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Chapter 11

Glycemic Control in Elderly Diabetics with Dementia

Vinod Kumar

INTRODUCTION

Burgeoning population of older persons is leading contributor to increasing prevalence of type 2 diabetes mellitus and many age related disorders. Dementia is one such disorder that presents serious challenges in the management of diabetes. Impairments of memory, comprehension, decision making and orientation in dementia interfere with the self-management of diabetes and lead to higher susceptibility to hypoglycemia, dehydration, falls and incontinence. Several scientific organizations have come up with guidelines for managing type 2 diabetes mellitus in older patients with different types of morbidities including dementia. In this paper, emphasis has been laid for the need of proper selection of simplified antidiabetic regimens, desired glycemic goals and the importance of support for such patients from formal and non-formal care providers.

DIABETES AND DEMENTIA INTERRELATIONS

Both diabetes and dementia pose enormous public health challenges. They can greatly compromise quality of life in old age. Both are chronic, progressive, and irreversible disorders leading to significant morbidity and mortality. Dementia has additional challenges of diagnostic unawareness of its early symptoms, confusion with features of normal ageing, relentless disease progression despite medications, and ultimate inability to recognize one's own self, complete dependence on others, and premature death. Prevalence of dementia among 65+ and 75+ diabetics is 16% and 24%, respectively.[1,2] In India, out of 60 million diabetics, about one-fifth are elderly patients while over 4 million Indians have dementia.[3] With 60+ and 80+ Indian population poised to jump from 76 and 6 million, respectively, to 324 and 48 million between the period 2000 and 2050,[4] future trajectories of the two diseases will be huge.

Although initial studies failed to find increased prevalence of cognitive impairment among type 2 diabetic patients[5-7] and reports from some developing countries that diabetics and nondiabetics had similar scores on screening tools,[8,9] there is now an overwhelming evidence that dementia and cognitive decline occur among diabetics not only more frequently but also faster when compared to nondiabetics.[10,11] Yet, follow-up of many years may be required to identify this so called faster cognitive decline in diabetics. Spauwen et al., Yaffe et al., and Fontbonne et al. reported statistically significant cognitive decline among type 2 diabetics versus control subjects in their follow up studies spanning for 12, 9, and 4 years, respectively.[12-14] Similar conclusions were drawn in a study restricted to type 2 diabetic women.[15] Yaffe et al. also observed worse cognitive function and greater decline in those with poor glycemic control.

Early symptoms of dementia are forgetfulness, repetitiveness, short-term memory loss, and difficulty in finding right words. Later, disorientation in space and time (difficulty finding their own room or toilet and inability to identify day from night), impaired reasoning, comprehension, and decision making can occur. Difficulty, managing social situations, money and finances, and even the activities of daily living (ADL) can advance to loss of basic functions which everyone learns in childhood such as holding urine (incontinence) and feeding.[16] It is not hard to imagine the problems in self-

TABLE 1: Practical clinical tips if diabetes and dementia coexist

Diabetic patients when develop dementia can	Dementia patients when develop diabetes can
Forget taking medicines or forget they have already taken (risk of taking twice)	Cannot find toilet in the house and develop risk of incontinence
Forget taking meals (hypoglycemia) and liquids (dehydration) or forget they have eaten	Increased falls (injuries and fractures) due to visiting and looking for toilets often
Indecision in adjusting the insulin dose or taking wrong dose (hypoglycemia or hyperglycemia)	If hyperglycemia, dehydration can lead to confusion
Forget how to do an injection or unable to identify their medicines	Inability to put their distress in words (so they may cry or shout)

caring for one's own diabetes with slowly developing functional dependence that happens in dementia. Table 1 illustrates what can happen to a diabetic if he develops dementia and to a demented if he develops diabetes.

CHALLENGES IN GLYCEMIC CONTROL IN ELDERLY DIABETICS WITH DEMENTIA

Elderly diabetics have special issues in their management and importantly, much attention has been paid for their glycemic control in the past few years. Guidelines have been developed all over the world with increasing focus on their cognition and functional status as well as their cardiovascular and hypoglycemic risks.[17-27] All of these advocate for customizing the glycemic management tailored according to the needs of individual elderly diabetic patients.

Although, many clinicians are conversant with general rules of treating elderly diabetics and do recognize the special needs of those who are severely demented and frail but are unable to identify those with early cognitive impairment and provide satisfactory standards of medical care from that angle. Hence, there is a need to screen elderly diabetics for cognitive function and also take into consideration related factors, such as malnutrition, weight loss, sarcopenia, frailty, functional dependence, and life expectancy, to prescribe right kind of antidiabetic medications. Apart from irreversible dementias like Alzheimer's disease and vascular dementia, clinicians also need to realize the significance of many coexistent but reversible or treatable medical conditions which cause cognitive problems and interfere with communication and self-care ability in the diabetic management, often requiring the services of a caregiver. Examples are dyselectrolytemia, chronic renal failure, chronic obstructive pulmonary disease (COPD) (anoxia), hypothyroidism, and vitamin B_{12} deficiency, latter being of special relevance to elderly diabetics who are on long-term metformin therapy. Kansal[28] demonstrated reversibility of cognitive impairment following specific treatment of underlying condition in 15 cases each of dyselectrolytemia, chronic renal failure, anoxia and in 8 cases of hypothyroidism and 7 cases of vitamin B_{12} deficiency.

General issues concerning elderly diabetics that impact their glycemic control are their heterogeneity and several consequences of aging. Heterogeneity is both in terms of clinical and functional status. Some may be young-old and functionally independent, others may be old-old (super old) with functional incapacity, both physically and mentally. Life expectancies are variable. Economic, social, and emotional deprivation affect some but not others. Duration of diabetes and prevalence of micro- and macrovascular diseases can be highly variable and some may be carrying on with their diabetes from their young or middle age with or without vascular complications. Other comorbidities like chronic kidney disease, COPD, chronic liver disease, and depression are also prevalent with variable magnitude.

Consequences of aging include wider glycemic variability, increased risk of hypoglycemia due to impaired counterregulatory mechanisms and failure to recognize it, age-related higher cardiovascular risk, deleterious effects of persistent hyperglycemia, altered pharmacokinetics, and geriatric syndromes [the 5 Is, i.e. **I**mpaired intellect (confusion, delirium, and dementia), **I**mbalance (with resulting falls and fractures), **I**mmobility (associated with frailty, sarcopenia, and impaired lower extremity performance), **I**ncontinence (multiple etiology), and **I**mpaired vision and hearing]. Finally, residing alone or in old age home is also important.

Additional issues concerning elderly diabetics with dementia that impact glycemic control in demented patients include 2–3 greater risk of hypoglycemia, recurrent hospitalizations, poor self-management ability, unacceptable hyperglycemia, home-boundness, and

residence in chronic care facility. Use of low-risk antidiabetic agents, simplifying treatment regimens, and active involvement of a trained caregiver are obvious choices for glycemic control.

Hypoglycemia in demented patients requires special attention. Poor appetite, changes in eating habits, weight loss, difficulties in understanding prescriptions, and wrong selection of antidiabetic agents all contribute to hypoglycemia risk in elderly diabetics with dementia. Failure to recognize hypoglycemic symptoms by demented patient precludes its speedy management. Thorpe et al.[29] observed tight glycemic control [glycosylated hemoglobin (HbA1c) <7%] in 52% of 15,880 elderly diabetics with dementia and many of them were older, had considerable weight loss, and were receiving sulfonylureas and/or insulin. Therapeutic implication of these observations is to minimize hypoglycemia risk through the use of safer antidiabetic agents in properly selected patients. Life expectancy of such patients is only 2–8 years and they are unlikely to experience benefits of tight glycemic control which takes years to accrue.

THERAPEUTIC APPROACH AND GLYCEMIC TARGETS FOR ELDERLY DIABETICS WITH DEMENTIA

Emphasis is on evaluation of elderly diabetics for cognitive impairment both initially and periodically, thereafter using an age and language validated screening tool such as mini mental status examination.[18,30] Reevaluation is recommended at each time of decline in clinical status. Increased difficulty with self-care should be considered a change in clinical status. The American Academy of Neurology guidelines recommend further screening of elderly subjects with cognitive impairment for reversible causes of dementia such as hypothyroidism, vitamin B_{12} deficiency, and depression.[31] Lately, it is emphasized that geriatric syndromes (of which cognitive impairment is one of the components) can occur with a higher frequency in elderly diabetics[32] and can affect self-care abilities and health outcomes including quality of life.[20]

Treatment targets for relatively healthy elderly diabetics with good cognitive and physical functioning are same as for young diabetics, i.e., HbA1c less than 7% but for many elderly diabetics, these need to be relaxed, i.e., HbA1c 7%-8% or even 9%.[20,25-27,32,33] Concept for relaxing the goals finds support from Action to Control Cardiovascular Risk in Diabetes (ACCORD) Trial in which HbA1c of less than 6% was associated with increased mortality. This should not, however, imply clinical inertia on the part of treating clinicians and desired glycemic goals at a minimum should avoid the deleterious consequence of persistent hyperglycemia; namely, dehydration, hyperosmolar coma, incontinence, cognitive decline, poor wound healing, sarcopenia, visual disturbances, and poor lower extremity performance. Table 2 summarizes HbA1c-related glycemic targets for elderly diabetics as per severity of their cognitive impairment, physical and functional health.

CHOICE OF ANTIDIABETIC AGENT

Selection of antidiabetic medication depends on its cost, duration of action, its disposal, simplicity of its administration, side effects including the risk of hypoglycemia, ability to lower fasting and postmeal blood sugars, and ability to minimize overall glycemic variability. Thus, drugs with gastrointestinal side effects

TABLE 2: Glycemic targets for elderly diabetics according to cognitive impairment, physical and functional health

Parameter	Categories		
	Patient one	Patient two	Patient three
Cognitive impairment	Nil	Moderate	Severe
Functional status	Independent	Dependent	Dependent
General health	Fair	Intermediate	Poor
Physical health			
Frail	No	Yes	Yes
Microvascular complications	Minimal	Moderate	Advanced
Comorbidities	Minimal	Moderate	Advanced
Life expectancy	>10–15 years	<5 years	<5 years
HbA1c target	7–7.5%	7.5–8.5%	>8.5%

HbA1c, glycosylated hemoglobin.

Note: A common goal is to keep glycemic variability at a minimum to avoid hyper and hypoglycemia both

are to be avoided in malnourished, sarcopenic, weight losing, and frail diabetics. Drugs which depress cognition cause hypoglycemia and are complex to administer are best avoided in elderly diabetics with dementia. The fact that relative contribution of postprandial hyperglycemia is higher than that of fasting blood glucose in the elderly age group should also be kept in mind.[34] Tables 3 and 4 give comparison of current options of antidiabetic agents in achieving glycemic control and such comparison in context to different types of elderly diabetics.[35]

Literature is replete with reports of increased risk of cardiovascular morbidity in all diabetics including elderly diabetics with or without dementia. Cardiovascular morbidity occurs even at prediabetic stage.[38] Management of diabetes will therefore not be complete without attending to factors other than glycemic control like

TABLE 3: Comparison of current options for glycemic control

Option	Hypoglycemia	Glycemic variability	Cost	Treatment complexity	Remarks
Diet	Low	Low	Low	Variable	–
Exercise	Low	Low	Low	Low	–
BW reduction	Low	NA	Low	Variable	Not for frail, PCM
Metformin	Low	Nil	Low	Low	CI: CKD, CLD, CHF, frail, PCM. GI effects, lactic acidosis, B_{12} deficiency (dementia)
SU	High	Nil	Low	Variable	Hypoglycemia risk, avoid glibenclamide
Insulin	High	Variable	Variable	Variable	Hypoglycemic risk, use long-acting analogs
TZD	Low	Nil	Moderate	Low	Fractures, CHF, macular edema, cognition, liver damage[36,37]
DPP4-I	Low	Low	High	Low	Effective with preserved B cell function
GLP1-RA	Low	Low	High	Moderate	Effective with preserved β-cell function
Meglitinides	Moderate	Low	Moderate	High	Do not combine with SU/AGI
AGI	Low	Low	Moderate	High	GI side effects, social problems

AGI, alpha-glucosidase inhibitors; BW, body weight; CHF, congestive heart failure; CKD, chronic kidney disease; CI, contraindications; DPP4-I, dipeptidyl peptidase-4 inhibitor; SU, sulfonylurea; TZD, thiazolidinediones; GLP1-RA, glucagon-like peptide-1 receptor agonists; GI, gastrointestinal; CLD, chronic liver disease; PCM, protein calorie malnutrition.

TABLE 4: Comparison of current options for different categories of patients

Option	Independent (category I)	Dependent frail (category II)	Dependent demented (category III)
Diet	Restrict carbohydrate	Calories, protein	Calories
Exercise	Muscle strengthen	Muscle strengthen	Activities
BW reduction	Healthy BW	No	No
Metformin	1st line	1st line	1st line
Sulfonylurea	2nd line	Alternate 1st line	±
Insulin	2nd line	Long-acting analog	Long-acting analog
TZD	2nd line	±	±
DPP4-I	2nd line	±	±
GLP1-RA	2nd or 3rd line	No	Cost
Meglitinides	2nd line	±	No
AGI	2nd line	No	±

BW, body weight; TZD, thiazolidinediones; DPP4-I, dipeptidyl peptidase-4 inhibitor; GLP1-RA, glucagon-like peptide-1 receptor agonists; AGI, alpha-glucosidase inhibitors.

aspirin prophylaxis, smoking cessation, and control of hypertension and dyslipidemia. This is, however, outside the scope of subject of glycemic control.

CONCLUSION

Challenges for glycemic control in patients having co-morbid dementia include poor self-management ability, difficulty understanding prescriptions, changes in eating habits, greater susceptibility to hypoglycemia and failure to recognize it, glycemic variability, home boundness, and in certain cases recurrent hospitalizations and residence in chronic care facilities. There is a need for using low risk first and second line hypoglycemic drugs and simplified therapeutic regimens and for achieving relaxed glycemic targets in accordance with the physical and mental functional status of individual patient. Strong support and care from the family when required is important. Slow progression of cognitive decline over years and its deceptive similarity in early stages to normal ageing makes a strong case for early detection of dementia by established diagnostic tools in order to improve diabetic care in older patients.

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