

Diabetes in the Elderly

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Abstract

With the ageing of populations even in developing countries and the epidemic of diabetes sweeping across India, elderly diabetics form a major fraction of patients in the physicians' daily practice. The clinical presentation of diabetes in this subgroup is somewhat different from the younger group of patients, and calls for emphasis on unusual features. Further, the diagnosis and management, including the choice of drugs are modified by the changed metabolism of the ageing patient. Lastly, the goals of therapy must be clearly defined keeping in mind the real danger of hypoglycemia in elderly diabetics.

INTRODUCTION

Advances in medical science and improved social conditions during the past few decades have increased the life expectancy of humans. This phenomenon of population ageing is universal. Almost 10% of the population in developed countries and 5 to 8% in the developing countries are over the age of 60 years. In India, the absolute size of the elderly population is considerable and the projected figure for the year 2001 is 70 million.¹

The prevalence of diabetes mellitus (DM) increases with age. In India, 20% of the elderly population has DM.² In addition, over 25% of older persons have impaired glucose tolerance (IGT).³ The majority of older individuals with diabetes have type 2DM.⁴

In the Diabetic Clinic at our hospital, about 45% (n= 680) are over 60 years old, with a male to female ratio of 3:2.

CARBOHYDRATE METABOLISM IN THE ELDERLY

Most studies have revealed rises in glucose levels, especially post prandial blood glucose levels that directly correlate with age. Fasting blood glucose increases by 1 to 2 mg/dL per decade, with postprandial blood glucose levels increasing up to 15 mg/dL per decade.⁶

The relative importance and mechanisms of deficient insulin secretion and action during ageing are still debated. The increased hyperglycemia may be due to delayed suppression of hepatic glucose output owing to impaired insulin release, and reduced rate of peripheral uptake. The predominant

problem of lean elderly diabetics is insulin deficiency. Obese patients have both insulin resistance and relative insulin deficiency. Major contribution also comes from extrinsic factors like diet, medication, activity, chronic illness and stress, which reduce the muscle mass and alter other organ functions resulting in glucose intolerance.⁶

DIAGNOSIS OF DIABETES IN THE ELDERLY

The current ADA guidelines for the diagnosis of DM, do not adjust glycemic criteria for age.⁷ This decision was based on the evidence that even mild hyperglycemia is associated with poor health outcomes as reported in younger individuals. Although IGT may be associated with an increased risk of cardiovascular disease, it does not predispose to chronic diabetic microvascular complications.

As post-challenge glucose levels in particular rise with increasing age, GTT is not indicated for diagnosis. The best screening test for DM in older adults is determination of fasting plasma glucose levels.⁸

Routine urine sugar testing for screening diabetes mellitus is inaccurate and is not recommended. Further, benign prostatic hyperplasia and diabetic autonomic bladder dysfunction are commonly found in elderly males and it alters the glucose content of urine due to the residual urine present in the bladder. In such patients, if at all urine sugar testing has to be done, the 'double-voiding technique' should be used. The patient should be asked to discard one sample and the next sample collected after half-hour should be used to assess urine sugar.

Because a substantial number of elderly patients have

undiagnosed diabetes, and these patients appear to have an increased incidence of macrovascular events, the current criteria recommend that a fasting glucose value be performed every 3 years in elderly patients at low risk for diabetes and yearly in patients at high risk, such as those with obesity, hypertension, family history, or the presence of complications commonly associated with diabetes.

CLINICAL PRESENTATION AND MANIFESTATIONS

Presentation of DM in the elderly may be confounding. At one extreme, routine screening is recommended, as they may be totally asymptomatic. At the other extreme, patients may have a host of dramatic symptoms attributed to other organ system problems. Urinary incontinence, mono-ocular neuropathy, and onset of sexual dysfunction are sometimes the first noticed symptoms in an elderly diabetic. They may also present with a minor infection that is difficult to control. A high index of clinical suspicion is necessary for all clinicians managing the elderly, and blood glucose concentration should be measured following any change of health status in the older people.

Several unique syndromes occur in elderly patients with diabetes. Diabetic neuropathic cachexia presents with weight loss, depression, and painful peripheral neuropathy, and generally is resolved without specific treatment in a few months. Diabetic amyotrophy occurs almost exclusively in older men with diabetes. Malignant otitis externa, a necrotizing infection usually caused by *Pseudomonas*, occurs primarily in elderly diabetics. The papillary necrosis that can occur with pyelonephritis develops primarily in this group. Spontaneously resolving intradermal bullae of the feet and the painful limitation of shoulder movements as in periartthritis of shoulder also occur. Finally, elderly persons with diabetes are at an increased risk of accidental hypothermia.^{9,10}

COMPLICATIONS OF DIABETES IN OLDER PERSONS

ACUTE METABOLIC COMPLICATIONS

Both diabetic ketoacidosis (DKA) and hyper-osmolar non-ketotic coma (HONK) can be seen in the elderly. DKA is rare and its features and management do not differ from those in younger diabetics, but its mortality is greatest in old age, particularly because of associated cardiovascular disease.¹¹

HONK almost always occurs in older people, and half the

time DM has not been previously diagnosed or treated.¹² The tendency of the elderly to develop HONK can be explained by a combination of impaired maintenance of serum osmolality, decreased thirst perception, and decreased access to water, especially in the bed-ridden, dependant patient in the setting of multiple medical problems. Reduced thirst perception renders the polydipsia less dramatic, thereby lessening recognition by self or others, ending in hyperosmolar coma.¹³ An acute infection is the most frequent predisposing factor (40 – 60%), with pneumonia being the most common infection. Other illnesses such as stroke, acute myocardial infarction, renal insufficiency, and medications such as glucocorticoids can also be predisposing factors.

Patients typically present with an altered sensorium, profound dehydration, and sometimes cardiovascular collapse. Focal neurological deficits, seizures, and central neurogenic hyperthermia that resolve with treatment can also be present. Leucocytosis is characteristic with counts up to 50,000 cells/cumm even in the absence of infection.⁶

The treatment of HONK involves frequent and careful monitoring. Although 4 – 6 liters of fluid may be needed in the first 12 hours, such rapid replacement may not be feasible in the older persons, who often exhibit poor cardiac reserve.¹⁴ In most cases, insulin and IV fluids can be safely started simultaneously. The exceptions are patients with hypokalemia or hypotension, to whom IV fluids should be given before insulin to prevent the worsening of hypokalemia or hypotension, which can occur in response to insulin and the resulting intracellular shift of glucose, potassium, and water.⁶

As a general rule, 0.1 unit of regular insulin per kilogram of body weight is given as an IV bolus, followed by an infusion of regular insulin at 0.1 U/kg/hr until blood glucose levels are reach 250 mg/dl. At this time, dextrose is added to the IV fluids and insulin infusion is decreased to 0.05 U/kg/hr. A decline in blood glucose of about 10% of the baseline value per hour is a reasonable goal in the elderly. Careful attention should be given to potassium replacement.

CHRONIC DIABETIC COMPLICATIONS

All the chronic diabetic complications develop faster in the elderly with poor glycemic control.¹⁰ A reduced insulin secretion is associated with a longer duration of diabetes and a greater prevalence of microvascular complications, while higher insulin levels are associated with the components of the metabolic syndrome.¹⁵

OCULAR COMPLICATIONS

Frequent complications include diabetic retinopathy, cataracts, and glaucoma. As most of the elder persons have cataracts, the assessment of diabetic retinopathy also becomes difficult. The prevalence of retinopathy tends to rise with age, with more than 25% of patients over 75 years presenting with retinopathy.¹⁶ Retinopathy, however, has not been correlated with age per se but with the duration of diabetes.¹⁷

NEUROPATHY

Neuropathy is the most common symptomatic chronic complication in diabetic patients and accounts for substantial morbidity in the elderly diabetic population. It is predominantly a disease of the older diabetic population, and shows a progressive course with limb amputation due to trophic ulceration as the final end-point of the disease.

The mechanisms underlying the development of diabetic neuropathy involve hyperglycemia induced metabolic abnormalities involving polyol pathway of peripheral nerve fibers and the supporting nutritive vascular supply.¹⁸ Since clinical diagnosis is often difficult due to age related changes in the peripheral and autonomic nervous system, diagnosis is based on nerve conduction studies, and autonomic function tests. Absence of ankle jerk may not be a good indicator of the presence of neuropathy in the elderly as it is absent in many non-diabetic elderly also.

Complications related to neuropathy are also commoner in the elderly diabetics. Falls are more frequent as a result of muscle weakness due to neuropathy and postural hypotension due to autonomic neuropathy. In symptomatic neuropathic patients, including those with painful neuropathy, symptomatic and palliative measures are often effective. Stepwise addition of antidepressants to simple analgesics has proven to be effective in patients with troublesome pain.¹⁸ However, the side effects caused by tricyclic antidepressants like sedation leading to falls, urinary retention in BPH, confusion and delirium must be carefully monitored for in the elderly. Other metabolic approaches like anti-oxidants and gamma-linolenic acid appear promising.¹⁹ During recent years a class of drugs has been developed that inhibits the activation of the polyol pathway in diabetic nerves. These so-called aldose reductase inhibitors hold promise for a targeted treatment regimen in the near future.¹⁸

Bladder dysfunction as a result of autonomic neuropathy is

quite common and has to be differentiated from benign prostatic hyperplasia in males. Both these conditions are responsible for the increased incidence of urinary tract infections in the elderly diabetics.

NEPHROPATHY

Advancing age and gradually falling creatinine clearance with contribution from co-existing hypertension and atherosclerosis lead to a high prevalence of nephropathy in the elderly diabetics. ACE inhibitors may be started at the stage of microalbuminuria to prevent progression to overt nephropathy. Improved metabolic control with diet and drugs has been demonstrated to reduce urinary protein excretion.²⁰

CORONARY HEART DISEASE (CHD)

Patients with type 2 diabetes have a 2 to 4 fold risk of developing cardiovascular disease. CHD is one of the major causes of death in elderly diabetics. In a study done at New Delhi, hypercholesterolemia was present in 64% and hypertriglyceridemia in 42% of elderly diabetics, with 26% having coronary artery disease.²¹ In the presence of dyslipidemia, obesity and hypertension, elderly diabetics exhibit a dramatic acceleration of atherosclerosis, with resulting CHD (Syndrome X). Hyperinsulinaemia is also an important risk factor for CHD. The presentation of CHD in these subjects is also atypical. They may have asymptomatic CHD that ends in painless myocardial infarction (MI) and acute left ventricular failure or sudden cardiac death. As a rule, every elderly diabetic presenting with acute onset of breathlessness must have an ECG done to rule out MI, even in the absence of chest pain. Furthermore, chronic breathlessness and loss of cardiac reserve may manifest in the elderly diabetic due to diabetic cardiomyopathy. Angina equivalents such as dyspnea and tiredness on exertion may replace classical anginal pain due to advanced autonomic neuropathy.

Long-term instability of fasting plasma glucose has been found to be a novel predictor of cardiovascular mortality in elderly diabetics.²²

INFECTIOUS COMPLICATIONS

Older diabetic patients often fail to mount a fever in response to infections, thereby delaying the recognition of serious infections. They are also at a high risk of developing tuberculosis.¹⁰ The presentation of tuberculosis may also be atypical with lower lobe tuberculosis or fulminant tubercular pneumonia, especially in high prevalence areas like our

country. Infections are common in diabetics due to hyperglycemia and reduced leukocyte function with impaired chemotaxis, which is more pronounced in the elderly. As mentioned earlier, UTI is quite common. Other common infections include necrotizing fasciitis, candidiasis and malignant external otitis media. Astute recognition and appropriate treatment is essential.

MONITORING

Patients should be monitored with regular laboratory evaluations, including fasting blood (or plasma) glucose determinations, to assess therapeutic response and obtain the minimum effective dosage of antidiabetic medications. Whenever possible, self-monitoring of blood glucose by the patients should be encouraged. Urine glucose concentrations correlate poorly with blood glucose, and should be avoided. Following initiation of treatment and subsequent dosage titration, control can be determined by evaluating glycosylated hemoglobin (HbA_{1c}) levels at intervals of approximately 3 months.

MANAGEMENT

As with any older patient, a holistic approach is needed in the context of the overall health, lifestyle, environment, and wishes.²³ For younger patients, many consider aggressive care with the goal of achieving euglycemia as the standard therapy. But in the older diabetic, there are two levels of care - basic and aggressive. Basic care is indicated for those individuals in whom the primary goal of treatment is the prevention of symptomatic hyperglycemia. The average glucose levels to achieve this goal are approximately 200 mg/dl of postprandial sugar or the level at which glycosuria is minimal. The elimination of glycosuria is important, as this predisposes the diabetic to volume depletion, hypotension and poor tissue perfusion. Glycosuria also causes weight loss due to loss of calories in the urine, catabolic state, loss of lean body tissue and may predispose to infections and other complications of malnutrition.

Aggressive care is appropriate when the goals of treatment include the prevention of long-term complications. Euglycemia with a fasting glucose level less than 110 mg/dl is optimal, with normal levels of glycosylated hemoglobin. There are several benefits of euglycemia, both immediate and long term (Table1).

TABLE 1: BENEFITS OF EUGLYCEMIA

Immediate:

- Less nocturia, polyuria and hypovolemia.

- Better leukocyte function and chemotaxis, hence, fewer infections
- Better wound healing

Long term:

- Slower progression of retinopathy, cataracts, neuropathy and nephropathy
- Reduced lipoprotein A and glycosylated hemoglobin, with resultant reduction in cardiovascular mortality.

The decision regarding the treatment goals is the most important in the management of DM in the elderly. The patient and the treating physician should make this decision jointly. Current medical problems and the estimated life expectancy have to be kept in mind while deciding on the type care to be given. Until further studies are available that can help us in deciding the type of care to be given to the elderly, many elderly patients deserve the same consideration as younger adults regarding aggressive management of their disease. Age per se should not be considered as an indication for providing only basic care to any elderly diabetic.

Regardless of the treatment goals decided, all older diabetics should receive care that meets minimum standards as shown in Table 2. The four standard modalities of diabetes treatment – diet, exercise, oral hypoglycemic agents, and insulin – all merit consideration in older diabetics also. Pharmacological therapy of an elderly diabetic poses many problems. Drugs may be used inappropriately, when the effects of treatment may be worse than the symptoms for which it was given. Polypharmacy is a common problem, often due to the presence of multiple co-existing diseases, but sometimes drugs are prescribed by several doctors who are not individually aware of the patient's other medications, leading a host of drug interactions. Drug compliance is also poor in the elderly due to deficient memory, sight or hearing, or due to unacceptable adverse effects. Pharmacodynamics of many drugs is altered in the elderly due to many physiologic changes, increasing the propensity for drug toxicity.

TABLE 2: MINIMUM STANDARDS OF CARE FOR OLDER ADULTS WITH DIABETES MELLITUS

Initial Evaluation

- Complete history and physical examination
- Geriatric assessment (functional assessment)
- Laboratory examination: fasting blood glucose, glycosylated hemoglobin, fasting lipid profile, creatinine, urinalysis, and ECG.
- Ophthalmological evaluation
- Dietary assessment

Continuing Care

- Use of treatment as needed to meet target glucose levels
- Assessment of blood glucose levels as frequently as needed to make sure that goals are being met
- Annual assessment for diabetic complications
- Annual review of geriatric (functional) assessment

The American Diabetic Association (ADA) has set a target fasting blood glucose of <120 mg/dl and a hemoglobin A1c level within 1% of the upper limit of normal as a therapeutic goal of diabetes management. Although the ADA has indicated that age per se should not be an excuse for suboptimal control of blood glucose, it may be neither feasible nor appropriate to attempt to achieve such tight control in many older patients with DM. Thus the goals of diabetes management in older adults should be individualized. Factors such as patient's estimated life expectancy, coexistent medical condition, economic issues, and availability of support services should always be considered when setting therapeutic goals in elderly diabetics.

Finding from the UKPDS study showed that tight diabetic control in individuals with type 2 diabetes was associated with lower micro vascular complications. Tight glucose control in the UKPDS, however, resulted in only marginal reduction in the incidence of macro vascular complications (16%) that did not achieve statistical significance (UKPDS, 1998). This smaller effect of tight glycemic control on the frequency of cardiovascular complication in individuals with type 2 DM greatly emphasize the importance of managing other cardiovascular risk factor such as hypertension, smoking, dyslipidaemia and central obesity in these patients to minimize the incidence of cardiovascular disease, the

primary killer of patients with type 2 DM.

DIET

Many elderly are managed with diet alone with various degrees of success. But, the elderly may find it more difficult to adhere to a strict dietary regimen than young adults. Moreover, there are many special considerations in the elderly like financial difficulties, mobility problems, poor food preparation skills, long-standing dietary habits, difficulty in following dietary instructions, decreased sense of taste and increased frequency of constipation, which hinder their ability and motivation to follow the advised dietary protocol.²⁴ It is important to tailor the dietary advice to the individual patient. Unnecessarily strict dietary control in a very old person with a short life expectancy may reduce the quality of life without any significant therapeutic benefits.²⁵

No specific modifications in the diet is currently recommended by the ADA have been recommended for older diabetics. However, vitamin and mineral supplements are indicated when the caloric intake falls below 1000 kilocalories per day to prevent deficiency syndromes.⁸

EXERCISE

The role of exercise as therapy in elderly diabetics is controversial. One study suggests that exercise, as a significant therapy for control of DM may not be feasible for older adults.²⁶

There are many potential benefits along with certain risks (Table 3). Most of the benefits are related to the improvements in the risk factors for cardiovascular disease, which is a significant complication of diabetes in the elderly. Because of the prevalence of silent coronary artery disease in this population, older adults with diabetes should undergo an exercise tolerance test in consultation with their treating physicians before they begin any exercise programme. The level of exercise be gradually increased and tailored to the exercise capacity of the patient. Patients must wear proper footwear during exercise, and care must be taken to avoid injury and falls that can be disastrous in the elderly. Hypoglycemia must be avoided by adequate snacks before starting the exercise.

Figure 1

Table 3: Potential benefits and risks of exercise in elderly diabetics. 8

Benefits	Risks
Improved exercise tolerance	Sudden cardiac death
Improved glucose tolerance	Foot and joint injuries
Improved maximal O ₂ consumption	Hypoglycemia
Increased muscle strength	
Decreased blood pressure	
Decreased body fat	
Increased muscle mass	
Improved lipid profile	
Improved sense of well being	

SULFONYLUREAS

Approximately 70% of the prescriptions for these anti-diabetics are for individuals over the age of 60 years.²⁷ The safety profile and easy dosage schedule make sulfonylureas the cornerstone of therapy in the treatment of type-2 DM in the elderly. Because type 1 DM is uncommon in older adults, most are eligible for a trial of oral agents when dietary management fails.⁸

Hypoglycemia, however, is a major safety concern with sulfonylureas. Up to 20% of patients taking sulfonylureas experience symptoms of hypoglycemia over a six-month period.²⁸ There are multiple factors associated with ageing that increase the risk of hypoglycemia, including the age related alteration of hepatic and renal functions that alter drug metabolism and excretion. Ageing is also associated with impairments in the autonomic nervous system and reductions in α -adrenergic receptor function suggesting decreased response to hypoglycemia in the elderly. This can be dangerous as they may not present with warning symptoms such as tremors, sweating or palpitation and may directly come with neuroglycopenic symptoms such as convulsions, focal neurological deficits or coma. The elderly are frequent users of drugs that are known to increase the risk for hypoglycemia, including β -blockers, salicylates, warfarin, sulfonamides, tricyclic anti-depressants and alcohol. Many elderly persons receive inadequate education regarding the signs and symptoms of hypoglycemia.²⁹ Severe hypoglycemia may follow glibenclamide use in the elderly. Metabolism of this drug yields two active metabolites, and in the elderly, the clearance of these metabolites appears delayed. For this reason, glipizide and gliclazide, which have shorter half-lives and few or no active metabolites, are

preferred sulfonylurea agents in the elderly diabetics.⁶

One more concern with sulfonylurea therapy has been the ability of these agents to cause vasoconstriction of small vessels, including the coronary arteries. The latest generation sulfonylurea, glimepiride, appears to be more selective than the earlier agents. Besides exhibiting less hypoglycemia compared to glibenclamide, this drug appears to be more specific for islet cell potassium channels. Thus, in contrast to earlier sulfonylureas, glimepiride is less likely to produce coronary artery vasoconstriction.⁶ Sulfonylurea tablets should be taken half-hour before meals. The drug should be started at a low dose, about half of the standard, and gradually increased if required.³⁰

BIGUANIDES

In overweight and obese diabetics, with normal renal functions and stable cardio-respiratory status, biguanides can be used if diet alone is not sufficient or as an add-on therapy with sulfonylureas. When used alone, they do not produce hypoglycemia. Metformin should not be used in conditions that are associated with increased generation of lactate or its decreased clearance, such as renal insufficiency, hepatic disease, alcoholism, severe congestive cardiac failure, severe peripheral vascular disease, and severe chronic obstructive pulmonary disease.³¹ Metformin should be administered immediately after meals to avoid gastrointestinal disturbances. Starting with a smaller dose can reduce this adverse effect.³⁰

■ - GLUCOSIDASE INHIBITORS

Acarbose is an ■ - glucosidase inhibitor and reduces post-prandial hyperglycemia with lesser effect on fasting glucose levels. The advantage of acarbose in the elderly is its safety profile. However, gastrointestinal disturbance is the major adverse effect of acarbose. Starting with a smaller dose and gradually increasing the dosage if required can minimize this.

REPAGLINIDE

Repaglinide is a short-acting insulinotropic antidiabetic agent. Acting principally by augmenting endogenous insulin secretion from the pancreas in response to a meal, this controls the postprandial glucose excursions.³² This is a short- acting drug and can be taken with meals. The safety and efficacy of repaglinide appear to be similar in geriatric and younger patients.

THIAZOLIDINEDIONES

There are currently three drugs in this group – troglitazone, rosiglitazone and pioglitazone – of which the former has been withdrawn due to fatal hepatotoxicity. At present, there is no evidence that the latter two drugs have a similar hepatotoxicity, but precaution should be taken in patients with liver dysfunction. These are used alone (monotherapy) or in combination with sulfonylureas, metformin, or insulin for the management of type 2 DM.³⁴ They act principally by increasing insulin sensitivity in target tissues, as well as decreasing hepatic gluconeogenesis. These are insulin sensitizers that act without stimulating insulin release from pancreatic beta cells, thus avoiding the risk of hypoglycemia. Hence these may be well suited for use in the elderly. The clinical usage recommendations and pharmacokinetics of thiazolidinediones in the elderly are similar to those in the younger diabetics.^{34,35} However, cardiac function must be assessed in all patients before starting these drugs as they can precipitate cardiac failure in patients with cardiac dysfunction. Liver enzymes should be monitored monthly for the first six months, every two months for the next 6 months, and every 3 to 6 months thereafter. Troglitazone has been withdrawn from the market in the US and most of Europe because of serious drug-related hepatic toxicity.

INSULIN

Insulin is indicated when treatment goals are not being met with diet, exercise, and oral medications. No specific regimen or form of insulin has been identified as particularly advantageous to the elderly. It is difficult to achieve euglycemia with a single daily dose of intermediate acting insulin.⁶ Although always a stressful therapy to initiate, insulin injections for the elderly can be particularly complex, predisposing to medication error. Problems include visual impairment and difficulty in drawing and injecting the exact dose of insulin, impaired manual dexterity, decreased sensation in the hands, limited access to injection sites, and difficulties in monitoring blood glucose. However, none of these considerations are absolute contraindications to insulin therapy, solutions can usually be found for each.⁸

INSULIN ANALOGUES

Insulin lispro is an analogue that has a more rapid onset and shorter duration of action compared with regular insulin. Therefore, it is associated with greater relative reductions in postprandial blood glucose concentrations and may provide greater patient convenience in terms of the timing of insulin injections in relation to meals with the added benefit of less

incidences of hypoglycemia. This is a specific advantage in the elderly as patients can be advised to take insulin immediately before meals precluding the need to wait for half-hour after taking injection.³⁷

In conjunction with long-acting insulin, such as insulin glargine or ultralente insulin, the rapid-acting analogues provide tight control of blood glucose levels throughout the day. Insulin glargine has a nearly peakless profile and lasts from more than 24 hours.³⁸ For geriatric use the initial dosage, dose increments, and maintenance dosage should be conservative to avoid hypoglycemia.

CONCLUSION

As age advances, the quality of life becomes more important than the length of life. A well-controlled elderly diabetic who has no major complications, and is adept at self-care, should be the goal of all physicians treating diabetic patients.

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