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MANAGEMENT OF DIABETES AMONG FRAIL OLDER ADULTS

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Jacqueline McMillan, MD, *University of Calgary*

Jayna M. Holroyd-Leduc, MD FRCPC, *University of Calgary*

Correspondence may be directed to Jacqueline.McMillan@albertahealthservices.ca.

Abstract

Diabetes in frail older adults has been associated with increased mortality, reduced functional status, and an increased risk of institutionalization. These individuals have double the mortality of age-matched controls with the most frequent cause of death attributable to macrovascular complications. Furthermore, they have worse quality of life and use more health care resources compared with younger adults. A diagnosis of diabetes is one of the strongest predictors of functional decline in older adults.

Older adults with diabetes often have comorbidities, functional impairments, and geriatric syndromes leading to frailty. The combination of diabetes and frailty produces a complex challenge.

This article will address diabetes care in an aging population, and the discussion will be based on current evidence and relevant clinical practice guidelines.

Résumé

Chez la personne âgée fragile, le diabète est associé à une augmentation de la mortalité et d'Institutionnalisation et une réduction du niveau fonctionnel. Le risque de mortalité est deux fois plus important que chez une population non diabétique du même âge, et il est surtout attribuable aux complications macro-vasculaires. Par ailleurs, comparativement aux personnes plus jeunes, ils ont une diminution de leur qualité de vie et utilisent davantage les ressources en santé. Un diagnostic de diabète est un des indicateurs les plus puissants de déclin fonctionnel chez les personnes âgées. Les personnes âgées diabétiques souffrent souvent d'autres comorbidités, de syndromes gériatriques et de perte d'autonomie fonctionnelle menant à la fragilité. La combinaison de diabète et de fragilité représente un défi complexe dans la prise en charge de ces patients.

Cet article discutera de la prise en charge du diabète dans une population vieillissante en se basant sur les données probantes et les plus récentes recommandations cliniques.

Case

Mr. DM is a 78-year-old man whose wife had died recently. Since his wife's death, he has been admitted to the hospital twice, once with pneumonia and most recently with severe hypoglycemia. He had been feeling unwell following poor oral intake but had continued taking his oral hypoglycemics. His neighbours found him drowsy and confused, and when paramedics arrived they found his blood sugar to be 2.1 millimoles per litre (mmol/L). Given this most recent hospitalization, he is considering moving into an assisted living facility. His children live several hours away, and they have expressed concerns about him living alone. They wonder if he may be depressed and describe him as growing more and more forgetful.

His past medical history includes type 2 diabetes mellitus, for which he takes metformin and glyburide. He does not have any microvascular complications from his diabetes (e.g. retinopathy, nephropathy, neuropathy). He had a transient ischemic attack (TIA) in 2004 and also has hypertension and gout. A few years ago, he had undergone bilateral cataract surgery. His other medications include acetylsalicylic acid (ASA), enalapril, allopurinol, and occasional acetaminophen.

Introduction

This case illustrates many of the unique challenges of managing diabetes in older adults. Diabetes in this population has been associated with increased mortality, reduced functional status, and an increased risk of institutionalization.[1] The mortality rate in older adults with diabetes is double that in age-matched controls, with the most frequent cause of death attributable to macrovascular complications (e.g. MI, stroke, peripheral vascular disease).[2] Furthermore, older people with diabetes have worse quality of life and use more health care resources compared with younger adults.[2] A diagnosis of diabetes is one of the strongest predictors of functional decline in older adults.[3]

Older adults with diabetes often have comorbidities, functional impairments, and geriatric syndromes leading to frailty.[4] The combination of diabetes and frailty produces a complex challenge. Frailty is a clinical syndrome that can be defined by the presence of three of the following: unintentional weight loss (>10 pounds [lb]), exhaustion, weakness (decreased grip strength), slow walking speed, and low physical activity.[5] This article will address diabetes care in an aging population, and the discussion will be based on current evidence and relevant clinical practice guidelines.

Search Strategy

We searched Medline, EMBASE, and PubMed from 2003 to February 2013. The following key search terms were used: diabetes mellitus, older adults, aged, management, guidelines, glycemic targets, and glycemic control, and 108 citations were retrieved. The inclusion criteria were (1) the majority of the patients being over age 65 years, (2) study design being a systematic review, a randomized controlled trial, a case control or cohort study, (3) the focus of the study being diabetes management in older adults. Articles were excluded if (1) they were non-English, (2) the study design was a case report, a case series, or an editorial, (3) only the abstract was available; 19 articles met inclusion criteria. Additional papers were obtained from review of the reference lists of the retrieved articles. We also included clinical practice guidelines that specifically addressed the management of the older adult, including the recent CDA 2013 practice guidelines. Further information about the search can be obtained from the authors.

Diabetes in Long-Term Care

In 1998, the Canadian Study of Health and Aging estimated the prevalence of diabetes in long-term care to be 17.5%.[6] Diabetes has been found to be an independent predictor of long-term care placement.[7] Long-term care residents with diabetes require more nursing time, have 6.4 major comorbidities compared with 2.4 among residents without diabetes,[8,9] are more likely to fall, are transferred to hospitals more often, require more medications, and have more pressure ulcers compared with other residents.[9,10]

Barriers to diabetes management in long-term care include high resident-to-staff ratios, knowledge deficiencies, lack of practice guidelines, pessimism about the care of older adults with diabetes, the belief that complications are inevitable, ambivalence about glycemic control, and lack of randomized controlled trial data within this population.[8,11] Recommendations for long-term care include hypoglycemia and sick-day management protocols, with the goals of avoiding metabolic complications, hospitalizations, infections, and pressure ulcers.[12]

Hypoglycemia in Older Adults with Diabetes

Hypoglycemia is prevalent but underrecognized in older people.[12] Adults over the age of 75 years have twice the number of emergency visits for hypoglycemia compared with the general population.[13] Hypoglycemia increases the risk of falls, cognitive impairment, hospitalization, and, if severe, seizures and death.[12] Patients at increased risk include those on insulin or oral agents such as long-acting sulfonylureas, those with polypharmacy, those with cognitive impairment and malnourishment, and those recently discharged from hospital.[2,12]

Many pathophysiological changes contribute to the increase in the prevalence and severity of hypoglycemia among older adults.

Impairments in the secretion of counterregulatory hormones; decreased hepatic gluconeogenesis; autonomic neuropathy; and impaired or absent hypoglycemic symptoms such as sweating, tachycardia, and tremors.[2] This is potentially compounded by cognitive impairment and the physical inability to respond to and treat low blood sugar.[14] Hospitalization for hypoglycemia should prompt a referral to a diabetes specialist.[12]

Cognitive Impairment, Fitness to Drive, Depression, Nutritional Status, and Polypharmacy

Cognitive dysfunction is twice as likely in older adults with diabetes compared with age-matched persons without diabetes.[14] The risk of dementia is increased in patients with type 2 diabetes experiencing hypoglycemia that is severe enough to require hospitalization.[15] A patient's fitness to drive should be assessed on an individual basis, with consideration given to such factors as risk for and ability to treat hypoglycemia, retinopathy, neuropathy, and cardiovascular disease. In many provinces, patients are required to disclose the diagnosis of diabetes mellitus to the motor vehicle licensing authority.

Depression is common in patients with diabetes. Although it is uncertain whether better glycemic control improves cognitive outcomes, it has been shown to improve affect in those with depression.[2]

Older adults with diabetes are at higher risk for nutritional deficiencies.[2,16] Canadian Guidelines and the American Medical Directors Association recommend against restrictive diets, which are likely to worsen nutritional deficits.[12] Special diets for diabetes are not recommended for adults with diabetes who are residents in long-term care.[16]

Polypharmacy has a number of attendant risks, and many prescription medications, including β-blockers, corticosteroids, thiazides, and atypical antipsychotics, raise glucose levels. Often there are strong indications for each of these medications, and therefore it becomes necessary to carefully analyze the risks and benefits of each medication.

Changes in the Pathophysiology of Diabetes with Aging

Diabetes in the older adult is metabolically distinct.[2,16] It is characterized by elevated postprandial glucose levels,[16–18] so fasting glucose may not be the best screening tool. In addition, normal aging is associated with an increase in glycated hemoglobin (HbA1c), therefore, HbA1c cannot be reliably used for the diagnosis of diabetes in older adults.[16] Instead, postprandial glucose values are good predictors of outcome in older adults.[16] Also unique to older adults is the degree of hyperglycemia required before the onset of glucosuria.[2]

In addition to the usual diabetes risk factors, many older individuals also have high levels of inflammatory cytokines, take multiple medications, and have numerous comorbidities. These factors can all independently alter glucose metabolism.[2]

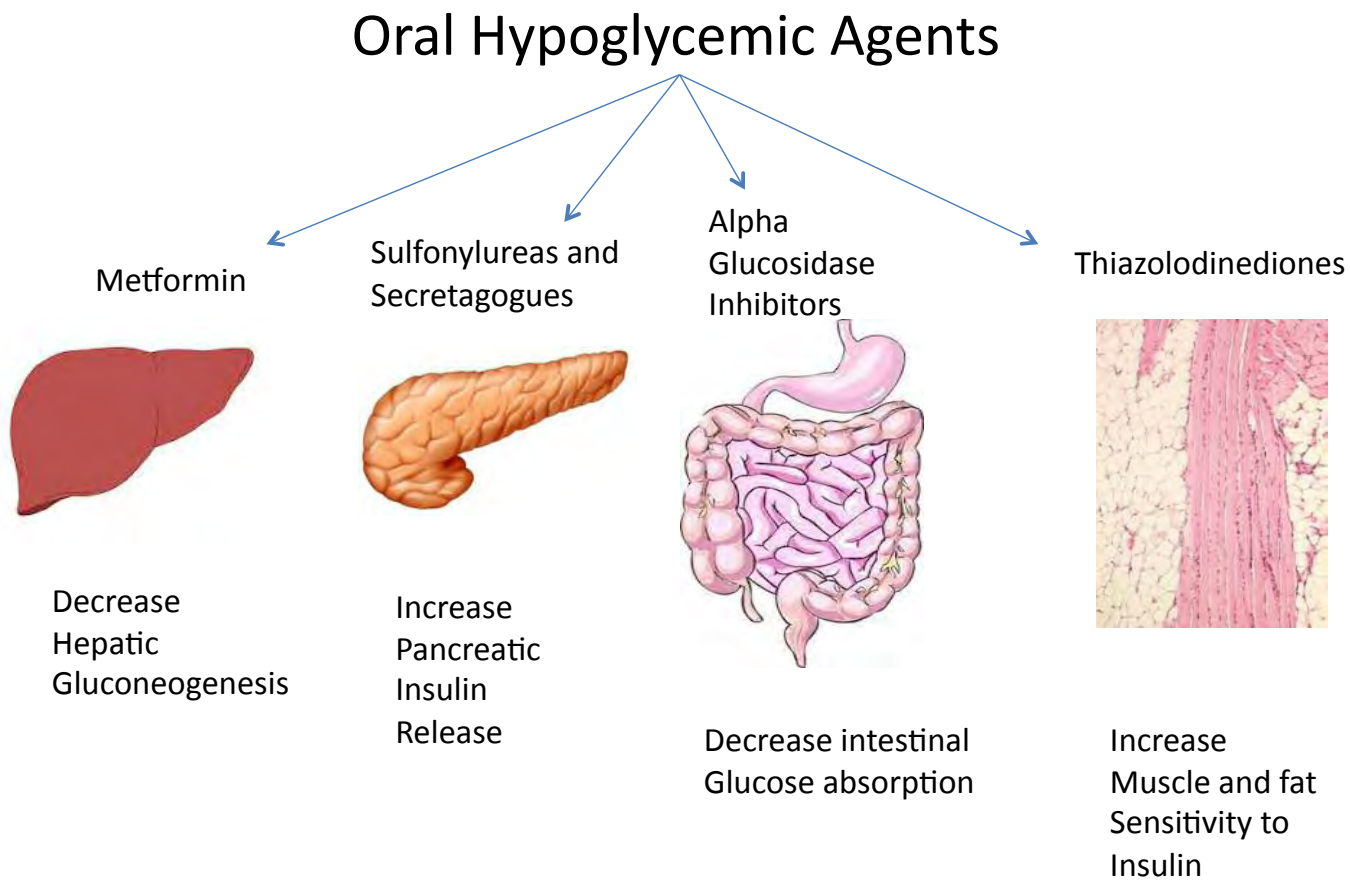
Treatment Goals in Older Adults

Frail and healthy older adults warrant individualized treatment targets.[11] The timeline of benefit for glycemic control is estimated to be 8 years.[19] In healthy older adults with few comorbidities and a life expectancy of at least 5 to 10 years, the same targets should be sought as in younger diabetics. This includes targeting a HbA1c less than 7% and blood pressure less than 130/80 mm Hg.[1,12,16,19,20]

Conversely, in frail patients with limited life expectancy (<5 years), intensive glycemic control may be unnecessary. Frailty is a better predictor of morbidity and mortality in older adults with diabetes compared with age or comorbidity.[21] The 2013 CDA guidelines recommend aiming for an HbA1c level of less than 8.5% and preprandial and fasting plasma glucose between 5 and 12 mmol/L in the following individuals: those with a limited life expectancy, high functional dependency, multiple comorbidities, and extensive history of coronary artery disease at risk for ischemia; those with a history of recurrent severe hypoglycemia and hypoglycemia unawareness; and those with a longstanding history of diabetes, in whom it has been difficult to achieve an HbA1c level of less than 7% despite multiple trials.[16]

The evidence for intensive glycemic therapy comes from randomized controlled trials in younger diabetics, and the microvascular benefit requires 5 to 10 years to be realized.[14,19] Three recent trials, designed to evaluate the benefit of intensive glycemic control on cardiovascular events and mortality, have included older patients with diabetes. The ACCORD (Action to Control Cardiovascular Risk in Diabetes) trial was terminated early at 3.5 years because of an increase in mortality in the intensive-treatment group (target HbA1c <6%) without any significant benefit in the combined primary outcomes of myocardial infarction, stroke, and cardiovascular events.[22] A post hoc analysis of the ACCORD study determined that for each year increase in baseline age, there was a 3% increase in the risk of hypoglycemia requiring medical attention (hazard ratio [HR], 1.22; 95% confidence interval [CI], 1.01–1.46).[23]

The ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation) trial[24] and the Veterans Affairs Diabetes Trial[25] both evaluated intensive glycemic control (HbA1c <6.5% and <6%, respectively) in patients with type 2 diabetes. Neither trial found a significant difference in the macrovascular outcomes in the intervention groups compared with standard therapy.[24,25] In the ADVANCE trial, severe hypoglycemia was more common in the intensive-treatment arm (HR, 1.86; 95% CI, 1.42–2.40).[24]



In contrast, intensive glycemic control is of well-proven benefit in preventing microvascular complications in type 2 diabetes; therefore, the American Diabetes Association (ADA) recommends an HbA1c level of less than 7% for microvascular benefits.[26]

Risk factor reduction and modification of hypertension and lipids decreases macrovascular risk in patients with diabetes.[2] Observational studies find no benefit to systolic blood pressure less than 120 mm Hg versus less than 140 mm Hg and indicate that low diastolic blood pressure may, in fact, be a risk factor for mortality in older adults.[19] The timeline of benefit for blood pressure and lipid control is estimated at 2 to 3 years, suggesting that antihypertensive medications and statins are of benefit to those whose life expectancy exceeds this.[19] No large trials of lipid-lowering therapy specific to older adults with diabetes have been conducted; however, pravastatin in patients aged 70 to 82 years (not limited to those with diabetes) resulted in a 15% reduction in coronary artery disease events.[27,28]

The Canadian Hypertension Education Program (CHEP) 2013 Guidelines recommend blood pressure less than 130/80 mm Hg in those with diabetes.[20] In patients with cardiovascular or kidney disease, including microalbuminuria, an angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) is recommended as first-line therapy.[20] Appropriate choices for patients with diabetes who do not have cardiovascular or renal disease include ACE, ARB, dihydropyridine calcium channel blocker (CCB), or a thiazide-diuretic.[20]

Specific Agents

Pharmacological agents should be initiated for all patients who do not meet target HbA1c less than 7% within 2 to 3 months of lifestyle management.[16] This corresponds to fasting plasma glucose or preprandial glucose values of 4 to 7 mmol/L and 2-hour postprandial glucose values of 5 to 10 mmol/L. In those with an initial HbA1c greater than 8.5%, pharmacologic agents should be initiated immediately, and two agents may be required.[16] As outlined above, these recommendations do not apply to frail older adults, in whom an HbA1c of 7.1% to 8.5% is appropriate.[16]

A number of oral hypoglycemic agents are included in the arsenal against diabetes. Metformin is the first-line oral hypoglycemic used in older adults in the absence of contraindications to its use.[16] Metformin is a peripheral insulin sensitizer that decreases hepatic

gluconeogenesis. The expected reduction in HbA1c with single-agent metformin is 1 to 1.5% with a negligible risk for hypoglycemia.[16] Metformin also results in improved cardiovascular outcomes in overweight patients.[29] Hepatic failure and estimated glomerular filtration rate (eGFR) of less than 30 millilitres per minute (mL/min) are absolute contraindications, and this agent should be used cautiously if the eGFR is 31 to 60 mL/min. Side effects of metformin include gastrointestinal complaints, many of which can be averted by using a low initial starting dose and slow titration, and vitamin B_{12} deficiency. Metformin tends to be weight neutral. Although metformin has not been evaluated in randomized controlled trials among older adults, it appears to be safe and effective.[2,16]

A second option is a meglitinide (e.g., repaglinide or nateglinide). These are insulin secretagogues with minimal to moderate risk of hypoglycemia and an expected reduction in HbA1c of 0.7%.[16] Furthermore, they have the added benefit of lowering postprandial blood glucose values.[16]

Long-acting sulfonylureas such as glyburide are not recommended in older adults because of the risk of severe or even fatal hypoglycemia that increases exponentially with age.[14,16,30-33] Sulfonylureas should be avoided completely in those at increased risk of hypoglycemia;[16] however, if they are used, gliclazide is the preferred sulfonylurea in older adults.[2,14]

α-glucosidase inhibitors (e.g. Acarbose) are effective in older adults but are poorly tolerated because of gastrointestinal side effects.[16] Thiazolidinediones are also effective but have attendant increased risks of edema, fractures, and congestive heart failure.[34,35] Rosiglitazone, but not pioglitazone, may increase the risk of cardiovascular events and death.[36-41]

Studies of the newer dipeptidyl peptidase-4 inhibitors (including saxagliptin and sitagliptin) in adults over 65 years have found these agents to be effective in reducing HbA1c values without increasing the risk of hypoglycemia compared with placebo.[42-44]

Insulin may be started at diagnosis in patients with profound hyperglycemia or later in the course of the disease in patients who are not meeting HbA1c targets.[16] The clock drawing test can be used to identify older adults who may have difficulty with insulin use.[45] Premixed insulin is preferred over mixing insulin as needed, and prefilled pens are preferred over syringes to avoid medication errors.[16] A trial of insulin glargine, which was added to the oral regimen versus twice daily premixed 30/70 insulin in patients with diabetes who were over 65 years of age, found that patients on glargine experienced less hypoglycemia and greater reduction in both HbA1c and fasting plasma glucose values compared with those on 30/70-insulin.[46] Insulin detemir has also been found to be associated with less risk of hypoglycemia compared with neutral protamine Hagedorn (NPH) insulin in older adults with type 2 diabetes mellitus.[47] Sliding-scale insulin is discouraged, as it can lead to more blood glucose fluctuations and hypoglycemia.[16]

Cautious titration of antidiabetic medications is essential. Among those with type 2 diabetes over the age of 50 years, whose treatment was intensified from oral monotherapy to additional oral agents or insulin, there was a U-shaped association between HbA1c and mortality such that for lower and higher HbA1c, the mortality increased, with the nadir at 7.5%.[48]

Key Points

1. *In relatively healthy older adults target HbA1c less than 7%.*
2. *In frail older adults with a limited life expectancy (<5 years), high functional dependency, multiple comorbidities, extensive history of coronary artery disease at risk for ischemia, or history of recurrent severe hypoglycemia – aim for HbA1c < 8.5% and preprandial and fasting glucose between 5 and 12 mmol/L.*
3. *Long-acting sulfonylureas such as glyburide are not recommended in older adults because of risk of severe hypoglycemia.*

Summary

The management of diabetes in older adults is complex and requires careful consideration of comorbidities, functional and cognitive status, life expectancy, and patient preferences. For many frail older adults with diabetes, intensive glycemic control may not be the best option; rather, more lenient targets may be appropriate. Older adults are often excluded from randomized controlled trials, and therefore recommendations are based on consensus guidelines. The pathophysiology of diabetes in the older adults is unique, with multiple factors contributing to an increase in the incidence and severity of hypoglycemia. Furthermore, the prevalence of diabetes in long-term care is increasing, and the management of these patients is complex.

Conclusion of Case

Glyburide was discontinued and a more appropriate agent was to be added if metformin alone did not result in a level of HbA1c less than 8.5%. A statin was added to the patient's current medications. Mr. DM also received education about diabetes, including how to manage hypoglycemia and what to do when he becomes unwell and is unable to consume adequate calories. His mood and cognition would be re-evaluated when his blood sugar levels became more stable.

Conflict of Interest

None to declare.

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