Diabetes in Old Age : An Emerging Epidemic

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Abstract

Diabetes in the elderly is emerging as one of the most important public health problems of the 21st century. In developing countries, the majority of people with diabetes are in the age range of 45-64 years. A better understanding on the pathogenesis of diabetes in the aging population is required to successfully treat and prevent its devastating complications. Changes in body composition with accumulation of fat in the abdomen is a key factor in the causation of diabetes in the aging population. The size and strength of skeletal muscle, a major tissue involved in glucose metabolism, also declines leading to muscle weakness and a reduction in physical activity. These changes lead to marked reduction in energy expenditure and abdominal fat accumulation causing insulin resistance. Recent evidence suggests that four months of aerobic exercise can improve muscle oxidative capacity similarly in younger and older people, but that insulin sensitivity is less likely to improve in older people. It appears that older people need to exercise more frequently to improve their insulin sensitivity. Diagnosis and management of diabetes in the elderly requires special attention since age, genetics, body composition and lifestyle factors all interact. Increasing evidence suggests that postprandial hyperglycemia is more sensitive to diagnose diabetes in elderly people than in the young. Age related changes in body function and cognition demand special caution in the selection of hypoglycemic drugs in the elderly. Targets of diabetes therapy in the elderly have to be individualized, considering the age of the patient, remaining life-expectancy and severity of co-morbid conditions. Short acting insulin secretogogues are preferred to avoid prolonged and frequent hypoglycemia. Judicious choice of insulin sensitizers, timely introduction of insulin, meticulous control of hypertension and hyperlipidemia are critical to prevent complications.

Introduction

We start to grow old the day we are born. Growing old is a common destiny of all species. With increasing life expectancy, the numbers of older people are growing in our society. There are many illnesses that occur in association with age. Type 2 diabetes is the classical example of a disease that increases with age. Changes in lifestyle, including diet and physical activity, and the increasing numbers of elderly people are both key factors for the worldwide epidemic of diabetes. Diabetes in the elderly is emerging as one of the most important public health problems of the 21st century.[1] Diabetes and its complications take a major toll on the quality of life of the elderly and the health care costs of the society.[2] Both diabetes and aging increase the risk for arteriosclerosis and cardiovascular mortality. Diabetes further increases the risk of cardiovascular mortality in older people.[3]

Spence in 1920 was the first to document impairment of glucose metabolism in subjects over the age of 60 years.[4] The cause for increased occurrence of type 2 diabetes and impaired glucose tolerance in the elderly population remains to be clearly defined. A better understanding of the underlying mechanisms responsible for diabetes in old age is critical to develop strategies to treat elderly with diabetes and to prevent the disease. The management of older people with diabetes requires special care and attention.

Age per se should not be a reason for sub-optimal control of blood glucose.[5] Although no studies have specifically addressed glycemic control in individuals above the age of 60 years, the UKPDS[6,7] included a substantial number of older persons, indicating the benefit of providing such treatment in all ages.

The current review will discuss the pathophysiology of diabetes in the elderly, the preventive and treatment approaches and its complications.

Aging And Diabetes- Epidemiology

The vast majority of cases of diabetes in the elderly are type 2. However, healthcare for people with type 1 diabetes has improved and now there are increasing numbers who are

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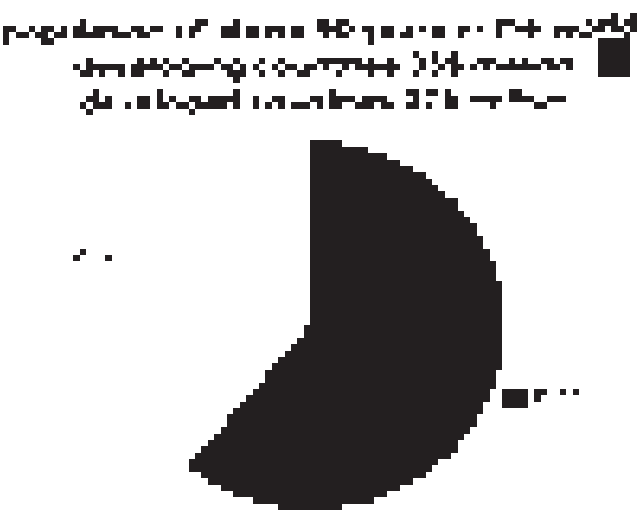

Fig. 1 : World population of elderly people. Data from WHO statistics.[9] 61% of people older than 60 years of age live in developing nations.

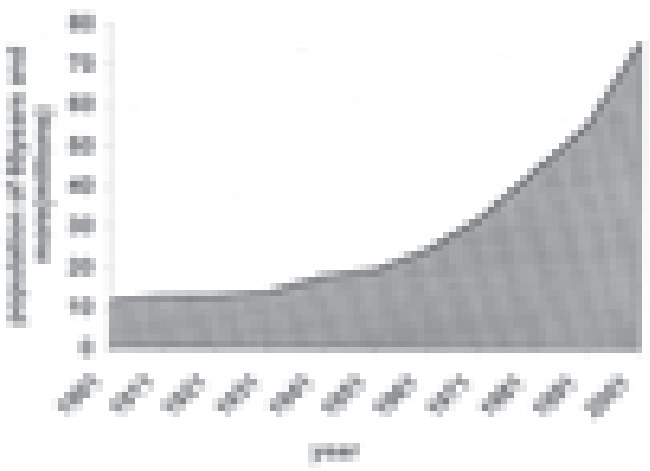

Fig. 2 : Growth of the elderly population in India from 1901-2001. Data obtained from 96.

entering into the geriatric age group.[8]

Of the approximately 580 million elderly people (60 years and more) in the world today, around 355 million live in developing countries (Fig. 1). In the United States, 10,000 people turn 50 years of age every day and one out of every five people are now over 65 years. In India there has been a rapid rise in the number of elderly with nearly 80 million people over 60 years (Fig. 2), which is equal to the entire population of the largest European country. By 2020 it is projected that three-quarters of all deaths in developing countries could be age-related. Non-communicable diseases such as diseases of the circulatory system, cancers and diabetes will cause the largest share of these deaths.[9]

The number of people with type 2 diabetes is increasing in the world at large and Asian Indians have the highest prevalence.[10] The number of adults with diabetes in the world is projected to rise from 135 million in 1995 to 300 million in the year 2025. The major part of this numerical increase will

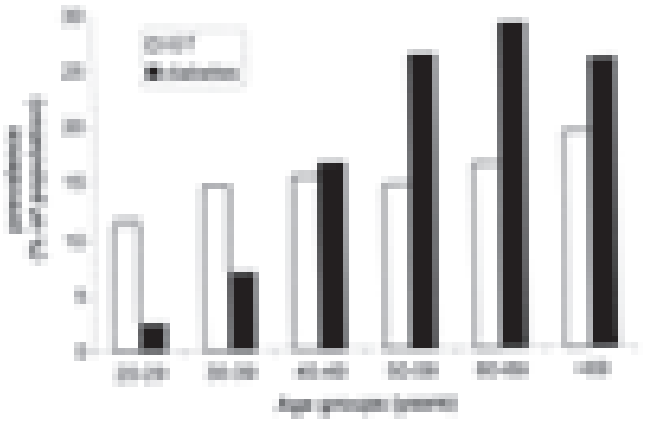

Fig. 3 : Age specific prevalence of impaired glucose tolerance (IGT) and type 2 diabetes in India. Data obtained from 97.

occur in developing countries, especially in Asia.[11] The countries that are projected to have the most cases of diabetes in 2025 are India (57 million), China (38 million) and the USA (22 million). The greatest increase between 1995 and 2025 is expected to occur in India (195%).[11] In developing countries, the majority of people with diabetes are in the age range of 45-64 years,[12] whereas in the developed countries the majority of people with diabetes are aged ≥ 65 years.[13]

In a study conducted among asymptomatic elderly individuals in India, prevalence of diabetes mellitus was 13.0 %.[14] In a study in rural South India, the age-adjusted rates for known diabetes in the middle-aged and elderly subjects were unexpectedly high, considering the poor socio-economic circumstances, decreased health awareness and decreased access to medical facilities.[15] In a study conducted in Trivandrum, the capital city of Kerala State, overall prevalence of type 2 diabetes was found to be 16.3%.[16] This is comparable to the prevalence of diabetes among Indians residing in Singapore. The prevalence is even higher among people of Indian origin in Fiji.[17-19] These data suggest that increasing life-expectancy (as in Kerala State) and changes in lifestyle and nutrition may result in substantially higher incidence of diabetes in India than currently established.

In both India (Fig. 3) and the United States (Fig. 4) the prevalence of diabetes rises with advancing age. There is also an increase in the number of people who display signs of impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), conditions that precede the development of clinical diabetes and are reported risk factors for vascular complications. As a result of these trends, approximately half of all diabetes cases occur in people older than 55 years of age 20. Approximately 20% of the United States population aged 65 and older (~7 million people) have diabetes (Fig. 4). People with diabetes represent 18% of all nursing home residents and tend to be younger than non-diabetic residents. Up to 20% of those 80 years old develop diabetes.

Pathogenesis Of Diabetes In The Elderly

Fasting plasma glucose increases by 1-2mg/dl per decade

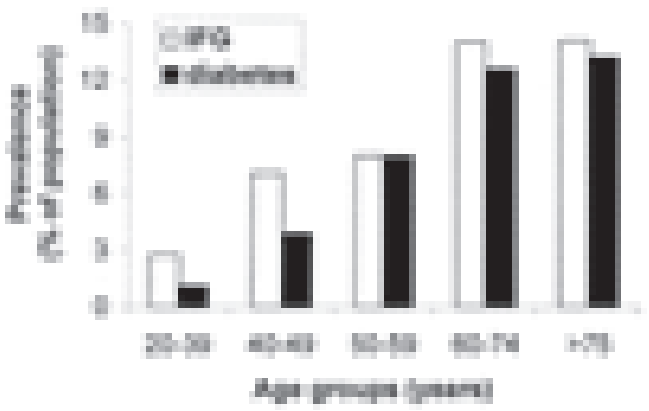

Fig. 4 : Age-specific prevalence of impaired fasting glucose and diabetes in United States. Data obtained from 98.

Fig. 5 : Pathogenesis of type 2 diabetes in the elderly. Aging is associated with reduction in lean body mass. The loss of lean mass, particularly skeletal muscle can lead to muscle weakness, reduced endurance capacity, and increased fatigability. These changes, in association with reduced physical activity, can contribute to the reduction in energy expenditure, increased body fat, and insulin resistance. Eventually this leads to the development of hypertension, diabetes, and dyslipidemia. Genetic predisposition can play a key role in the development of adverse health conditions.

and 2-hour postprandial plasma glucose increases by 8-20mg/dl per decade after 30 to 40 years.[8] Impairment of glucose tolerance with age is well recognized.[21] (Figs. 3 and 4). Whether this glucose intolerance is part of aging process or is it the emergence of true diabetes has been a source of debate. Though aging may have a direct effect, deterioration of glucose tolerance in not always an inevitable concomitant of aging.[22]

With advancing age lean body mass decreases and percent adiposity increases, but there may be little or no change in total body weight. Aging is associated with sarcopenia, referred to as the universal and involuntary decline in skeletal muscle mass. This results in loss of muscle strength and contributes to the eventual inability of the elderly individual to carry out tasks of daily living.[23] A major mechanism of insulin action is facilitating glucose uptake by the muscle. A reduction in lean body mass means the eventual inability to dispose glucose. Reduced metabolically active lean tissue mass and reduced physical activity levels of older people predisposes them becoming obese.

Another important change with age is the shift of muscle fiber composition to predominantly type I (slow twitch) fibers, which are less glycolytic than type II (fast twitch) fibers. The contractile fiber type of the muscle is determined by the expression of slow and fast isoforms of myosin heavy chain. Some studies have reported associations between the predominant muscle fiber type and level of glucose tolerance in obesity or diabetes. Preliminary evidence also suggests that the shift in fiber type towards a predominance of type I fibers in the elderly contributes to the increase in impaired glucose tolerance although these studies are still on-going.

The weight gain that commonly occurs between fourth and seventh decades of life contributes to insulin resistance, particularly the abdominal accumulation of fat.[24] In a study conducted with a subset of 186 males in the Baltimore Longitudinal Study of Aging (BLSA), age per se appeared to have no influence on the levels of insulin or glucagon. Instead, the data suggested that the presence of obesity altered plasma glucose, insulin, and glucagon levels.[25] Thus, intra-abdominal fat accumulation can be regarded as a key factor in causing diabetes in the aging population.[26]

It should be noted that an early study from the BLSA group concluded that age does have an independent effect on glucose tolerance.[27] The data were obtained from 743 community dwelling subjects. They tested whether the effect of age on glucose tolerance remains when data were adjusted for fatness, fitness, and fat distribution. The differences between the young and middle-aged groups were not significant, but the old groups had significantly higher 2 hour glucose values than young or middle-aged groups underscoring the independent role of aging.

We recently completed a study that supported the idea that accumulation of abdominal fat is more important than age per se in determining the decrease in insulin sensitivity in older people.[28] There are data that suggest that age related decline in muscle mitochondrial functions might be responsible for development of insulin resistance.[29,30] Additional evidence from gene array studies,[31,32] as well as other metabolic studies[33,34] in type 2 diabetes patients demonstrated a link between defective oxidative phosphorylation pathway in skeletal muscle and development of insulin resistance. However all of these studies to date have been associative and therefore the link between insulin resistance and abdominal fat and muscle mitochondrial function is not firmly established. This is illustrated by a recent study in which it was shown that a four month program of progressive aerobic exercise resulted in similar increases in muscle mitochondrial capacity and reduction of abdominal fat in young, middle-aged and elderly people who were previously sedentary.[28] In contrast, insulin sensitivity was only improved in the young group (Fig. 6). This study demonstrates that abdominal fat and muscle oxidative function may be only indirectly related to insulin-mediated glucose metabolism.

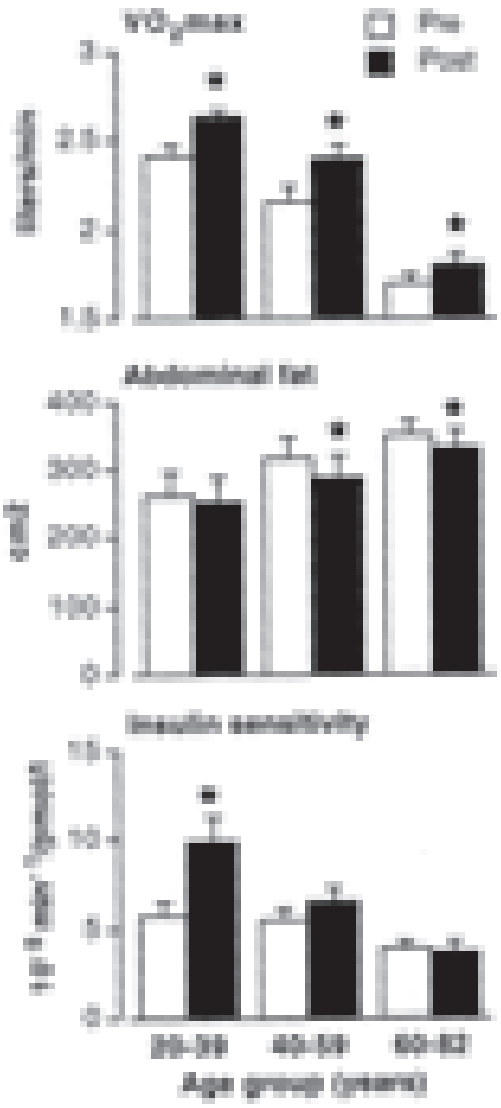

*Fig. 6 : Effects of aerobic exercise training on aerobic capacity, abdominal fat and insulin sensitivity in people of different ages. Sedentary men and women completed a four months of bicycle exercise, which improved aerobic capacity (VO2max) in each age group. By design body weight was maintained during the study within 2% of initial values, but middle-age and older groups still had a significant reduction in abdominal fat. Insulin sensitivity, measured by intravenous glucose tolerance test, was improved after training only in the younger group. * pre-post difference within group ($p < 0.05$). Before training there were significant effects of age on each variable. Adopted from 28.*

It is clear that age and obesity are risk factors for diabetes but obviously not all elderly people become diabetic. Genetic factors are likely to be involved. Analysis of the genetics of type 2 diabetes has revealed the complexity of the disease, i.e., its inheritance is neither autosomal dominant nor recessive.[35-37,38] The complex, non-Mendelian inheritance of type 2 diabetes is secondary to environmental contributions to disease risk and, more importantly, to the polygenic nature of type 2 diabetes, i.e., onset of the disease requires the simultaneous presence of a subset of susceptibility genes that affect insulin sensitivity and secretion.[39] The genetic mechanism involved in type 2 diabetes remains to be clearly defined. There is little doubt that people who are genetically predisposed to become diabetic develop the disease when they become older, physically less active and gain excess body fat. There may still be contributing environmental factors which are not yet fully understood.

There are many hormonal changes that occur with aging. Leptin levels are positively correlated to insulin resistance in older people and amylin secretion is associated with delayed return of glucose levels to baseline.[40] However the putative role of amylin in the hyperglycemia of aging and type 2 diabetes mellitus remains controversial.[41] Age-related decreases in growth hormone, androgens, testosterone (especially in men), and dehydroepiandrosterone levels may contribute to diabetes since the fall in these hormones may cause loss of lean tissue, accumulation of fat and reduced physical performance.

Hepatic glucose sensitivity to insulin and beta cell sensitivity is reportedly unaltered by aging.[42] However a recent study demonstrated that the deterioration of glucose tolerance with aging is a combined effect of decreases in both insulin secretion and action. Severity of this defect is determined by the amount of fat and not by age per se.[43] These conclusions were based on oral and intravenous glucose tracer studies performed in 67 elderly and 27 young subjects. Fasting glucose levels as well as glycemic response above basal were higher in the elderly when compared to young subjects. Insulin action, measured with either an oral meal test or an intravenous glucose infusion method, was lower in the elderly. However, when insulin action was statistically adjusted for differences in percent visceral fat and total body fat, the differences between elderly and young people were removed.

Thus, the conclusion reached by the majority of studies performed in this area is that the development of insulin resistance and diabetes in older people is due more to changes in body composition than aging per se.[28,43,44]

Geriatric Syndromes

Elderly diabetic patients have unique management problems due to aging and disabilities unrelated to diabetes. Atypical presentation of a typical illness is common especially in people over 75 years of age. Homeostatic strain caused by the onset of a new disease often leads to symptoms associated with a different organ system, particularly one compromised by pre-existing disease.[45] Thus the "weakest link" organ systems will manifest the symptoms. Acute confusion, depression, incontinence, falling and syncope account for the common presenting features whatever be the underlying disease. In other words, the organ systems usually associated with a particular symptom are less likely to be the source of that symptom. For example, an 80-year-old diabetic patient with acute myocardial infarction may present to the emergency room with acute confusion. A thorough knowledge of the geriatric syndromes (geriatric giants) are

absolutely essential for the accurate diagnosis and management.[46]

Unique Clinical Features Of Diabetes In Elderly

The early symptoms of diabetes are absent in as many as half of the patients (Table 1). Polydipsia is unlikely, because thirst is impaired with normal aging.[1] If symptoms do occur, they are generally nonspecific (confusion, failure to thrive, incontinence, etc.). Often, diabetes presents for the first time in an elderly person who is hospitalized with a complication that may be related to diabetes, such as a myocardial infarction or a stroke. In frail elderly nursing home patients, nonketotic hyperosmolar coma may be the first sign of diabetes. Renal threshold for glucose increases with age, so that no sugar is spilled into the urine until the glucose level is markedly elevated.[1] Polyurea usually accompanies glycosuria and therefore polyurea occurs only in higher blood sugar values in the elderly than in younger people.

Table 1: Atypical presentations of diabetes in the elderly

1.	Confusion
2.	Falls
3.	Failure to thrive
4.	Neuropathy
5.	Coronary artery disease
6.	Visual symptoms
7.	Hyperosmolar coma

Several unique syndromes occur in elderly patients with diabetes.[1] 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 patients with diabetes; so also is the papillary necrosis that can occur with pyelonephritis.

Diagnosis

Evidence to date indicates that postprandial blood glucose (2 hrs OGTT) is a more reliable indicator of diabetes in the elderly than fasting blood sugar. The DECODE (Diabetes Epidemiology: Collaborative analysis of Diagnostic criteria in Europe) study analyzed data on close to 30,000 subjects from twenty European epidemiological studies. The fasting criteria tended to diagnose younger and more obese subjects than the 2-hour criteria.[47] Another analysis of existing population-based European studies from the DECODE Study Group revealed that one-third of the older diabetic subjects who were undiagnosed at baseline had isolated post-challenge hyperglycemia.[48] The oral glucose tolerance test provides additional prognostic information and enables detection of individuals with impaired glucose tolerance who have the greatest attributable risk of death.[49,50] Thus in older adults 2 hour hyperglycemia seems to be more common than faster hyperglycemia.[51] These studies underscore the importance of measuring 2 hour-post challenge plasma glucose in older individuals.

Complications

Diabetes is the sixth most common cause of death among elderly adults.

Considerable progress has been made, or will be made in the coming years, in reducing risk for the traditionally recognized microvascular (retinopathy, nephropathy, neuropathy), and macrovascular (coronary heart disease, stroke, peripheral arterial disease) complications of diabetes.

The prevalence of microvascular complications is reported to be very high in elderly diabetes in general.[52] In a study conducted at Medical College Hospital, Trivandrum, S. India,(unpublished observations) we examined sixty uncomplicated, type 2 diabetes patients above the age of 65 years with history of diabetes for at least 10 years. The incidence of peripheral neuropathy in this group was found to be as high as 77%. Dyslipidaemia was present in 78% of patients.

As diabetes increasingly becomes a disease of elderly people, there are other complications that must also be addressed (Table 2). These include cognitive disorders, physical disability, falls and fractures, and other geriatric syndromes.[52] The potential for diabetes to cause cognitive impairment among the aged is well-documented.[53] Five out of seven cohort studies associated diabetes with roughly a doubling of the overall risk of dementia.[5352;54] However all these studies lacked data to determine the specific mechanisms underlying the association between diabetes and cognitive decline.[55] The specific association with Alzheimer's disease may be weaker but the association with stroke mediated dementia is considerably stronger. The consistency of the association between diabetes and cognitive disorders indicates that exploration of preventive measures is warranted. Genetic linkage studies suggest that people carrying the epsilon 4 allele of the apolipoprotein E gene who also have atherosclerosis, peripheral vascular disease, or diabetes mellitus are at substantially higher risk of cognitive decline.[5254]

Table 2 : Unique complications of diabetes in elderly

1.	Cognitive decline
2.	Physical disability
3.	Drugs related (hypoglycemia)
4.	Falls
5.	Fractures
6.	Geriatric syndromes

Diabetes is also associated with greater risks of disabilities related to mobility and daily tasks among elderly people.[56] Findings from the National Health and Nutrition and Examination Surveys indicate that people with diabetes have about two to three times the prevalence of inability to walk 400 meters, do housework, prepare meals, and manage money. Diabetic women become disabled at approximately twice the rate of non-diabetic women and have an increased risk of

falls and hip fractures.[56,57] The association of diabetes with physical disability is explained in part by classic complications of diabetes (for example, coronary heart disease, peripheral arterial disease, and visual impairment), but a 60% excess prevalence of disability remains after controlling for these factors.[57]

Occurrence of severe hypoglycemia associated with the use of oral agents or insulin increases exponentially with age. This increased risk of hypoglycemia in elderly people is related, in part, to reduced responses of glucagon, the most important counter-regulatory hormone.[1] Because of this glucagon deficiency, elderly subjects are critically dependent on epinephrine to prevent hypoglycemia. Hypoglycemic episodes may trigger serious events like myocardial infarction or stroke.[58]

Unfortunately, few epidemiological studies have examined the impact of diabetes on functional outcomes (cognitive or physical function), and almost no randomized clinical trials have examined the effect of treatments on these outcomes.[55]

Prevention Of Diabetes In Aging Population

Several approaches have been proposed for the prevention of diabetes.[59-61] Table 3 summarizes the important steps. Nutrition therapy and regular physical activity are the most important interventions.[62] It is less clear how much exercise is required for older people to improve their insulin sensitivity. It was reported that when healthy older people perform very vigorous exercise they experience the same acute increase in insulin sensitivity as younger people.[63] However, another study found that older people who had been vigorously training for many years had lower insulin sensitivity than well-trained younger people.[64] In that study[64] though, the older trained group had insulin sensitivity values that were similar to or greater than young or older sedentary people, which demonstrates the important benefit of long-term regular exercise.

Table 3 : Steps for prevention of diabetes in elderly people

- Regular physical exercise (best to start when young)
- Adopting healthy lifestyle measures
- Awareness/Education
- Diets low in saturated fats
- Maintain ideal bodyweight
- Screening
- Cessation of smoking
- Treatment of dyslipidemia
- Treatment of blood pressure
- Drugs

Many older people cannot sustain an exercise program at high intensity or prolonged duration. Therefore, we recently tested whether a moderate intensity exercise program performed over a shorter period (four months) could have similar benefit on insulin action in people of different ages.[28] In this group of previously sedentary people there was a significant decline in insulin sensitivity with advancing age, which was more strongly related to the age-related increase in abdominal fat. There was also a decline in skeletal muscle markers of mitochondrial oxidative capacity. It has been proposed that a decline in mitochondrial function in skeletal muscle in people who are elderly, obese or with type 2 diabetes could limit the ability to metabolize glucose and contribute to insulin resistance. A total of 65 people completed the 16 week bicycle training program, with similar improvements in aerobic capacity (Fig. 6) and mitochondrial biogenesis 28 across the age span. There was a small but significant decline in abdominal fat in middle age and older groups but improvement in insulin sensitivity was only apparent in younger people (Fig. 6). These results suggest that older people may need to exercise longer, more vigorously, or more regularly to obtain a significant improvement in insulin action. Weight loss may also be an important consideration. By design participants in the study maintained their body weight within 2% of initial values. It has been shown that exercise and weight loss can have additive effects on improvement of insulin action in overweight men.[65] Thus, the amount of exercise needed for older people to improve insulin sensitivity and the interaction with weight loss, specifically fat loss requires further investigation.

Drugs have also been evaluated for the prevention of diabetes. Both intensive lifestyle intervention and metformin were shown to reduce the incidence of diabetes, but lifestyle intervention have the greatest effect in prevention of diabetes.[59]

Treatment

The goal of treatment of type 2 diabetes is to begin early and balance the risk/benefit ratio of aggressive therapeutic intervention for the patient. However, some studies have shown that the usage rate of drug treatment for diabetes declines with older age, perhaps because of the concern about side effects or reduced treatment benefits due to competing risks of death.[66]

Treatment goals

Although the American Diabetes Association has made recommendations for the care and treatment of type 2 diabetic patients, there are currently no specific ADA guidelines for treatment of elderly patients.[67,68] Thus, there may be wide variations in the approach to care for older patients among different healthcare professionals.

As the number of older people with diabetes increases, outcomes such as cognitive and physical disability will become greater concerns because of their implications for quality of life, loss of independence, and demands on caregivers. Clinicians will need to modify the guidelines for each individual patient based on their co-morbidity and functional status. In healthy subjects with good functional status the target HbA1c should be less than 7%.[69] Tight

glucose control is most worthwhile for healthy people who can expect to live at least 10 more years.[70] Clearly, additional studies of diabetes treatment in the elderly are required so that clinicians can better understand the benefits and risks of glycemic control in older people.[66]

Special considerations

Treatment decisions are influenced by a variety of factors. Drug-induced hypoglycemia is the main consideration and the most important limiting factor in instituting tight metabolic control in the elderly.[71] Perception or awareness of hypoglycemia may be impaired in elderly people especially with long duration of diabetes and other cognitive defects. Vascular and neuropathic complications are already present in a significant number of elderly diabetic patients at the time of diagnosis.[72]

Other contributing factors to the high prevalence of hypoglycemia include lack of knowledge or awareness of the warning symptoms of hypoglycemia and autonomic symptoms. This problem may persist even when the patient has been educated regarding the nature of these symptoms. When elderly subjects do experience symptoms of hypoglycemia, they tend to be less intense and more nonspecific than in younger people.

Depression, impaired cognitive function, and lack of recognition of thirst and subsequent dehydration are important factors to be taken into account. Elderly people are also predisposed to falls, pressure ulcers, amputations and chronic infections, especially pulmonary tuberculosis.[40] Chronic hyperglycaemia will result in a decreased pain threshold and incontinence. Adherence to dietary therapy, physical activity and medication regimes may be compromised by concomitant illnesses and psychosocial limitations.[71]

The treatment plan can be broadly divided into diet, exercise and drugs.

a) Diet

There is no single recommended dietary plan for people with diabetes.[5] Rather, medical nutrition therapy for older people with diabetes should be individualized, with consideration given to usual eating habits and other lifestyle factors. The fundamental principle is to provide a nutritionally balanced diet. In general, normal body weight should be maintained. (The normal body mass index of Indians needs to be determined since they develop diabetes and related illnesses at what is considered the normal range of BMI by the World Health Organization. In comparison, Europeans and North Americans are more likely to develop diabetes if their body mass index is in the overweight or obese range). Good diabetes control by itself results in some weight gain, because of reduced loss of energy as glycosuria and increased resting energy expenditure, in patients with previously poor glycemic control. This factor should be considered when simultaneous drug and diet treatments are started to improve glycemic control. In people who are overweight or obese a low caloric diet is important. In cases of severe obesity the low calorie National Cholesterol Education Program guidelines diet should be followed. However since many diabetic patients of Indian origin are not considered morbidly obese, the need for this type of diet should be carefully tested before recommending its use in this population. In patients with renal insufficiency, the intake of protein has to be restricted and it should be predominantly high quality protein.

b) Exercise

Exercise is a readily available form of non-pharmacological intervention, which can increase insulin action and has many beneficial effects like improved perfusion to tissues. Exercise has an acute, insulin-like action on glucose transport across the plasma membrane of muscle cells.[26] The ability of muscle contraction to stimulate glucose uptake is independent of the insulin-mediated pathway. Thus, people who are insulin resistant can achieve improved glycemic control with exercise. However, patients on oral drugs or insulin may be at increased risk for exercise-induced hypoglycemia and hence careful blood sugar monitoring should be performed, especially at the start of the exercise programme.[8] Appropriate adjustment of diet and drugs in necessary to avoid hypoglycemia. Regular exercise training should be advocated for all people with diabetes because it has been shown to improve insulin action and reduce cardiovascular complications.

c) Pharmacological management

Regular physical activity and dietary measures aimed at bodyweight normalization and improvement of insulin action are the cornerstones of therapy in type 2 diabetes.[73] In the United Kingdom Prospective Diabetes Study (UKPDS) it was clearly shown that patients with type 2 diabetes mellitus who were intensively treated with oral blood glucose-lowering agents or insulin developed less microvascular complications, irrespective of age.[74,75] The question of whether achievement of strict metabolic control is also of benefit in elderly patients is still unanswered.

When used appropriately drugs may be the single most important intervention in the care of an older patient, but when used inappropriately they may endanger the life of the individual by causing serious adverse drug reactions.[76] As with the use of any medicine in old age, the basic principle should be 'start low, go slow". The drug should be used at first at low doses and then slowly increased until either the desired treatment effect is achieved or side-effects reach an unacceptable level.[8] Daily low dose aspirin therapy is found to be very beneficial in the elderly if no other contraindications exist.[77]

Ultimately, because of the progressive nature of the disease and the progressive decline in pancreatic beta-cell function, insulin therapy is almost always obligatory to achieve optimal glycemic goals.[78]

Oral Agents

Table 4 provides salient features of medications and special precautions in the elderly. The variation in the ease of tablet breaking and accuracy between different tablet formulations affect bioavailability and patient compliance.[79] This fact has

to be kept in mind when prescribing oral medications for the elderly. Sulphonylureas are usually well tolerated. Hypoglycemia is the most frequently occurring adverse effect, which can be serious and damaging in the elderly. This adverse effect has to be kept in mind, especially in case of elderly living alone. Recent Census Bureau statistics indicate that elderly people account for 38% of the 23.6 million people in the United States who live alone. Hypoglycemia has been associated primarily with long-acting sulphonylureas, like chlorpropamide and glibenclamide (glyburide).[58,80] Therefore, shorter-acting compounds like tolbutamide and gliclazide that are well-tolerated appear to be the best choice to treat elderly patients. Glimepiride has fewer and less severe effects on cardiovascular variables than glibenclamide (glyburide) and is safe in elderly. To avoid hypoglycemia, dosage is usually started at 1 mg/day, slowly titrated depending on blood glucose values, at 1- to 2-week intervals to a usual dosage range of 1 to 4 mg/day (maximum 6 mg/day in the UK or 8 mg/day in the US).[81]

Table 4 : Precautions while using oral drugs and insulin in elderly diabetes patients

Drug	Specific precautions/adverse effects in elderly
Sulfonylureas	Hypoglycemia with long acting preparations (chlorpropamide, glibenclamide), prefer short acting (tolbutamide, gliclazide, glipizide)
Biguanides (metformin)	Avoided if age >80years, creatinine more than 1.4mg%, acute illness/hospitalized elderly, significant renal, hepatic, cardiac disease
Meglitinides (repaglinide, nateglinide)	Insulin secretion tends to decrease postprandially, similar safety profile as that of sulphonylureas
Alpha-glucosidase inhibitors (acarbose)	Ideal for elderly patients with mild hyperglycemia, Gastrointestinal adverse effects more in elderly start at 25mg, not to be combined with lispro insulin, weak agent for monotherapy
Thiazolidonediones (rosiglitazone, pioglitazone)	Safe in elderly, weaker antihyperglycaemic effect useful in elderly patients with impaired renal function, may cause weight gain, edema; monitor liver enzymes
Insulin	Errors in mixing and dose measurements, hypoglycemia, diabetes education

Insulin

Undoubtedly insulin is the natural replacement therapy to compensate for the progressive loss of beta cell function in type 2-diabetes.[82] Generally, older patients with diabetes mellitus can be managed for years, often decades, with nutritional therapy and oral agents.[83] Some elderly people lose virtually all their endogenous insulin secretary capacity over time with no endogenous insulin. Hypoglycaemia is clearly the most significant risk of insulin therapy. If mild and easily treated, hypoglycemia is not a major concern. On the other hand, nocturnal hypoglycaemia and, in particular, hypoglycaemia unawareness, are clear signs that the insulin regimen should be modified. Hypoglycemic episodes in the elderly may trigger serious events like myocardial infarction or stroke. In elderly patients in whom regular meals cannot be guaranteed, continuing with sulphonylurea therapy and adding a basal insulin supplement can be a safe and effective way of preventing hyperglycaemic symptoms.

Management Of Related Disorders

Hypertension

In diabetic patients with hypertension the blood pressure goal is less than 130/80 mm Hg.[84] Combinations of two or more drugs are usually needed to achieve the target blood pressure goal. Thiazide diuretics, beta-blockers, ACE-inhibitors, ARBs, and CCBs are beneficial in reducing cardiovascular disease and stroke incidence in patients with diabetes.[84]

Both hypertension and diabetes carry an increased risk of cardiovascular and renal disease and are commonly associated conditions.[85,86] The prevalence of hypertension in the diabetic population is particularly high, increasing from 40% of middle-aged patients with type 2 diabetes mellitus to approximately 60% by age.[75] Hypertension increases an already high risk of cardiovascular disease events associated with diabetes mellitus and is also a risk factor for the development of microalbuminuria and retinopathy. Three recent clinical trials have addressed the effects of aggressive intervention in diabetes, particularly older patients with type 2 diabetes mellitus.[87] The UKPDS revealed the importance of treating the high blood pressure in diabetic patients. Aggressive antihypertensive treatment is safe and well tolerated, and resulted in fewer cardiovascular events in the subset of patients with diabetes.[88] The higher level of cardiovascular risk in the elderly explains why use of antihypertensives provides a greater benefit in older versus younger hypertensive patients. Even in hypertensive patients over the age of 80, the benefits of drug-induced blood pressure reduction have been demonstrated in terms of prevention of nonfatal complications.[85]

Hyperlipidemia

The prevalence of cardiovascular illnesses increases as age advances. Mortality risk is high for diabetic patients with a history of myocardial infarction and for this reason aggressive treatment of dyslipidemia is indicated.[90] The goals of therapy should be the same in all age groups. The LDL goal is less than 100 mg%. Statin therapy is proven to reduce mortality in all age groups, including very elderly individuals.[91,92] Resins may be added to statins if necessary to reach the LDL goal. The initial therapy for hypertriglyceridemia is improved glycemic control. Additional triglyceride lowering can be achieved with statins (for subjects with both high LDL and triglyceride levels) or fibric acid derivatives (gemfibrozil or fenofibrate).[90]

Miscellaneous

Low dose aspirin should be administered if there are no contraindications. Immunization recommendations for the elderly population should be strictly followed in diabetes patients.[93] Immunization against influenza and pneumococcal disease is an important part of preventive service.[94] Pneumococcal vaccine has to be given only once while

influenza vaccinations should be given annually. The adult immunization recommendations of the American Geriatrics Society also suggest vaccination against other illnesses such as tetanus, which should be given every ten years.[93]

Patient Education

Patient education is critical in the management of diabetes in elderly. Group health education classes are cost effective and more encouraging for active participation. Many elderly diabetic patients are enthusiastic and motivated learners and are actively involved in all aspects of their treatment.[58] When elderly patients are appropriately educated they can self-monitor their blood glucose level as accurately as younger patients. Topics of discussion should include insulin dose adjustment with self monitoring of blood glucose, identification of hypoglycemia symptoms, dietary choices, exercise, and smoking cessation.[95] Glucose meters should be easy to use, have large display screens and memory capabilities, and require little maintenance.

Including family members in the assessment and education process is very essential. Periodic review and reassessment of treatment goals are important. Regular reinforcement is needed to sustain the behavioral changes, since functional and cognitive status may change in older adults over short periods of time.[69]

Conclusion And Summary

Diabetes in the elderly population is growing into epidemic proportions throughout the world. Though there are some disease similarities in older and middle-aged people, understanding the pathophysiology, clinical features and treatment of the elderly diabetic population presents additional challenges. Tight metabolic control should be the goal of therapy, but may not be safe in all the elderly patients because of co-morbidities and risk of hypoglycemia. Long acting sulphonylureas should be avoided because of the risk of hypoglycemia. The majority of the elderly may ultimately require insulin to achieve acceptable metabolic control. Whether on insulin or on oral drugs, self-monitoring of blood glucose will help reduce the risks of serious hypoglycemia.[69] Treating high blood pressure and lowering lipids are more beneficial in the elderly, a group highly susceptible to cardiovascular morbidity and mortality. Daily small dose aspirin should be advocated if no contraindication exists. Physical exercise improves muscle strength and endurance and improves insulin sensitivity. Older people, unlike the young have to perform more regular and daily exercise to improve and sustain insulin sensitivity. Lifestyle modifications to prevent weight gain, especially abdominal accumulation of fat, are important for prevention and treatment of diabetes. Targets of glycemic control have to be determined with due consideration of age, remaining life-expectancy, co-morbid conditions and severity of vascular complications. Further studies are required to delineate the exact etiology of glucose intolerance and to make age-specific treatment recommendations.

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