

Clinical Management of Diabetes in the Elderly

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The population of the United States is aging. The elderly are increasingly comprising a larger proportion of newly diagnosed diabetic patients. In 1993, 41% of the 7.8 million people diagnosed with diabetes were over 65 years of age.¹ Managing type 2 diabetes in the elderly population is difficult because of complex comorbid medical issues and the generally lower functional status of elderly patients. Nationally published guidelines often do not apply to geriatric care, and practitioners' individualized approaches to therapy are highly variable. Understanding the special dynamics of geriatric patients will aid in the optimum management of their diabetes.

Physiology of Aging

Many age-related changes affect the clinical presentation of diabetes. These changes can make the recognition and treatment of diabetes problematic. It is said that at least half of the diabetic elderly population do not even know they have the disease.² Part of the problem is that, because of the normal physiological changes associated with aging, elderly diabetic patients rarely present with the typical symptoms of hyperglycemia.³ The renal threshold for glucose increases with advanced age, and glucosuria is not seen at usual levels.⁴ Polydipsia is usually absent because of decreased thirst associated with advanced age. Dehydration is often more common with hyperglycemia because of elderly patients' altered thirst perception and delayed fluid supplementation. More often, changes such as confusion, incontinence, or complications relating to dia-

betes are the presenting symptoms.

Alterations in carbohydrate metabolism in the elderly include the loss of first-phase insulin release.⁵ The initial surge in postprandial insulin does not occur in all elderly diabetic patients.⁶ In contrast to lean elderly and younger adults with diabetes, there is no impairment in glucose-induced insulin release as seen by a normal second-phase insulin secretion among obese elderly patients.⁵ This suggests that the primary impairment in obese elderly patients is insulin resistance, whereas lean elderly patients have impaired glucose-induced insulin release.

Lean elderly diabetic patients may even display features of autoimmune changes normally attributed to younger type 1 diabetic patients.⁷ Islet cell antibodies and marked insulin deficiency are increasingly seen in lean elderly diabetic patients.^{5,8} Thus, it is important to remember that both type 1 (insulin-dependent) and type 2 (non-insulin-dependent) diabetes occur in the elderly.

Hypoglycemia is often a risk of diabetes treatment in the elderly. Studies of healthy elderly patients have shown that glucose counterregulation involving glucagon, epinephrine, and growth hormone responses to hypoglycemia are diminished, which may contribute to the reduction in autonomic warning symptoms.⁹ Although classic overt symptoms of hypoglycemia may be absent, symptoms of cognitive impairment and long-term implications regarding dementia need to be researched.

In elderly patients with diabetes, the epinephrine response is actually enhanced. Thus, there are often symp-

toms present with severe hypoglycemia (blood glucose levels <50 mg/dl) that are not present with moderate hypoglycemia.⁹

Other complicating aspects of the physiology of aging include changes in the pharmacokinetics of both insulin and oral medications. Changes in drug absorption, distribution, metabolism, and clearance must be considered when treating any condition in elderly patients. These alterations affect individual drug choices and dosing decisions.

Diagnosis

The current diagnoses of diabetes in the elderly are the same as those of younger adults. The current American Diabetes Association (ADA) criteria for diagnosis of diabetes are: two fasting plasma glucose levels ≥ 126 mg/dl on two separate occasions, a random plasma glucose ≥ 200 mg/dl with symptoms, or a 2-h oral glucose tolerance test (OGTT) ≥ 200 mg/dl (Table 1). Because it is also recommended that anyone over 45 years of age be screened, all elderly individuals should be screened annually for diabetes.

Recent literature from the DECODE trials that included elderly subjects are revealing that an OGTT ≥ 200 mg/dl increases the risk of all-cause mortality even in the presence of a normal fasting glucose.¹⁰ Although measuring fasting plasma glucose levels increases the detection of diabetes in the young, it may actually miss 31% of cases in the elderly.^{11,12} In elderly patients, a 2-h OGTT may be useful in diagnosing diabetes if there is clinical uncertainty.

All complications of diabetes can

Table 1. Criteria for the Diagnosis of Diabetes Mellitus

Symptoms of diabetes plus casual plasma glucose concentration >200 mg/dl (11.1 mmol/l). Casual is defined as any time of day without regard to time since last meal. The classic symptoms of diabetes include polyuria, polydipsia, and unexplained weight loss.

or

Fasting plasma glucose (FPG) >126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h.

or

2-h PG >200 mg/dl (11.1 mmol/l) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.

In the absence of unequivocal hyperglycemia with acute metabolic decompensation, these criteria should be confirmed by repeat testing on a different day. The third measure (OGTT) is not recommended for routine clinical use.

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occur in the elderly at higher rates. This includes, but is not limited to, autonomic neuropathy, nephropathy, retinopathy, erectile dysfunction, and foot ulcers. Clinicians should also be aware of and primed to recognize some unique syndromes occurring more commonly in elderly diabetic patients.⁴ These include:

1. Diabetic neuropathic cachexia. This syndrome typically occurs in men and is associated with painful peripheral neuropathy, anorexia, depression, and weight loss. The syndrome may resolve without treatment within a few months.³
2. Diabetic neuropathy. This can occur suddenly and can be focal and asymmetric. Diabetic third-nerve palsies are the most common mononeuropathy in the elderly, although other nerves can be affected. Usually, these are spontaneously reversible over several weeks.
3. Amyotrophy. This proximal muscle weakness and muscle wasting can coexist with polyneuropathies and may be treatable with immune therapy. It should be considered in all elderly diabetic patients who report new difficulty rising from chairs.
4. Malignant otitis externa. This condition is more common in elderly

diabetic patients and should be a diagnostic consideration when older patients report severe ear pain.

5. Papillary necrosis. This should be considered in elderly patients with sudden deterioration in renal function. Urinary infections should be treated aggressively.
6. Osteoporosis. Preventive measures should be considered for elderly diabetic patients. Diabetes is a known risk factor for osteoporosis and has been shown to increase the risk of falls, resulting in increased fractures.¹³

Treatment

Goals of therapy for elderly diabetic patients should include an evaluation of their functional status, life expectancy, social and financial support, and their own desires for treatment. A full geriatric assessment performed before establishing any long-term diabetes therapy may aid in identifying potential problems that could significantly impair the success of a given therapy. Often, elderly patients have cognitive impairments, limitations in their activities of daily living, undiagnosed depression, and difficult social issues that need to be addressed.

The ideal HbA_{1c} target of $<7\%$ may be difficult to achieve in the elderly, but

is recommended for all adults. Research is lacking regarding the benefit of tight control in the oldest elders (>80 years of age). Major large prospective trials to date have not reported conclusive data on intensive blood glucose control and improved vascular endpoints for the geriatric population.

Diabetes is associated with lower levels of cognitive functioning and greater cognitive decline in elderly.¹⁴ Prospective trials have not shown consistent improvements in cognition with tight control, although observational studies note improved cognitive functioning with lower HbA_{1c} levels.¹⁵ The mechanisms by which diabetes is associated with cognitive impairment remain unclear.

Therapy should be chosen based on the individual needs and issues of each patient. Coexisting health problems, such as dementia or psychiatric illnesses, may require a simplified approach to diabetes care.

The risks of hypoglycemia are higher in the cognitively impaired. Elderly patients often have impaired awareness of the autonomic warning symptoms of hypoglycemia even when they have been educated about them. They may also have delayed psychomotor responses to intervene in the correction of hypoglycemia.¹⁶ Therefore, each patient's risk for hypoglycemia should be considered, and therapy should be individualized accordingly.

As with any diabetic patient, overall goals should aim at reduction of all cardiovascular risk factors, smoking cessation, improvement in exercise, elimination of obesity, and optimal control of hypertension. In frail elderly patients, particular attention should be given to functional goals and to avoiding therapies that may cause loss of independence or early institutionalization.

Current options for therapy include diet and exercise as recommended by the ADA. Many nursing homes and long-term care facilities now offer exercise programs for the physically challenged. Exercise can improve insulin sensitivity

and should be encouraged for those who are deemed able to participate after safety evaluations have been performed.

Dietary compliance is often not feasible for elders who exhibit difficulties with instrumental activities of daily living, because their functional capabilities may limit their ability to prepare basic meals. Restricting caloric intake in long-term care patients should be done with much caution. Many already have insufficient caloric intake because of confusion, dysphagia, and diminished appetite. Often, a consultation with a dietitian and home evaluations by social workers can provide some insight. As with most of geriatrics, a multidisciplinary approach to the evaluation and treatment of each patient will provide the most fruitful results.

For elderly patients who require medical therapy, the following options are available.

1. Alpha-glucosidase inhibitors (e.g., acarbose [Precose] and miglitol [Glyset]). These agents delay digestion of complex carbohydrates and disaccharides. Although less effective than other agents, they should be considered in all elderly patients with mild diabetes. Gastrointestinal side effects may limit therapy or may benefit those who suffer from constipation. Liver functioning may be impaired at high doses, but this has not been a clinical problem.
2. Biguanides (e.g., metformin [Glucophage]). The benefit of metformin in the elderly is that it does not cause hypoglycemia when used independently. However, it is used with caution in the elderly because it can cause anorexia and weight loss.¹⁷

Before starting therapy, all elderly patients should have their creatinine clearance calculated. Serum creatinine is a poor correlate because of low muscle mass in the elderly. Metformin should not be administered if the creati-

nine clearance is <60 mg/dl.

3. Thiazolidinediones (e.g., rosiglitazone [Avandia] and pioglitazone [Actos]). These are true insulin sensitizers and enhance insulin effects by activating the PPAR alpha receptor.¹⁸ Rosiglitazone has been shown to be safe and effective in elderly patients.¹⁹ It does not cause hypoglycemia. However, it should be avoided in patients with heart failure. Thiazolidinediones are comparatively expensive drugs, but for elderly patients who can afford them, they are potentially very useful.
4. Sulfonylureas (e.g., glipizide [Glucotrol], glyburide [Micronase, Diabeta, Glynase]) and other types of secretagogues (e.g., repaglinide [Prandin] and nateglinide [Starlix]). Traditional sulfonylureas are still widely used as first-line therapy. First-generation agents such as chlorpropamide should be avoided in the elderly because of their long half-life and increased propensity for hypoglycemia in the elderly. Although sulfonylureas can cause hypoglycemia in the elderly, the incidence is relatively low if short-acting agents are used.^{20,21}

Repaglinide is unrelated to the sulfonylureas but also promotes insulin secretion from pancreatic β -cells. Unlike with sulfonylureas, in the absence of exogenous glucose, insulin release is lessened with repaglinide.

Nateglinide is unrelated to the sulfonylureas and repaglinide, but it also acts on pancreatic β -cells as an insulin secretagogue. Both repaglinide and nateglinide are used around meal times and are short-acting, which may lessen the risk of hypoglycemia. With the exception of nateglinide, insulin secretagogues should be used with caution in patients with renal dysfunction. All insulin secretagogues should be avoided in those with liver disease.

4. Insulin. The risk of severe hypoglycemia associated with insulin increases with age.^{5,22} Initiation of insulin in elderly type 2 diabetic patients should be done with the involvement of a multidisciplinary team. A complete geriatric assessment should be performed first to assure that patients can comply with their regimens and to identify potential complicating factors. If there are identified caregivers, provisions for adequate respite programs should be offered to avoid caregiver burnout.

Conclusion

Ideal geriatric care requires a multidisciplinary approach. Successful diabetes care in the aging population requires an understanding of the physiology of aging, recognition of the special issues facing the elderly, and interaction with geriatricians, diabetologists, pharmacists, social workers, diabetes educators, and dietitians to ensure the most efficacious treatment. When prescribing insulin or oral agent regimens for this population, providers should pay special attention to possible side effects and drug interactions. More research is needed to help us understand the full impact of diabetes on this expanding and complex segment of our population.

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Note of disclosure: Dr. Chau is a stock shareholder in Pfizer, Inc., which manufactures drugs for the treatment of diabetes.