elderly there is an increased frequency of an FPG ≥125 mg/dL concurrent with an OGTT of ≥200 mg/dL, which indicates the need for especially careful screening of these patients. Moreover, CVD is more than twice as common in these individuals, and they may be at greater risk of treatment-related complications.

Pathophysiology

Several factors contribute to the prevalence of diabetes in the elderly. A family history of diabetes influences the chance of developing the disease, as does the individual’s race. Certain lifestyle factors also contribute to the development of diabetes: weight, especially with centrally distributed body fat; diet, especially the consumption of high amounts of saturated fat and low amounts of complex carbohydrates; and lack of physical activity. In general, it is possible to attribute glucose intolerance to several other factors, including decreased lean body mass, increased visceral adiposity, decreased relative insulin secretion, and peripheral insulin resistance.

Other hormones have a role in regulating glucose levels. Although there are some exceptions, in general, total testosterone levels decline in adults with each year of age. Testosterone levels, specifically lower levels in older men and higher levels in women, may be risk factors for the development of diabetes. A study of Japanese patients with type 2 diabetes showed a significantly lower level of free testosterone compared to healthy men in each decade of life between 40 and 60 years old. However, advanced age may not entirely explain the lower testosterone levels in older men with type 2 diabetes. Studies in lab animals have shown that diabetes has a negative effect on testicular function, reducing testosterone secretion.

Androgen ablation therapy has also been associated with an increased incidence of diabetes and CVD, while administration of exogenous testosterone has been shown to improve insulin sensitivity and glucose homeostasis. Amylin and the incretin hormones also influence glucose homeostasis; this influence will be described in greater detail in other sections of this supplement.

Aging is also a factor in the development of diabetes. Aging is associated with a deterioration in the ability of the beta cells to secrete insulin, leading to great fluctuations in both rapid (13 minutes) and ultradian (120 minutes) oscillations of insulin secretion, which may ultimately be responsible for decreased glucose tolerance in the elderly.

The Complications of Diabetes in Elderly Patients

Elderly individuals with diabetes use almost twice as many healthcare resources as those without diabetes. They experience a higher frequency of chronic disease and have a poorer quality of life than their nondiabetic peers. Aging is associated with morbidity and, in elderly diabetics, complications of diabetes add to this morbidity. As the duration of an individual’s diabetes increases, so does the frequency of both microvascular and macrovascular complications. Elevated A1C levels and risk factors, such as smoking, high cholesterol, and hypertension, also increase the frequency of such complications. Moreover, there is an increased incidence of depression and impaired cognitive function among elderly diabetics, who are also at risk for vascular dementia and possibly Alzheimer’s disease.

The risk of macrovascular complications is anywhere from 2 to 5 times greater in elderly diabetic patients than in patients with normal glucose tolerance. Macrovascular complications (i.e., CVD, cerebrovascular disease, and peripheral vascular disease) are associated with 50–70% of the deaths from diabetes. The principal cause of death in elderly diabetics is CVD and, in fact, the mortality of diabetes itself may be underestimated, because cardiovascular causes, rather than diabetes, are often listed on death certificates.

Elderly patients with diabetes are also at an increased risk of microvascular complications. In about one-third of elderly persons with type 2 diabetes, diabetic retinopathy is the sole or major cause of blindness. These patients may also have an increased frequency of other ocular diseases, including senile cataract, senile macular degeneration, and open-angle glaucoma. The prevention of these complications requires optimal blood glucose control. It should be noted that, in the United Kingdom Prospective Diabetes Study (UKPDS), it was found that individuals who received intensive therapy to control their blood glucose levels experienced statistically significantly less deterioration in retinopathy after 6 years. The elderly also have an increased risk of diabetic nephropathy, which is compounded by arteriosclerosis, hypertension, congestive heart failure, and drug-induced renal problems.

Aging exponentially increases the risk of severe or fatal hypoglycemia associated with the use of oral agents or insulin, due to a reduced glucagon response that leaves the elderly patient dependent on epinephrine. Hyperosmolar coma is also particularly common in patients with diabetes who are elderly, residing in LTC, and mentally impaired or otherwise unable to express thirst or access fluids. There is a 50% mortality rate from hyperosmolar coma in those aged 50 years and older, compared to just 5% in those younger than age 50.
The Challenges and Opportunities of Diabetes

Diabetes can also affect various aspects of physical and mental functioning. In a study of older African Americans, patients with diabetes reported worse general health (P<0.001) and poorer performance on instrumental activities of daily living (P=0.017) than patients without diabetes.29 Hyperglycemia has been demonstrated to decrease cognitive function, and diabetes mellitus is associated with an increased incidence of dementia.28 Also, elderly patients with diabetes have a higher incidence of depression and impaired cognitive function than those without diabetes.28 Depression, in turn, is associated with an increased level of functional impairment and increased mortality, as shown in a study examining older Mexican American diabetic patients.30,31

From 1991 to 2004, Bethel and colleagues performed a longitudinal analysis comparing Medicare beneficiaries who were newly diagnosed with diabetes (n = 35,772) to a control group of those without diabetes (n = 25,563) with respect to complications of the disease. The findings from this study are summarized in Table 2.24 According to the study, seven out of 10 Medicare beneficiaries experienced a complication of diabetes, compared to four out of 10 in the control group (P<0.0001). Of particular note is the fact that congestive heart failure (CHF) is second only to the sum of all lower extremity complications (LECs).22

However, LECs are prevalent in elderly diabetic patients. Peripheral and autonomic neuropathy, when combined with problems such as arthritis, peripheral arterial disease, and decreased vision, places the elderly at greater risk of foot ulcers, infections, and amputation. In fact, two-thirds of all amputations among those with diabetes occur in older diabetic patients.22 Bethel and colleagues found that LECs were the most common complications in both the diabetes and control groups.22

Table 2. Prevalence of Complications, 1994–2004†‡

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Any adverse outcome‡</td>
<td>535</td>
<td>544</td>
<td>605</td>
<td>642</td>
<td>685</td>
<td>706</td>
<td>918</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>296</td>
<td>423</td>
<td>516</td>
<td>575</td>
<td>617</td>
<td>655</td>
<td>679</td>
</tr>
<tr>
<td>Muscular ischemia</td>
<td>75</td>
<td>127</td>
<td>171</td>
<td>212</td>
<td>241</td>
<td>286</td>
<td>296</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>216</td>
<td>306</td>
<td>385</td>
<td>435</td>
<td>472</td>
<td>511</td>
<td>576</td>
</tr>
<tr>
<td>Cerebrovascular</td>
<td>131</td>
<td>232</td>
<td>312</td>
<td>378</td>
<td>437</td>
<td>488</td>
<td>463</td>
</tr>
<tr>
<td>Stroke</td>
<td>88</td>
<td>143</td>
<td>191</td>
<td>226</td>
<td>251</td>
<td>279</td>
<td>313</td>
</tr>
<tr>
<td>Diabetic nephropathy</td>
<td>51</td>
<td>92</td>
<td>145</td>
<td>196</td>
<td>250</td>
<td>511</td>
<td>304</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>41</td>
<td>60</td>
<td>88</td>
<td>119</td>
<td>160</td>
<td>201</td>
<td>212</td>
</tr>
<tr>
<td>ESRD</td>
<td>16</td>
<td>26</td>
<td>42</td>
<td>51</td>
<td>48</td>
<td>46</td>
<td>50</td>
</tr>
<tr>
<td>Diabetic retinopathy</td>
<td>47</td>
<td>107</td>
<td>163</td>
<td>214</td>
<td>261</td>
<td>312</td>
<td>220</td>
</tr>
<tr>
<td>Low vision or blindness</td>
<td>0</td>
<td>22</td>
<td>33</td>
<td>43</td>
<td>52</td>
<td>64</td>
<td>53</td>
</tr>
<tr>
<td>LECs</td>
<td>266</td>
<td>472</td>
<td>612</td>
<td>710</td>
<td>778</td>
<td>835</td>
<td>728</td>
</tr>
<tr>
<td>Sample, No.</td>
<td>35,772</td>
<td>27,543</td>
<td>22,338</td>
<td>18,604</td>
<td>16,085</td>
<td>13,303</td>
<td>33,772</td>
</tr>
</tbody>
</table>

Diabetes and Cardiovascular Disease

As previously noted, the forms of CVD are among the most dire and prevalent complications of diabetes. Elderly patients with diabetes have a 2 to 2.5 times higher risk of mortality from CVD than their peers.25 According to the CDC, heart disease and stroke cause about 65% of the deaths in people with diabetes; the death rate from heart disease and the risk of stroke in these individuals are 2 to 4 times higher than they are in those without diabetes.2 Thus, CVD is the leading cause of death among adults with diabetes.34

Furthermore, in a study comparing patients with diabetes to an age- and sex-matched control group of patients without diabetes, CHF was found to be from 2 to 8 times more prevalent among those with diabetes.3 The American Heart Association (AHA) has stated that “diabetes mellitus deserves to be designated a major risk factor for CVD” due to the large body of data that show this connection and has committed itself to emphasizing diabetes in its scientific and educational programming.36

IFG has been identified as a predictor of mortality from ischemic heart disease. It has been shown that insulin resistance, coagulation abnormalities, obesity, physical inactivity, heredity, and advancing age are all factors that lead to the development of both coronary disease and diabetes. The metabolic syndrome comprises several of these factors.37

As far back as 1974, the Framingham study demonstrated that the incidence of heart failure in those with diabetes was anywhere from 2 to 5 times greater than it was in those without diabetes. Several studies have since identified diabetes as a major factor in the risk of developing heart failure. Almost 50% of people with diabetic heart failure also have diabetes.38 As diastolic dysfunction develops, several morphologic changes occur in the hearts of those with diabetes, including myocyte hypertrophy, increased matrix collagen, interstitial fibrosis, and intramyocardial microangiopathy. The altered myocardial glucose and fatty acid metabolism of patients with diabetes are the probable causes of these changes. The advanced glycation end-products—result of the chronic hyperglycemic effect on proteins—decrease the compliance of the blood vessels and myocardium, which leads to contractile dysfunction.34

According to the AHA, patients with diabetes and ischemic heart disease can have enhanced myocardial dysfunction, leading to accelerated heart failure (ie, diabetic cardiomyopathy). There are numerous underlying factors to this severe coronary atherosclerosis, prolonged hypertension, chronic hyperglycemia, microvascular disease, glycosylation of myocardial proteins, and autonomic neuropathy.36 As previously mentioned, the components of the metabolic syndrome predispose patients to both CVD and diabetes. One of those components—insulin resistance—has the following significant risk factors:

- **Atherosclerogenic dyslipidemia.** Sometimes referred to as diabetic dyslipidemia, this condition is characterized by elevated very-low-density lipoproteins (VLDLs), small LDL particles, and low-high-density lipoprotein (HDL) cholesterol. This lipid triad can promote atherosclerosis, independent of elevated LDL cholesterol. Patients with atherogenic dyslipidemia can also have an elevated serum total apolipoprotein B.36

- **Hypertension.** An established risk factor for CVD, hypertension also increases the risk of stroke and diabetic nephropathy.36

- **Prothrombotic state.** Due to alterations in their coagulation mechanisms (eg, increased fibrinogen levels, increased plasminogen activator inhibitor-1, and various platelet abnormalities), patients with diabetes are prone to arterial thrombosis.36

Healthcare costs for individuals with both diabetes and CVD can be high. In a study of over 32,000 patients enrolled in an HMO for 12 months, divided evenly between diabetes and nondiabetics, it was found that patients with both CVD and diabetes incurred medical costs of over $10,000/year, on average. Those without either disease incurred medical costs of only $2,562/year, and those with one—but not both—of the diseases incurred medical costs of $4,402 to $6,396/year (Figure 3).39 When considering costs, it must be remembered that acute myocardial infarction and CHF are 2.78 and 2.71 times more likely, respectively, in those with diabetes. Inpatient costs, such as those from heart attacks and heart failure, represent about 51% of medical care costs for those with both CVD and diabetes, compared to 31% of medical care costs for those without CVD.39

Managing Diabetes in Long-Term Care

<table>
<thead>
<tr>
<th>Disease</th>
<th>Costs incurred by those with diabetes (US $)</th>
<th>Costs incurred by those without diabetes (US $)</th>
<th>Cost of diabetes as % of total medical costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Diabetes</td>
<td>2562</td>
<td>6400</td>
<td>31.8%</td>
</tr>
<tr>
<td>CVD</td>
<td>82,563</td>
<td>40,315</td>
<td>50.9%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>23,740</td>
<td>12,050</td>
<td>51.0%</td>
</tr>
</tbody>
</table>


dm, type 2 diabetes mellitus; ESRD, end-stage renal disease; LEC, lower extremity complication.

*p*values for complications with prevalence rates less than 10 per 1,000 persons in 2004 are not listed.

*All complications and complications with prevalence rates less than 10 per 1,000 persons in 2004 are not listed.*
THE MANAGEMENT OF TYPE 2 DIABETES IN LONG-TERM CARE FACILITIES

The goal of diabetes management in any population is control of hyperglycemia—in other words, the lowering of blood glucose to a desired target—and the management of associated complications. Achieving glycemic levels that are as close to the nondiabetic range as possible has been shown to reduce substantially the risk of the diabetes-related complications discussed earlier.44 Managing diabetes among residents of LTC facilities, however, requires special considerations, because these individuals are uniquely prone to certain problems that complicate treatment decisions (eg, dementia, depression, frailty, multiple coexisting medical conditions, undernutrition, increased risk of hyperglycemia, and adverse drug reactions).45 Diabetes cannot be managed in isolation; CVD, including hypertension and dyslipidemia, as well as functional status, individual preferences, comorbidities, and overall prognosis must all be considered.46

The ADA has developed specific recommendations for the management of diabetes, and the ADA has refined those guidelines for the management and treatment of diabetes in LTC facility residents. These recommendations are presented in the following sections.

Recognition and Screening

The management of diabetes begins with the screening of all patients at risk for the disease. In LTC facilities, some residents may already have a confirmed diagnosis and treatment regimen, while others may develop diabetes during their stay at the facility. The ADA stresses the importance of screening for diabetes or pre-diabetes in asymptomatic individuals.47 Residents should receive a physical examination whenever there is a suspicion of diabetes, including when they are admitted, when a visit by a medical practitioner is required, and when significant changes in health status occur.42 Residents with FPG or other risk factors should receive annual tests of fasting blood glucose.41

Table 3. Possible Symptoms, Signs, and Consequences of Hypoglycemia and Hyperglycemia in the Frail Elderly44

<table>
<thead>
<tr>
<th>Hypoglycemia</th>
<th>Hyperglycemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confusion or disorientation</td>
<td>Blurred vision</td>
</tr>
<tr>
<td>Poor concentration and coordination</td>
<td>Weight loss</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>Dehydration</td>
</tr>
<tr>
<td>Generalized weakness</td>
<td>Confusion, worsening dementia</td>
</tr>
<tr>
<td>Altered behavior, aggression</td>
<td>Lethargy</td>
</tr>
<tr>
<td>Altered personality and mood (eg, apathy, depression)</td>
<td>Falls</td>
</tr>
<tr>
<td>Falls</td>
<td>Functional decline</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>Nonketotic hyperosmolar coma</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>Worsening incontinence</td>
</tr>
<tr>
<td>Seizures</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td></td>
</tr>
<tr>
<td>Coma, death</td>
<td></td>
</tr>
</tbody>
</table>

Source: American Medical Directors Assoc.

Managing Diabetes in Long-Term Care

Evaluation of Complications

After a diagnosis of diabetes has been confirmed, the ADA guidelines suggest that the resident should be evaluated for the nature and severity of any complications. The UKPDS found that, using the ADA’s diagnostic criteria as of 1998, 50% of patients with diabetes had already developed complications by the time they were diagnosed.48 The initial determination of the severity of diabetes complications requires a detailed physical examination to assess oral health, vision, cognition, cardiovascular complications, neuropathy, skin condition, lower extremity deformities, and ulceration. Laboratory tests should initially include a complete blood count and basic serum chemistry, including renal and hepatic function and urine microalbumin level. Before ordering additional tests, information should be obtained from recent hospital records, community physicians, and from the resident’s family to prevent duplicating efforts and incurring unnecessary expenses.49

Metabolic Control

Even when it may not be possible to prevent the complications of diabetes, it is important to note that improved glycemic control decreases the rate at which complications progress, improves the resident’s well-being, and may reduce hospitalizations. Thus, it is reasonable to strive for glycemic control that is as good as possible, given the resident’s preferences and level of comfort with the treatment.50 The glucose values of residents of LTC facilities—especially those of residents with poor control—should be reviewed frequently, and targeted interventions should be determined at each review.51 The Diabetes Control and Complications Trial (DCCT) provided evidence of a correlation between A1C levels and blood glucose. As can be seen in Table 4, lower A1C values usually correlate with lower mean plasma glucose levels.52 Lower A1C values have also been associated with a reduction in the risk of complications in the elderly.53

Table 4. Correlation Between A1C Level and Mean Plasma Glucose Levels on Multiple Testing over 2–3 Months52

<table>
<thead>
<tr>
<th>A1C (%)</th>
<th>Mean Plasma Glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>mg/dL</td>
<td>mmol/L</td>
</tr>
<tr>
<td>6</td>
<td>135</td>
</tr>
<tr>
<td>7</td>
<td>170</td>
</tr>
<tr>
<td>8</td>
<td>205</td>
</tr>
<tr>
<td>9</td>
<td>240</td>
</tr>
<tr>
<td>10</td>
<td>275</td>
</tr>
<tr>
<td>11</td>
<td>310</td>
</tr>
<tr>
<td>12</td>
<td>345</td>
</tr>
</tbody>
</table>

The AMDA guidelines recommend that clinicians develop individualized short- and long-term treatment goals that address the resident’s disease severity, cardiovascular risk factors, and overall prognosis. These goals may include the following:54

• Setting appropriate target ranges for blood glucose control (ie, FPG, postprandial glucose, and A1C)
• Maintaining adequate nutrition
• Reducing the risk of LECs
• Educating the resident and family members about the disease and its management
• Controlling pain and neuropathic symptoms
• Reducing the progression of complications, if possible
• Setting goals for the management of dyslipidemia, if appropriate
• Maximizing functional status and increasing physical activity, within the resident’s limits
• Discussing and documenting end-of-life care

THE TREATMENT OF TYPE 2 DIABETES

According to the ADA, glycemic control is fundamental to the management of diabetes.55 There is epidemiologic evidence to suggest that tight glycemic control can reduce the burden of CVD. This evidence has been confirmed by preliminary data from the Veterans Affairs Diabetes Trial, which is currently in its final stages,46 therefore, it is reasonable to try for the best possible control.51

Ideal treatment recommendations for the management of type 2 diabetes include a target fasting blood glucose of less than 130 mg/dL and a postprandial blood glucose of less than 180 mg/dL, with an A1C of less than 7%, in general, and less than 6% for an individual patient without significant hypoglycemia.56 These recommendations may not be ideal in all settings. The management of an older adult in the LTC setting should be tailored to the individual resident. In a well-functioning elderly person, the ADA goal of an A1C of less than 7% may be attainable. However, a higher level of A1C, ranging from 7% to 8%, may be more appropriate in the presence of comorbidities, frailty, and increased risk of hypoglycemia or drug side effects.57

The glycemic control guidelines of the American Geriatrics Society (AGS) suggest a target A1C of 8% for frail elderly individuals. The guidelines also stress that therapy must be determined on an individual patient basis.58 Because of the increased renal threshold that comes with advanced age, it is not appropriate to determine these levels by urinary glucose testing; rather, blood glucose levels should be monitored through frequent fingersticks.59
The Challenges and Opportunities of managing Diabetes in Long-Term Care

Throughout the course of treatment, healthcare practitioners must be particularly alert to any signs or symptoms of hypoglycemia, the consequences of which can be severe if left unrecognized or untreated. Hypoglycemia can be difficult to recognize; its risk factors include advanced age, inconsistent caloric intake, high doses of insulin, use of rapid-acting insulin with delayed meal consumption, hepatic or renal disease, change in activity level, and hypoglycemia unawareness. It is especially difficult to recognize in frail elderly patients with diabetes, because these individuals may exhibit disorientation, incoordination, altered mental status, or falls for reasons other than hypoglycemia.

The treatment of elderly patients with type 2 diabetes is similar to that of younger individuals, although the ADA guidelines caution that not all frail patients can tolerate the glucose standards recommended by the ADA.15,14 The ADA guidelines suggest a three-tiered approach to treatment, beginning with lifestyle modification (ie, diet and exercise when appropriate), followed by the initiation of oral hypoglycemic agents, and, finally, the initiation of insulin therapy to achieve control.14

Lifestyle Modifications

Preventing the onset or progression of diabetes is crucial. Studies show that the early achievement of glycemic control can preserve beta-cell function and slow the progression of macrovascular and microvascular complications.1 Individuals who are at high risk of developing diabetes, including persons with IGT or IFG, should be counseled regarding the many states that follow-up counseling, including monitoring for the education to improve glucose control.3 Weight loss resulting of LtC facilities.

immune dysfunction, increased infections, and hip fracture. 48 with a number of negative effects, including pressure ulcers, and reducing the intake of saturated fats to less than 7% of total calories.1 However, fat increases the palatability of food and that takes into account the resident’s usual eating habits and ethnic/cultural food preferences. The ADA guidelines include the following specific recommendations with regard to MNT:12

• Adjust dosages of oral agents and/or insulin to balance food consumption.
• Control portion size and total caloric intake, based on the individual’s weight and level of activity.
• Increase the consumption of dietary fiber to help reduce gastrointestinal problems.
• Avoid restricting fat.
• Discuss the role of meal planning with the resident and the resident’s family.

To improve glycemic control, assist with weight maintenance, and reduce CVD risk, the ADA recommends at least 150 minutes per week of moderate-intensity aerobic activity and resistance training three times a week when no contraindications are present.1 These recommendations must, of course, be moderated for elderly residents, who may be incapable of participating in an exercise regimen because of multiple comorbidities and limited mobility.13 An increase in physical activity can be recommended to patients with diabetes, with intensity, duration, and frequency tailored to individual needs and abilities. The involvement of a physical or activity therapist may be beneficial as well.12 Previously sedentary patients should undergo a medical evaluation and cardiovascular testing, if necessary, prior to initiating any changes to daily activity.1 In the general population, the benefits of weight loss and exercising are great; in addition to lowering glucose levels, exercise can improve CVD risk factors such as blood pressure and atherogenic lipid profiles.2,8 The effect of exercise programs in elderly populations with diabetes has not been fully evaluated, and results are conflicting.9

Pharmacologic Therapy for Diabetes

When lifestyle modifications do not achieve glycemic control within 3 months of initiation, oral agents may be added to a resident’s treatment regimen. These agents are most effective in residents whose FPG levels are below 300 mg/dL.11 The choice of agent must be tailored to a resident’s specific needs, taking into account comorbidities and the likelihood of adverse drug reactions.10 Table 5 provides a concise review of traditional agents.

Alpha-glucosidase inhibitors. These agents, acarbose and miglitol, help control postprandial glucose by delaying the digestion and absorption of simple sugars from the gastrointestinal tract, allowing time for the body to augment insulin secretion.12 They have also been shown to enhance and prolong the release of glucagon-like peptide-1 (GLP-1), an incretin hormone, which appears to play a role in mediating satiety.13 They may be used as initial therapy in elderly patients—especially those who are obese—with modest

Table 5. Traditional Oral Hypoglycemic Agents

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Initial Dosage</th>
<th>Maximum Dosage</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pioglitazone (Actos®)</td>
<td>15 or 30 mg once daily</td>
<td>45 mg once daily</td>
<td>Thiazolidinediones*</td>
</tr>
<tr>
<td>Pioglitazone + Metformin (ActosPlusMet®)</td>
<td>If inadequately controlled on metformin monotherapy: Either 15 mg/500 mg or 15 mg/850 mg once daily or twice daily</td>
<td>45 mg once daily</td>
<td></td>
</tr>
<tr>
<td>Rosiglitazone (Avandia®)</td>
<td>4 mg once daily or 2 mg twice daily</td>
<td>8 mg once daily or 4 mg twice daily</td>
<td></td>
</tr>
<tr>
<td>Rosiglitazone + Metformin (Avandamet®)</td>
<td>2 mg/500 mg twice daily</td>
<td>4 mg/1,000 mg twice daily</td>
<td></td>
</tr>
<tr>
<td>Rosiglitazone + Glimepiride (Avandaryl®)</td>
<td>4 mg/1 mg or 4 mg/2 mg once daily</td>
<td>8 mg rosiglitazone and 4 mg gliclazide once daily</td>
<td></td>
</tr>
<tr>
<td>Metformin (Glucophage®)</td>
<td>500 mg twice daily or 850 mg once daily in the morning</td>
<td>2,550 mg in 3 divided doses</td>
<td>Biguanides*</td>
</tr>
<tr>
<td>Metformin extended release (Glucophage® XR)</td>
<td>500 mg once daily in the evening</td>
<td>2,000 mg once daily</td>
<td></td>
</tr>
<tr>
<td>Gliburide + Metformin (Glycovan®)</td>
<td>1.25 mg/250 mg once daily or twice daily</td>
<td>20 mg/2,000 mg once daily</td>
<td></td>
</tr>
</tbody>
</table>

Alpha-glucosidase inhibitors. These agents, acarbose and miglitol, help control postprandial glucose by delaying the digestion and absorption of simple sugars from the gastrointestinal tract, allowing time for the body to augment insulin secretion.12 They have also been shown to enhance and prolong the release of glucagon-like peptide-1 (GLP-1), an incretin hormone, which appears to play a role in mediating satiety.13 They may be used as initial therapy in elderly patients—especially those who are obese—with modest
should have their renal function checked routinely; if serum creatinine is elevated to levels equal to or above 1.5 mg/dL in men or 1.4 mg/dL in women, metformin should be discontinued. The loss of muscle mass (sarcopenia) associated with aging results in low to normal serum creatinine in the elderly, despite decreased renal function; therefore, serum creatinine may not be an accurate indicator of renal function. In patients older than 70, creatinine clearance should be calculated using the Cockcroft-Gault equation, and metformin should only be prescribed if the calculated creatinine clearance is greater than 50 mL/min. If the clearance falls between 30 and 60 mL/min, the dose should be reduced by 50%. Moreover, these effects can be minimized by titrating the dosage upward slowly. Metformin is not recommended for patients aged 80 years and over, unless measurement of creatinine clearance demonstrates that renal function is not reduced.

Thiazolidinediones (TZDs). The agents of this class enhance peripheral insulin sensitivity and thus improve insulin-mediated glucose uptake in muscle, in adipose tissue, and to a lesser extent, in the liver. TZDs have been shown to reduce FPG by about 35 to 40 mg/dL and A1C by 1% to 1.5%. Troglitazone, the first drug of this class that was available, produced several cases of severe liver toxicity and has been removed from the market. Rosiglitazone is indicated for first-line use among elderly obese patients, particularly those who cannot tolerate metformin. Both agents may reduce macrovascular morbidity and mortality; however, these agents are associated with a substantially higher incidence of edema and anemia among elderly patients. In August 2007, the US Food and Drug Administration (FDA) announced that an updated label with a boxed warning on the risks of heart failure was needed for the entire TZD class. The FDA’s review of rosiglitazone and the possible increased risk of heart attacks associated with its use is still ongoing.

Sulfonylureas. These agents are divided into first-generation (acetohexamide, chlorpropamide, tolbutamide, and tolbutamidine) and second-generation (glibenclamide, glipizide, and glyburide). Both generations lower FPG by increasing the release of insulin; however, the second-generation agents, which are most commonly used in practice, are more potent and have improved pharmacokinetic and safety profiles. Sulfonylureas are indicated as first-line therapy in lean elderly patients with diabetes and have been shown to reduce FPG by about 60 to 70 mg/dL and A1C by 1.5% to 2%. Metformin reduces FPG by about 60 to 70 mg/dL and A1C by 15% to 2%, and it is useful in combination with sulfonylureas. The UKPDS found that, with metformin, there was a reduction in diabetes-related end points, deaths, and myocardial infarction compared to diet therapy. Metformin is contraindicated in patients with significant liver, renal, and cardiac disease, because of its association with the occurrence of lactic acidosis. However, according to a recent study, the use of metformin in patients with heart failure has not increased the incidence of lactic acidosis; therefore, the drug’s use in these patients warrants further consideration. The drug is eliminated unchanged by the kidneys, and its half-life is prolonged in patients with renal impairment. Thus, the progressive decrease in renal function that comes with aging will change metformin’s pharmacokinetic profile. Patients managed according to the Challenges and Opportunities of

The pharmacokinetics of the sulfonylureas changes with advancing age; impaired absorption and elimination is noted, particularly with glyburide. The most common and severe side effect associated with sulfonylureas is hypoglycemia, which can lead to permanent neurological damage and death in the elderly and can easily be misdiagnosed as a cerebrovascular event. There is a lower incidence of hypoglycemia with tolbutamide, gliclazide, and possibly glipizide, and chlorpropamide is contraindicated in the elderly as a result of this problem. Glyburide can also be associated with pronounced hypoglycemia, and the high prevalence of chronic kidney disease in LTC has led many practitioners to choose glipizide over glyburide.

Insulin. This is the oldest of the currently available medications to treat diabetes, and it remains the most effective at lowering glucose levels. Insulin is now thought of less as a hypoglycemic agent and more as a therapeutic agent for delaying the progression of complications from diabetes and decreasing the risk of adverse cardiovascular events. The drug is indicated for older diabetic patients who fail to respond to neoglycologenic therapy, oral antihyperglycemic agents, or both, and for patients with extremely high FPG levels (over 500 mg/dL). It is also indicated for obese elderly patients as an adjunct therapy to metformin; this combination can reduce the weight gain often associated with insulin, reduce insulin requirements, and improve glycemic control.

Impaired awareness of hypoglycemia has been observed among elderly patients with type 2 diabetes. When initiating insulin in the LTC setting, it is extremely important that insulin be dosed conservatively and titrated slowly. Patient and staff should be educated about the signs and symptoms of hypoglycemia so they can be addressed immediately. Figure 4 contains an algorithm for the initiation and adjustment of insulin regimens.

Insulin, an amino acid protein, is available in several forms. Regular insulin—crystalline-zinc in a neutral pH buffer—was at first extracted from bovine pancreas. After it was discovered that the onset and duration of insulin could be altered through the addition of basic proteins and neutral protamine Hagedorn (NPH) insulin and Lente insulin were developed. In the 1990s, insulin was developed using human recombinant DNA, and eventually all animal-derived insulins were phased out of production.

The most recent rapid- or short-acting bolus (ie, mealtime) insulins are lispro, aspart, and glulisine. These insulins have a 1-hour onset of action but no peak; detemir is used once

### Table 5. Traditional Oral Hypoglycemic Agents

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<tr>
<th>Drug Name</th>
<th>Initial Dosage</th>
<th>Maximum Dosage</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Repaglinide (Prandin®)</strong></td>
<td>16 mg/day</td>
<td>Administer 15 to 30 min before each meal</td>
<td>Elderly patients and patients previously treated with hypoglycemic agents or patients with hemoglobin A1C &lt; 8%. – Give 0.5 mg three times daily – Give 1 to 2 mg three times daily</td>
</tr>
<tr>
<td><strong>Nateglinide (Starlix®)</strong></td>
<td>120 mg three times daily, 60 mg three times daily in elderly patients</td>
<td>Administer 15 to 30 min before each meal</td>
<td>120 mg three times daily</td>
</tr>
<tr>
<td><strong>Acarbose (Precose®)</strong></td>
<td>25 mg three times daily</td>
<td>100 mg three times daily</td>
<td>Administer with first bite of each main meal</td>
</tr>
<tr>
<td><strong>Miglitol (Glyset®)</strong></td>
<td>25 mg three times daily</td>
<td>100 mg three times daily</td>
<td>Administer with first bite of each main meal</td>
</tr>
</tbody>
</table>

**GLUCOSE INHIBITORS**

**Insulin.** The oldest of the currently available medications to treat diabetes, and it remains the most effective at lowering glucose levels. Insulin is now thought of less as a hypoglycemic agent and more as a therapeutic agent for delaying the progression of complications from diabetes and decreasing the risk of adverse cardiovascular events. The drug is indicated for older diabetic patients who fail to respond to neoglycologenic therapy, oral antihyperglycemic agents, or both, and for patients with extremely high FPG levels (over 500 mg/dL). It is also indicated for obese elderly patients as an adjunct therapy to metformin; this combination can reduce the weight gain often associated with insulin, reduce insulin requirements, and improve glycemic control.

Impaired awareness of hypoglycemia has been observed among elderly patients with type 2 diabetes. When initiating insulin in the LTC setting, it is extremely important that insulin be dosed conservatively and titrated slowly. Patient and staff should be educated about the signs and symptoms of hypoglycemia so they can be addressed immediately. Figure 4 contains an algorithm for the initiation and adjustment of insulin regimens.

Insulin, an amino acid protein, is available in several forms. Regular insulin—crystalline-zinc in a neutral pH buffer—was at first extracted from bovine pancreas. After it was discovered that the onset and duration of insulin could be altered through the addition of basic proteins and neutral protamine Hagedorn (NPH) insulin and Lente insulin were developed. In the 1990s, insulin was developed using human recombinant DNA, and eventually all animal-derived insulins were phased out of production. The most recent rapid- or short-acting bolus (ie, mealtime) insulins are lispro, aspart, and glulisine. These insulins have a 1-hour onset of action but no peak; detemir is used once...
or twice daily and peaks less than NPH. Detemir has led to improved glycemic control without weight gain, giving it a substantial advantage over other insulin formulations. In most studies, analog insulin has been found to lower postprandial glucose and reduce hypoglycemic episodes more than human insulin. Regular insulin must be injected about 30 to 45 minutes before eating, postprandial glucose will rise before the insulin peaks. Short-acting analogs, such as aspart and lispro, can be used closer to meals (10 to 15 minutes before) and are thus preferred to meals (10 to 15 minutes before) and are thus preferred

Table 6 lists various clinical situations and suggested insulin regimens to deal with them. It is important for healthcare practitioners to insist that, although previously the rule of thumb for mixing insulin was to mix so-called clear (ie, regular or lispro) insulin before cloudy (ie, intermediate or long-acting) insulins, the introduction of glargine has invalidated this rule. Glargine must not be mixed with any other insulin, because doing so could alter its effectiveness and release pattern. The aforementioned classes of drugs can be used alone or in combination with each other to take advantage of differing mechanisms of action. The AMIDA guidelines suggest the initiation of a second or, possibly, third class of drugs if, despite initial treatment, FPG remains above 140 mg/dL or AIC is greater than 7.0%. Table 7 lists some choices for combination therapy.

Table 6. Suggested Insulin Regimens for Different Clinical Situations

<table>
<thead>
<tr>
<th>Clinical Situation</th>
<th>Suggested Insulin Regimen (in order of lowest hypoglycemic risk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adding insulin to oral agent(s)</td>
<td>• Basal once daily in morning or at bedtime (eg, glargine) • Pre-supper insulin mixture (eg, 75/25 lispro or 70/30 aspart insulin) • Detemir 1–2 times daily • Intermediate-acting insulin once daily at bedtime (eg, NPH)</td>
</tr>
<tr>
<td>Risk of nocturnal hypoglycemia</td>
<td>• Long-acting or basal once daily in morning or at bedtime (eg, glargine) • Intermediate-acting insulin (eg, NPH) at bedtime instead of before supper</td>
</tr>
<tr>
<td>Well-controlled with consistent eating pattern</td>
<td>• Basal insulin once daily in morning or at bedtime and rapid (aspart, lispro, glulisine) at meals • Twice-daily insulin mixture (eg, aspart 70/30 insulin or 75/25 lispro before breakfast and supper) • Split mixed intermediate and short-acting (eg, NPH + regular twice daily before breakfast and supper)</td>
</tr>
<tr>
<td>Poor control</td>
<td>• Basal insulin once daily and rapid (aspart, lispro, glulisine) at meals • Rapid-acting insulin before meals + NPH 1–2 times a day • Split mixed (eg, NPH + regular 2–3 times daily before breakfast and supper) • Short-acting insulin (regular) before meals + NPH 1–2 times a day</td>
</tr>
</tbody>
</table>

Table 7. Examples of Combination Therapy Choices

| Alpha-glucosidase inhibitor + metformin | • Fixed-dose (single pill) therapy |
| Thiazolidinedione + metformin | Thiazolidinedione (rosiglitazone) + metformin |
| Thiazolidinedione (rosiglitazone) + metformin | Thiazolidinedione (rosiglitazone) + metformin |
| Thiazolidinedione + metformin + thiazolidinedione | Thiazolidinedione (pioglitazone) + metformin |

Rapid-acting insulin analog or premixed insulin analogs may be used in special situations. Insulin–oral medications, all oral medications may be used in combination with insulin, therapy combinations should be selected based on the patient’s self-monitoring of blood glucose profiles. Initiate/intensify combination therapy using options listed above when AIC levels are 8–10% to address fasting and postprandial glucose levels. Initiate/intensify insulin therapy when AIC levels are >10%.

Options include:

- Secretagogue + metformin
- Secretagogue + thiazolidinedione
- Secretagogue + α-glucosidase inhibitor
- Thiazolidinedione + metformin
- DPP-4 inhibitor + metformin
- DPP-4 inhibitor + thiazolidinedione
- Secretagogue + metformin + thiazolidinedione
- Secretagogue (glyburide) + metformin

Rapid-acting insulin analog or premixed insulin analogs may be used in special situations. Insulin–oral medications, all oral medications may be used in combination with insulin, therapy combinations should be selected based on the patient’s self-monitoring of blood glucose profiles. Initiate/intensify combination therapy using options listed above when AIC levels are 8–10% to address fasting and postprandial glucose levels. Initiate/intensify insulin therapy when AIC levels are >10%.
The Challenges and Opportunities of Managing Diabetes in Long-Term Care

The Newest Medications for Diabetes Treatment

Newer antihyperglycemic agents have emerged to address the adverse metabolic effects, such as weight gain and worsening of the lipid profile, and the risks of hypoglycemia, gastrointestinal side effects, and edema that are associated with the conventional agents. Ultimately, the conventional therapies that have been the mainstay of treatment for diabetes have not adequately maintained long-term glycemic control, as is evident in the wide glycemic fluctuations and postprandial hyperglycemia that are often associated with their use. The newer antihyperglycemics that are described below have been developed to overcome these shortcomings.

Extended-release metformin. As discussed, metformin decreases hepatic glucose production and intestinal absorption of glucose and improves insulin sensitivity by increasing peripheral glucose uptake and use. A new formulation of metformin is now available in extended-release 500 mg and 1,000 mg tablets. These extended-release tablets have been shown to reach maximum plasma concentration at approximately 7 to 8 hours when taken postmeal. This formulation has been shown to provide systemic exposure (ie, area-under-the-curve) equivalent to the immediate-release version and up to 35% higher systemic exposure. In a double-blind, randomized, placebo-controlled, multicenter study of patients with type 2 diabetes who were randomized to either traditional immediate-release metformin at 500 mg in the morning and 1,000 mg in the evening or extended-release metformin at 1,500 mg once daily, 2,000 mg once daily, 2,000 mg once dosed (500 mg in the morning and 1,000 mg in the evening), each of the extended-release metformin regimens was found to be at least as effective as the immediate-release regimen. Also, the once-daily dosing of the extended-release formulation was as effective as the BID dosing of the immediate-release formulation. In a similar study that randomized patients to placebo and glyburide, extended-release metformin 1,500 mg or 2,000 mg once daily plus glyburide, or extended-release metformin 1,000 mg twice daily plus glyburide, changes in glycemic control across the extended-release regimens were comparable, and the difference in the A1C from baseline in the metformin plus glyburide groups and in the placebo group was statistically significant (P<0.003).

Extended-release metformin carries a boxed warning that is especially relevant to the elderly: the drug can accumulate to levels in excess of 5 µg/mL during treatment and result in lactic acidosis, which is fatal in 50% of cases. Thus, the renal function of elderly patients treated with extended-release metformin should be carefully monitored. Healthcare practitioners should be vigilant for nonspecific symptoms such as malaise, myalgias, respiratory distress, increasing somnolence, and nonspecific abdominal distension.

Inhaled insulin. The mechanism of action of insulin has been discussed in previous sections; it does not differ for inhaled insulin. Human insulin inhalation powder is absorbed as quickly as subcutaneous rapid-acting insulin analogs and more quickly than subcutaneous regular human insulin. In clinical studies, inhaled insulin reached peak concentration within 10 to 105 minutes for subcutaneously administered regular human insulin. In studies comparing inhaled insulin as monotherapy or add-on therapy in patients with type 2 diabetes who were previously treated with oral agents (ie, an insulin secretagogue and either metformin or a T2D), the patients receiving inhaled insulin experienced greater reductions in A1C levels from baseline and more patients achieved A1C levels below 7%.

The most commonly reported adverse event with insulin therapy, including inhaled insulin, is hypoglycemia. Other adverse events with inhaled insulin include cough, dyspnea, respiratory events, and decreased pulmonary function. The FDA requires testing of pulmonary function before the initiation of inhaled insulin therapy, 6 months after initiation, and annually thereafter. As of October 2007, Pfizer, the maker of Exubera, the only commercially available inhaled insulin formulation, voluntarily ceased any further production of the medication. This decision was based on poor utilization of the medication, not on any safety considerations.

Incretin-based therapy. The incretin effect, which is enhanced insulin secretion following oral vs. intravenous glucose administration, is dependent on glucose-dependent insulinoptotropic (GIP) hormone and GLP-1. GIP and GLP-1, which are secreted in response to food consumption, affect the stomach, liver, pancreas, and brain in several ways that impact glucose levels by stimulating glucose-dependent insulin secretion, by inhibiting gastric emptying, and by inhibiting glucagon secretion. GLP-1 is degraded by the enzyme dipeptidyl peptidase-4 (DPP-4). Agents with differing mechanisms of action have been developed to activate GLP-1 and to inhibit degradation by DPP-4.

Long-acting GLP-1 agonists. Exenatide, a synthetic peptide that has incretin-mimetic actions, is currently the only FDA-approved long-acting GLP-1 agonist; however, a longer-acting formulation of exenatide and lixilaglutide, another GLP-1 agent, is in clinical development. Exenatide is indicated as adjunctive therapy for patients with type 2 diabetes mellitus who are taking metformin, a sulfonylurea, a T2D, a combination of metformin and a sulfonylurea, or a combination of metformin and a T2D, but who have not achieved adequate glycemic control.

Exenatide has been shown to produce a significant drop in A1C, due to a significant effect on postprandial plasma glucose concentrations. In a recent study of exenatide in type 2 diabetes patients at 82 weeks and at 2 years, A1C reductions from week 0 (7.0%–7.9%) were sustained through years 2 (7.0%–6.9%); P<0.05 versus baseline), with 50% of the population achieving A1C ≤7%. At week 30, exenatide was associated with a significant reduction in mean (SD) body weight from baseline [−2.0 (2.2) kg], and there were continued reductions after 2 years [−4.7 (0.3) kg; P<0.001 versus baseline]. At 82 weeks, clinically relevant improvements in blood pressure, HDL-C, and triglycerides; the greatest improvement in risk factors for CVD occurred among patients who experienced the most weight reduction.

Based on data demonstrating the efficacy of exenatide when used with a T2D, or with or without metformin, exenatide has been approved for use with T2Ds. With exenatide, 62% of the subjects who had elevated A1C despite therapy with T2D (alone or with metformin) achieved A1C ≤7%, compared to 16% with placebo. The most frequent adverse event was nausea, which was dose-dependent and tended to decline over time. Reductions in weight were shown not to be dependent on nausea, because weight loss was also seen in subjects who did not report nausea.

Long-term clinical studies are required to determine the role of the incretin effect in therapy in older adults. It has been studied in patients in the seventh and eighth decades of life and has been shown to be safe; however, data on the appropriateness of its use in this population is necessary before it can be considered for inclusion in treatment regimens.

PPG inhibitors. By inhibiting GLP-1 breakdown, DPP-4 inhibitors increase meal-stimulated active GLP-1 and GIP levels twofold to threefold. Sitagliptin is currently the only agent in this class that is FDA-approved. Studies show that it is effective in improving glycemic control when used alone or in combination with metformin or a T2D. When sitagliptin was added to therapy for type 2 diabetic patients with inadequate glycemic control on a T2D, the percentage of patients achieving the target A1C <7% was 45%, compared to 23% with placebo. Sitagliptin is administered once daily as monotherapy or as combination with metformin or a tTZD, the patients receiving inhaled insulin experienced greater reductions in A1C levels from baseline and more patients achieved A1C levels below 7%.

Sitagliptin is approved long-acting GLP-1 agonist; however, a longer-acting formulation of exenatide and lixilaglutide, another GLP-1 agent, is in clinical development. Exenatide is indicated as adjunctive therapy for patients with type 2 diabetes mellitus who are taking metformin, a sulfonylurea, a T2D, a combination of metformin and a sulfonylurea, or a combination of metformin and a T2D, but who have not achieved adequate glycemic control.

Although not yet approved by the FDA, vildagliptin—also a DPP-4 inhibitor—has demonstrated efficacy in patients with poor glycemic control and with regard to weight loss in obese individuals. Vildagliptin targets islet dysfunction; it improves the ability of the islet's alpha and beta cells to sense and respond to sugar in the blood. In combination with pioglitazone (a T2D), vildagliptin led to a 10% reduction in A1C in clinical trials; two-thirds of patients who received this combination achieved an A1C of ≤7%. Adverse events with this combination were similar to those with the individual agents, and patients taking the combination experienced no significant additional weight gain and less edema than those taking only pioglitazone. Vildagliptin's side effects, including hypoglycemia and edema, were similar to placebo in monotherapy trials; the most common side effects of vildagliptin are cold/flu-like symptoms, headaches, and diarrhea.

Pramlintide. This agent is a synthetic analog of amylin, a beta-cell hormone that, like GLP-1 and GIP, is secreted with insulin in response to eating. Amylin is a neuroendocrine hormone that regulates glucose by suppressing glucagon, slowing gastric emptying, and potentially affecting eating behavior and weight control. As previously mentioned, the ongoing degradation of beta-cell function in insulin-dependent patients with type 2 diabetes leads to impaired postprandial insulin and amylin response. Clinical trials involving the administration of pramlintide to these patients demonstrated a reduced postprandial hyperglycagionemia, a slowed rate of gastric emptying, and improved postprandial glucose excursions. A reduction in A1C of 0.5% to 0.7% was achieved without increases in insulin use or severe hypoglycemia. Pramlintide’s side effects, including nausea, vomiting, increased circulatory time, increased gastric emptying, and improved postprandial glucose excursions; A reduction in A1C of 0.5% to 0.7% was achieved without increases in insulin use or severe hypoglycemia. Pramlintide’s side effects, including nausea, vomiting, increased circulatory time, increased gastric emptying, and improved postprandial glucose excursions; A reduction in A1C of 0.5% to 0.7% was achieved without increases in insulin use or severe hypoglycemia.

Pramlintide is administered subcutaneously and has been shown to decrease C-reactive protein and increase adiponectin, both of which are associated with inflammation and insulin resistance.

The most common adverse event reported with pramlintide was mild-to-moderate nausea, which dissipated early in treatment. To improve glycemic control, pramlintide should be administered three times daily—conjunction with insulin therapy—with major meals. Patients using pramlintide should have their blood glucose levels monitored frequently and should reduce their dosages of rapid- and short-acting insulin by half. It should be noted that pramlintide is not often used in the nursing home setting.
BARRIERS TO THE MANAGEMENT OF DIABETES IN THE ELDERLY AND IN RESIDENTS OF LTC FACILITIES

There is a belief among some healthcare practitioners that diabetes is a relatively benign condition of the elderly and that patients will die from something other than the complications of diabetes, which are often slow to develop. In one study of hospitalized patients aged 75 years and over, 53% of patients had elevated glucose blood levels; however, in half of these patients, the condition was ignored by the physician.13 As has been discussed in this supplement, the complications of diabetes, especially stroke, renal disease, and amputation, are more common among elderly individuals who have diabetes or hyperglycemia than among those who do not. Elderly individuals with diabetes or hyperglycemia are also more severely affected by these complications, and they suffer a comparably poorer quality of life.14

There is no denying that managing diabetes in elderly patients is more difficult and more time-consuming than managing diabetes in the disease in younger patients. The impairments of age—physical, mental, and social—all complicate treatment.15 Undernutrition and dehydration are prevalent in elderly patients, as are frequent urination, poor vision, increased infections, decreased awareness of thirst, and decreased sensation, all of which make the early diagnosis of diabetes, hyperglycemia, and hyperosmolar hyperglycemic conditions more difficult.15 Anorexia, which is also common in this population, may hinder the diagnosis of diabetes, hyperglycemia, and hyperosmolar hyperglycemic conditions more difficult.15 Anorexia, which is also common in this population, may hinder the diagnosis of diabetes, hyperglycemia, and hyperosmolar hyperglycemic conditions more difficult.15

Among elderly individuals, the prevalence of both diabetes and obesity is increasing. Therefore, LTC practitioners must be up-to-date in their understanding of diabetes, its prevention, and its management. Managing diabetes among older individuals is complex and requires the constant vigilance of all parties (e.g., the patient, caregivers, and family members). The consequences of diabetes and its complications are especially severe in elderly patients, and the prevention or delay of these complications should be the primary goal of disease management.

Among elderly individuals, it may not always be possible to institute the intensive therapeutic regimens that current guidelines recommend. The consequences of diabetes, and aging itself, often prevent the patient from engaging in recommended treatments—especially those relating to diet and exercise. Thus, healthcare practitioners must develop individualized treatment plans for each patient that account for the patient’s life expectancy, quality of life, and living situation. The guidelines developed by the ADA and summarized in these pages help guide healthcare practitioners and LTC facilities institute optimal treatment plans that may lead to dramatically improved health and functioning among LTC residents.

References

SUMMARY

Among elderly individuals, the prevalence of both diabetes and obesity is increasing. Therefore, LTC practitioners must be up-to-date in their understanding of diabetes, its prevention, and its management. Managing diabetes among older individuals is complex and requires the constant vigilance of all parties (e.g., the patient, caregivers, and family members). The consequences of diabetes and its complications are especially severe in elderly patients, and the prevention or delay of these complications should be the primary goal of disease management.

Among elderly individuals, it may not always be possible to institute the intensive therapeutic regimens that current guidelines recommend. The consequences of diabetes, and aging itself, often prevent the patient from engaging in recommended treatments—especially those relating to diet and exercise. Thus, healthcare practitioners must develop individualized treatment plans for each patient that account for the patient’s life expectancy, quality of life, and living situation. The guidelines developed by the ADA and summarized in these pages help guide healthcare practitioners and LTC facilities institute optimal treatment plans that may lead to dramatically improved health and functioning among LTC residents.

References


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