Review Article

Diabetes Mellitus in Elderly - An Overview

I Subramaniam*, J Levins Danny Gold**

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Introduction

The prevalence of diabetes mellitus increases with age in all populations. Type 2 diabetes mellitus is age related, affecting nearly 1 in 5 individuals over the age of 65 years. The prevalence of diabetes increases with age and it peaks at 60-69 years of age. With the demographic transition and population aging, diabetes mellitus will be a major public health problem in India. Management of elderly type 2 diabetes mellitus will include diet and low dose oral hypoglycemic agents, while few may require insulin.[1-5]

Carbohydrate metabolism in elderly diabetics

Most studies reveal that both fasting and post prandial blood glucose show an increase in the level as age advances. Fasting blood glucose increases by 1-2 mg per dl. per decade while post prandial glucose increases by up to 15 mg per dl. per decade increase in age.[1] Studies have concluded that the problem with elderly patients with diabetes is insulin deficiency and that obese elderly patients with diabetes have both insulin resistance and relative insulin deficiency.[6] The factors responsible for diabetes in the elderly are intrinsic as well as extrinsic. The intrinsic factors are beta cell dysfunction, obesity, insulin resistance and genetics. The extrinsic factors are stress, illness and drugs.[3]

Disease presentation and manifestations

Routine blood glucose screening is recommended in elderly patients as they are mostly asymptomatic. They may present with urinary incontinence, weight loss and weakness. Weight loss may reflect glucose loss as well as poor intake due to anorexia. Thirst perception is decreased in the elderly and polydipsia is less dramatic. Elderly diabetics may present with atypical features like orthostasis, unsteadiness and confusion.[4,7]

* Professor & Head, ** Senior Resident, Department of Medicine, Rajah Muthian Medical College and Hospital, Annamalainagar, Chidambaram, Tamilnadu

Address for correspondence:
Dr. I Subramaniam, MD
No. 78, Link Road, PO Panruti, Pin No. 607106, Distt. Cuddalore, Tamilnadu. India email: *mani2003md@yahoo.com*

Several specific syndromes in the elderly diabetics have been described.

1) Painful shoulder periarthrosis: This is seen in 10% of patients with moderate to severe motion limitation at the glenohumeral joint.[8,9]

2) Diabetic amyotrophy: This consists of asymmetric weakness, pain and wasting of the pelvic girdle and thigh muscles with minimal sensory changes. This condition is transient with spontaneous resolution within a year.[9,10]

3) Diabetic neuropathic cachexia: Elderly diabetics present with painful peripheral neuropathy, dramatic weight loss and depression. This also abates within a year.[11]

4) Diabetic dermopathy: Elderly diabetics can present with epidermal bullae of the feet. It resolves spontaneously.[9]

5) The increased frequency of depression, anxiety and forgetfulness has also been reported in older patients with diabetes mellitus.[7,12]

6) The combination of decreased muscle mass, decreased shivering, diminished peripheral blood flow, high surface to body mass ratio and impaired autonomic nervous system makes older patients with diabetes mellitus more prone to hypothermia.[4,9]

7) Renal papillary necrosis is common in old diabetics but it presents without flank pain or high fever.[10,13]

8) Older diabetics especially those in nursing homes are at high risk for tuberculosis.[9,10]

9) Serious infections such as malignant otitis externa owing to pseudomonas aeruginosa or polymicrobial necrotizing fascitis may occur in elderly diabetics.[9,10]

Diagnosis

Diabetes mellitus is present when 1) fasting blood sugar is more than 126 mg per dl 2) random blood sugar is more than 200 mg per dl. 3) two hour post prandial blood sugar after 75 grams of glucose is more than 200 mg per dl.[14]

Routine blood sugar testing should be done in individuals over 45 years every three yearly.[13] Hemoglobin Alc has low sensitivity and specificity in the elderly.[13] Serum fructosamine is an alternative screening test that is well standardized in the young but the data is limited in elderly.[9,15,16]

Hyperglycemic hyperosmolar non-ketotic syndrome (HHNS)

HHNS is a state of acute illness marked by dehydration and a blood glucose level greater than 600 mg per dl. together with a serum osmolality of more than 320 milli osmoles per kg, a serum pH greater than 7.3 and bicarbonate of 20 milli equivalent per liter or more. Blood urea nitrogen and creatinine are elevated. The anion gap is usually 15 milli equivalent or less and ketones are usually absent.[17,18]

The mechanism responsible for HHNS in the elderly diabetics are:

1) High levels of insulin reserve in HHNS prevents lipolysis but is inadequate to prevent hepatic glucose production.
2) Lower levels of counter regulatory hormones and free fatty acids.
3) Inhibition of lipolysis by the hyperglycemic osmolar state.[18]

Both diabetic ketoacidosis and HHNS can be seen in the elderly and in persons with type 1 and type 2 diabetes.[5] The tendency of the elderly to develop HHNS can be explained by a combination of age related impaired maintenance of serum osmolality, decreased thirst sensation and decreased access to water especially in the bed ridden dependent patient in the setting of multiple medical problems.[5] Acute infection like pneumonia is the commonest predisposing factor in 40 to 60 % of patients having HHNS. Other factors like stroke, myocardial infarction, renal insufficiency and medications like glucocorticoids are also predisposing conditions.[5,18] The onset of HHNS can be preceded by days or weeks of polyuria, polydipsia and weakness.

Patients typically present with:

1) altered sensorium
2) profound dehydration
3) cardiovascular collapse
4) focal neurological deficits
5) seizures
6) central hyperthermia
7) leukocytosis (may go upto 50,000 per cubic millimeter)

Treatment of HHNS:

1) replenish plasma volume
2) correct electrolyte imbalance
3) lower glucose towards normal
4) diagnose and treat the precipitating factors like infections

If circulatory collapse or severe hypotension is present normal saline is given initially. Half normal saline is administered to correct the water deficit. 4-6 liters of fluids may be needed in first 12 hours. Care should be taken in the elderly as they have poor cardiac reserve.[19,20]

As a general rule, 0.1 unit of regular insulin per kilogram of bodyweight is given intravenously as a bolus. This is followed by an infusion of regular insulin at 0.1 unit per kilogram of body weight per hour until blood glucose level reaches 250 mg per deciliter. After the blood glucose level goes below 250 mg per deciliter, dextrose saline is added to the intravenous fluid and insulin infusion is decreased to 0.05 units per kilogram body weight per hour. A decline of serum glucose of 10% per hour is a reasonable goal. Serum potassium replenishment should be done carefully. The general rule is that total body potassium is depleted despite a normal potassium level. Potassium chloride can be added early even in the presence of normal potassium level as long as urine output is maintained.[18]

Chronic Complications and glycemic control

Retinopathy, macroangiopathy, neuropathy and nephropathy develop faster in elderly diabetics with poor glycemic control.[9,21,22,23,24] Cardiac mortality and morbidity are higher in persons with elevated hemoglobin Alc.[19] Diabetes mellitus in the elderly is also associated with abnormal left ventricular function and structure.[25] Older patients with type 2 diabetes are also at a greater risk for cerebrovascular accidents.[26] Poor glycemic control contributes to retinopathy development and progression in the elderly.[27,28,29] In addition to the greater risk for retinopathy, older diabetics are also at higher risk for blindness from cataracts, macular degeneration and glaucoma than younger diabetic patients.[5]

Long term managment

Treatment of older diabetics is directed towards two goals.[30]

1) prevention of acute symptoms and acute complications like hyperosmolar coma and hypoglycemia.

2) prevention of chronic complications like retinopathy and nephropathy.

Good control of diabetes in elderly leads to:[31]

a) less nocturia, polyuria and hypovolemia
b) fewer infections and better wound healing
c) slower progression of retinopathy and cataract
d) slower progression of nephropathy and neuropathy
e) better control of dyslipidemia.

The criterias for better control of diabetes mellitus in the elderly include:

- Hemoglobin Alc less than 1% of the upper limit of normal
- Fasting blood glucose upto 140 mg per dl.
- Post prandial glucose upto 180 mg per dl.

Diet

Diet forms the fundamental aspect of therapy. Ideally, 25-30 calories per kilogram body weight should be the aim of a diabetic diet. Out of them, 55 to 60% of calories should be in the form of carbohydrates especially complex carbohydrates like whole grain cereals, pulses, beans, vegetables and salads. Twenty five percent of the calories should be in the form of fats. Protein should be taken at about 0.8 gram per kilogram body weight. 30-40 grams per day of naturally occurring dietary fibers have been found to be beneficial.[33] Therefore the entire success of dietary modifications in a diabetic subject depends on the judicious selection of carbohydrates, moderation in protein intake and a determined restriction of total fat intake.[34]

Exercise

Exercise has been found to be beneficial in many studies in people with diabetes mellitus. Exercise has been found to lower fasting glucose and hemoglobin Alc levels. It helps to improve glycemic control by increasing insulin sensitivity, maintaining body weight, reducing cardiovascular risk factors and inducing a sense of well being. Aerobic exercises like walking is more effective than isometric exercises in improving the glycemic status.[34]

Drug Therapy

Therapy is usually started with oral agents, failing which insulin is administered. The initial oral agent is usually one of the sulphonylureas. Sulphonylureas inhibit adenosine triphosphate sensitive potassium channels in the pancreatic beta cell plasma membrane resulting in depolarization and secretion of insulin.[35,36] The second generation sulphonylureas (glyburide and glipizide) are now preferred over the first generation drugs owing to fewer interactions and a more favorable safety profile. Liver metabolism of glyburide yields two active metabolites and in elderly the clearance of these metabolites is delayed.[37,38] Glipizide and gliclazide having a shorter half life with few or no active metabolites are preferred sulphonylureas in elderly diabetics. In particular glipizide with the osmotic gastro intestinal therapeutic delivery system is the least likely to be associated with hypoglycemia. The latest generation sulphonylurea (glimepiride) besides stimulating the release of insulin from functioning pancreatic beta cells has additional extrapancreatic effects.

Alpha glucosidase inhibitors such as acarbose retard the digestion of complex carbohydrates and disaccharides to absorbable monosaccharide by inhibiting alpha glucosidase in the intestinal brush border. This results in decreased post prandial glucose levels and a modest reduction in hemoglobin Alc levels.[39,40] Mild abdominal discomfort and flatulence are common side effects. It usually does not produce hypoglycemia, therefore can be used in the frail elderly.[13,26,36,39]

Metformin is a biguanide that decreases hepatic glucose release and increases muscle glucose uptake. In contrast to sulphonylureas which promote weight gain, metformin therapy is associated with weight loss.[41] Metformin also lowers coronary ischemic attack by lowering triglycerides and LDL cholesterol and in increasing high density lipoprotein.[42] The side effects of metformin are abdominal discomfort, anorexia, diarrhea and lactic acidosis. Metformin should not be used in conditions that are associated with increased production or decreased clearance of lactate such as renal insufficiency, hepatic disease, alcoholism, severe congestive heart failure and chronic obstructive pulmonary disease. Metformin therapy should be discontinued in serious infections, major surgery or radiologic procedures involving parenteral contrast administration. The potential risk of lactic

acidosis cautions it's use in frail elderly prone for lactic acidosis.[36,43,44] Metformin should not be used when serum creatinine exceeds 1.5 mg per dl in men and 1.2 mg per dl in women.

Thiazolidinediones enhance insulin sensitivity and also have a beneficial effect on lipids, decreasing triglycerides and increasing high density lipoproteins levels. These compounds interact with a group of nuclear receptors known as peroxisome proliferator-activated receptor-gamma (PPARγ).[45] The glitazones lower circulating insulin relative to plasma glucose but do not return glucose levels to normal. They appear to be useful in combination with other drugs rather than used alone. The glitazones have a synergistic action with that of metformin. Rosiglitazone and pioglitazone are currently approved agents. Water retention, weight gain and anemia are occasional side effects. Regular monitoring of liver enzymes should be done.

Meglitinides are the new class of insulin secretogogues. It acts by closure of the K^+ ATP channels in the beta cells. Repaglinide belongs to this group and it promotes insulin secretion in response to meals. This reduces in between meals hypoglycemia.

Insulin is indicated when treatment goals are not being met with diet, exercise and oral agents. It is stressful to initiate insulin injection for the elderly because of visual impairment, difficulty in drawing and injecting the exact dose of insulin due to decreased manual dexterity.[46,47] Furthermore hypoglycemia in the elderly can be associated with severe psychomotor deficits and altered counter regulatory hormone responses.[32,48,49]

With the advent of new therapeutic options for diabetes, it is feasible to tighten the glycaemic control in elderly with minimal risk of hypoglycemia.[50]

References

1 Morrow LA, Halter JB. Treatment of the elderly with diabetes. In Kahn CR, Weir GC (eds): Joslin's diabetes mellitus ed 13. Malvern PA, Lea and Febiger, 1994.

2 National public health institute, Helsinki, Finland. Age and sex - specific prevalence of diabetes and impaired glucose regulation in 11 Asian cohorts. *Diabetes Care* 2003, 26: 1770-1780

3 Hiltunen L, Kukinen H, Koski K, et al. Prevalence of diabetes mellitus in an elderly Finnish population. *Diabet Med* 1994; 11: 241-249.

4 Hogikyan RV, Halter JB. Aging and diabetes. In Porte D Jr, Sherwin RS (eds): Ellenberg and Rifkin's diabetes, Ed 5, Stamford CT, Appleton and Lange, 1997.

5 Singh I, Marshall Jr. Diabetes mellitus in the elderly. *Endocrinol Metab Clin North Am* 1995, 24: 255-272.

6 Meneilly GS, Dawson K, Tessier D. Alterations in the glucose metabolism in the elderly patients with diabetes. *Diabetes Care*, 1993; 16: 1241-1247.

7 Hiltunen.L, Keinanen, Laara E, et al. Self perceived health and symptoms of elderly persons with diabetes and impaired glucose tolerance. *Age Ageing* 1996; 25: 59-66.

8 Freidman NA, Laban MM. Periarthrosis of the shoulder associated with diabetes mellitus. *Am J Phys Med Rehabil* 1989; 68: 12-14.

9 Morley JE ,Kaiser FE. Unique aspects of diabetes mellitus in the elderly. *Clin Geratr Med* 1990; 6: 693-702

10 Morley JE, Mooradian AD, Rosenthal MJ, et al. Diabetes mellitus patients. Is it different? *Am J Geriatr Soc* 1994; 42: 965-967.

11 Ellenberg M. Diabetic neuropathic cachexia. *Diabetes* 1974; 23: 418-423.

12 Konen JC, Curtis LG, Summerson JH. Symptoms and complications of adult diabetic patients in a family practice. *Arch Fam Med* 1996; 5: 135-145.

13 Meneilly GS, Tessier D. Diabetes in the elderly. *Diabet Med* 1995; 12: 949-960.

14 Expert Committee on the diagnosis and classification of diabetes mellitus: report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* 1997; 20: 1183-1197.

15 Cefalu WT, Ettinger WH, Bell-Farrow AD, et al. Serum fructosamine as a screening test for diabetes in the elderly. A pilot study. *J Am Geriatr Soc* 1993; 41: 1090-1094.

16 Negoro H, Morley JE, Rosenthal MJ. Utility of serum fructosamine as a measure of glycemia in young and old diabetes and non-diabetic subjects. *Am J Med* 1988 85: 360-364.

17 Greene DA. Acute and chronic complications of diabetes in older patients. *Am J Med* 1986; 80: 39-53.

18 Umpierez GE, Khajavi M, KitabchI AE. Diabetic ketoacidosis and hyperglycemic hyperosmolar non ketotic syndrome. *Am J Med Sci* 1996; 311: 225-233.

19 Kuusito J, Mykkanen L, Pyorala K, et al. NIDDM and its metabolic control predict coronary heart disease in the elderly subjects. *Diabetes* 1994; 43: 960-967.

20 Lalau JD, Vermersch A, Hary L, et al. Type 2 diabetes in the elderly. An assessment of metformin. *Int J Clin Pharmacol Ther Toxicol* 1990; 28: 329-332.

21 Morisaki N, Yokote K, Tashiro J, et al. Lipoprotein (a) is a risk factor for diabetic retinopathy in the elderly. *J Am Geriatrics Soc* 1994; 42: 965-967.

22 Mykkanen L, Laakso M, Pyorala K. Asymptomatic hyperglycemia and atherosclerotic vascular disease in the elderly. *Diabetes Care* 1992; 15: 1020-1030.

23 Nathan DM.Singer DE, Godine JE, et al. Retinopathy in older type 2 diabetics. Association with glucose control. *Diabetes* 1986; 35: 797-801.

24 Rius F, Pizarro E, Salinas I, et al. Age as a determinant of glomerular filtration rate in non-insulin dependent diabetes mellitus. *Nephrol Dial Transplant* 1995; 10:1644-1647.

25 Lee M, Gardin JM, Lynch JC, et al. Diabetes mellitus and echocardiographic left ventricular function in free living elderly men and women. The cardiovascular health study. *Am Heart J*. 1997; 133: 36-43.

26 Mankovsky BN, Metzger BE, Moltch ME, et al. Cerebrovascular disorders in patients with diabetes mellitus. *J Diabetes complications* 1996; 10: 228-242.

27 Frank KJ, Dieckert JP: Diabetic eye disease. A primary care perspective. *South Med J* 1996; 89: 463-470.

28 Morisaki N, Watanabe S, Kobayashi J, et al. Diabetic control and progression of retinopathy in elderly patients: five year follow up study. *J Am Geriatr Soc* 1994; 42: 142-145.

29 Nguyen HT, Luzio SD, Dolben J, et al. Dominant risk factors for retinopathy at clinical diagnosis in patients with type 2 diabetes mellitus. *J Diabetes Complications* 1996; 10: 211-219.

30 Henry RR, Genuth S. Current recommendations about intensification of metabolic control in non- insulin dependent diabetes mellitus. *Ann Intern Med* 1996; 124: 175-177.

31 Bohannon NJV, Jack DB, Type 2 diabetes: Tips for managing your older patients. *Geriatrics* 1996; 51: 28-35.

32 Meneilly GS, Cheung E, Tuokko H, Counter regulatory hormone responses to hypoglycemia in the elderly patients with diabetes. *Diabetes* 1994; 403-410.

33 Coulston AM, Mandelbaum D,Reaven GM. Dietary Management of nursing home residents with non-insulin dependent diabetes mellitus. *Am J Clin Nutr* 1990; 51:67-71.

34 Shah SN, Phatak RB. Management of diabetes mellitus. API Textbook of Medicine 7th edition; Chapter 18: 1108.

35 Bloomgarden ZT. New and traditional treatment of glycemia in NIDDM. *Diabetes Care* 1996; 19: 295-299.

36 Mooradian AD. Drug therapy of non-insulin diabetes mellitus in the elderly. *Drugs* 1996; 51:931-941.

37 Seltzer HS. Drug induced hypoglycemia; a review of 1418 cases. *Endocrinal Metab Clin North Am* 1989; 18: 163-183.

38 Sonnenblick M, Shilo S, Glibenclamide induced prolonged hypoglycemia. *Age Ageing* 1986; 15: 185-189.

39 Chiasson JL, Josse RG, Hunt JA, et al. The efficacy of acarbose in the treatment of patients with non-insulin diabetes mellitus. *Ann. Intern Med* 1994; 121: 928-935.

40 Rosskamp R. Safety aspects of oral hypoglycemic agents. *Diabetolgia*1996; 39: 1668-1672.

41 Defrenzo RA, Goodman AM. Multicenter metformin study group. Efficacy of metformin in patients with non-insulin dependent diabetes mellitus. *N Engl J Med* 1995; 333: 541-549.

42 Fontbonne A, Charles MA, Juhan I, et al. The effect of metformin on the metabolic abnormalities associated with upper body fat distribution. *Diabetes Care* 1996; 19: 920-926.

43 Davidson MB, Peters A. An overview of metformin in the treatment of diabetes mellitus. *Am J Med* 1997; 102: 99-110.

44 Sulkin TV, Bosman D, Krentz AJ. Contraindications to metformin therapy in patients with NIDDM. *Diabetes Care* 1997; 20: 925-928.

45 Saltiel AR, Olefsky JM. Thiazolidinediones in the treatment of insulin resistance and type 2 diabetes. *Diabetes* 1996; 45: 1661-1669.

46 Bembaum M, Albert SG, Mcginnis J, et al. The reliability of self blood glucose monitoring in elderly diabetic patients. *J Am Geriatr Soc* 1994; 42: 779-781.

47 Cusi K,Cunningham GR, Comstock JP. Safety and efficacy of normalizing fasting glucose with bed time NPH insulin alone in NIDDM. *Diabetes Care* 1995; 18: 843-851.

48 Meneilly GS, Cheung E, Tuokko H. Altered responses to hypoglycemia of healthy elderly people. *J Clin Endocrinol Metab* 1994; 78: 1341-1348.

49 Shorr RI, Ray WA, Daugherty JR, et al. Incidence and risk factor for serious hypoglycemia in older persons using sulphonylureas or insulin. *Arch Intern Med,* 1997; 157: 1681-1686.

50 Bamett AH, Owens DR. Insulin analogues. *Lancet* 1997; 349: 47-51.