Brief Communication

Preventing microvascular complications in type 1 diabetes mellitus

Vijay Viswanathan

M. V. Hospital for Diabetes, M. Viswanathan Diabetes Research Centre, Chennai, Tamil Nadu, India

ABSTRACT

Patients with complications of diabetes such as retinopathy, nephropathy, and cardiovascular complications have increased hospital stay with greater economic burden. Prevention of complications should be started before the onset of type 1 diabetes mellitus (T1DM) by working on risk factors and thereafter by intervention upon confirmatory diagnosis which can prevent further damage to β-cells. The actual risk of getting microvascular complications like microalbuminuria and retinopathy progression starts at glycated hemoglobin (HbA1c) level of 7%. As per the American Diabetes Association, a new pediatric glycemic control target of HbA1c <7.5% across all ages replaces previous guidelines that had called for different targets by age. Evidence shows that prevalence of microvascular complications is greater in patients with age >20 years as compared to patients <10 years of age. Screening of these complications should be done regularly, and appropriate preventive strategies should be followed. Angiotensin converting enzyme inhibitors and angiotensin II receptor blocker reduce progression from microalbuminuria to macroalbuminuria and increase the regression rate to normoalbuminuria. Diabetic microvascular complications can be controlled with tight glycemic therapy, dyslipidemia management and blood pressure control along with renal function monitoring, lifestyle changes, including smoking cessation and low-protein diet. An integrated and personalized care would reduce the risk of development of microvascular complications in T1DM patients. The child with diabetes who receives limited care is more likely to develop long-term complications at an earlier age. Screening for subclinical complications and early interventions with intensive therapy is the need of the hour.

Key words: Nephropathy, neuropathy, retinopathy, type 1 diabetes mellitus

Introduction

Diabetes is a major public health problem associated with a huge economic burden in developing countries. A population based study reported that the total cost (direct and indirect) of diabetes care in India was 31.9 billion USD.[1] A similar study evaluated the cost of treating long term diabetic complications in India, with the main objective of assessing the direct cost of treating long term diabetic complications such as retinopathy, foot amputations, cardiovascular and renal diseases among hospitalized type 2 diabetes mellitus (T2DM) patients. The key findings of this study demonstrated that those patients with foot complications or with presence of two diabetic complications had a four times higher in patient hospital stay when compared to others. It was also found that patients having renal disease and cardiovascular and retinal complications spent three times more than diabetic patients without any complications.[2]

Prevention strategies for type 1 diabetes mellitus (T1DM) depend on the onset of diabetes. Prevention can be done before the onset of T1DM by working on risk factors namely genetic risk, use of antibodies, prediabetes conditions and thereafter by intervention when the child is diagnosed with diabetes to prevent further damage to β-cells.

Type 1 diabetes mellitus treatment emphasizes the need to develop new methods like "artificial pancreas" or an ideal insulin replacement therapy, which could

Access this article online	
Quick Response Code:	Website: www.ijem.in
	DOI: 10.4103/2230-8210.155382

Corresponding Author: Dr. Vijay Viswanathan, M. V. Hospital for Diabetes and Diabetes Research Centre, No. 4, West Mada Church Street, Royapuram, Chennai - 600 013, Tamil Nadu, India. E-mail: drvijay@mvdiabetes.com

achieve tight control without hypoglycemia. T1DM management can also involve development of better methods like "biological cure" by transplantation or regeneration for replacing beta cell function, and through an enhanced understanding or in-depth knowledge of immunopathogenesis (interaction of genes, environment and immune system) which can allow for more effective preventive therapies. Early stage T1DM treatment should focus on potential therapeutic targets for immune modulation specifically on β-cell/antigen-presenting cell, naive T-cells, and effector T-cells.[3]

Researchers question whether it is actually possible to prevent microvascular diabetic complications or is it only possible to treat the complications once they occur. Studies have shown that in T1DM the actual risk of getting microvascular complications like microalbuminuria and retinopathy progression starts at glycated hemoglobin (HbA1c) level of 7%.[4]

Based on the results of the Diabetes Control and Complications Trial, guidelines on the probable relationship between blood glucose/A1c and microvascular diabetic complications have been proposed. As per these guidelines, the HbA1c level should be <8.5% for children aged <6 years; <8% for children aged 6–12 years; and <7.5% for adolescents between the age of 13 and 19 years. These guidelines have been recently changed by the American Diabetes Association. A new pediatric glycemic control target of HbA1c <7.5% across all ages replaces previous guidelines that had called for different targets by age. The adult HbA1c target of <7% for T1DM remains the same, with individualized lower or higher targets based on patient need.[5]

A study of microvascular complications in T1DM patients involving 5,000 children showed that in 373 children (177 males, 196 females; mean age: 16.97 ± 10.12 years) with a follow-up period of 10 years or more, retinopathy was found to be the most common microvascular complication (females: 3.5%, males: 2.5%), followed by nephropathy which is defined as persistent microalbuminuria with or without a fall in glomerular filtration rate (males: 1.7%, females: 1.5%), neuropathy diagnosed with the vibration perception threshold (males: 0.5%, females: 1.5%), cardiovascular and foot complications (males: 1.1%, females: 1%) and hypertension (males: 0.5%). Further analysis based on age showed that the prevalence of retinopathy, neuropathy and nephropathy is greater in patients with age >20 years as compared to patients <10 years of age or between the ages of 10 and 20 years. Thus, if a patient is more than 20 years, screening of these microvascular complications should be done more often, and appropriate preventive strategies should be followed. Data analysis based on duration of DM in a similar cohort showed that in patients with diabetes more than 10 years of age, the prevalence of nephropathy was 27.25%, retinopathy was 24% and neuropathy was 8.5%.

Diabetic nephropathy, characterized by proteinuria, is prevalent in 15–40% of T1DM patients and in 5–20% of T2DM patients. It is found to be more common in African Americans, Asians, and Native Americans and considered to be associated with a risk of cardiovascular disease.

Results of a clinical study done to assess the prevalence of microalbumininuria (MAU) in South Indian diabetic subjects revealed that MAU was present in 10.3% patients with duration of diabetes <5 years, in 23.8% patients with duration of diabetes between 5 and 10 years and in 50% patients with duration of diabetes >10 years. It was observed that MAU occurs in T1DM after the age of 20 years and it was present in a large proportion of the study subjects.[6]

Angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor blocker (ARBs) reduce progression from microalbuminuria to macroalbuminuria and increase the regression rate to normoalbuminuria. For those with microalbuminuria, ACE-inhibitors and ARBs reduce the time to doubling of serum creatinine. Young people with microalbuminuria would potentially be taking ACE-inhibitors for decades. Side-effects include cough (for ACE-inhibitors), hyperkalemia, headache, and impotence.

Diabetic nephropathy can be controlled with tight glycemic and blood pressure control. Multifactorial disease management of nephropathy includes antihypertensive agents, good blood glucose control, and control of dyslipidemia; renal function monitoring, lifestyle changes, including smoking cessation and low-protein diet.[7]

The International Society for Pediatric and Adolescent Diabetes (ISPAD) recommends that annual screening for microalbuminuria should start from the age of 11 years to after 2 years of having diabetes. Microalbuminuria is characterized by an albumin excretion rate (AER) of 20–200 μg/min or AER of 30–300 mg/day; albumin/creatinine ratio (ACR) of 2.5–25 mg/mmoL in males and 3.5–25 mg/mmoL in females (random ACR is higher in females) and albumin concentration of 30–300 mg/L in an early morning urine sample.

Studies have shown that poor glycemic and blood pressure control increases the risk of retinopathy. Retinopathy can be classified into five stages: Background, preproliferative,

proliferative (T1DM), advanced diabetic eye disease and maculopathy (T2DM).[8] Diabetic retinopathy can be controlled with tight glycemic and blood pressure control and regular eye examinations. Retinopathy can be treated with laser photocoagulation and vitreoretinal surgery whenever necessary.[9]

International Society for Pediatric and Adolescent Diabetes recommends that screening for retinopathy should start from the age of 11 years to after 2 years of having diabetes. Minimum assessment for retinopathy should be by ophthalmoscopy through dilated pupils. The frequency of retinopathy screening, in general, should occur annually but should be more frequent if there are high risk features for visual loss. Laser treatment reduces the rate of visual loss for vision-threatening retinopathy.

Diabetic neuropathy can be prevented with tight glycemic control, which can reduce the risk or progression of neuropathy. Contributory factors, which need to be ruled out for the treatment of diabetic neuropathy include alcohol excess, Vitamin B12 deficiency, and uremia. Pain relief can be offered based on the dominant symptoms.[4] As per ISPAD recommendations, peripheral and autonomic neuropathy should be assessed by history and physical examination from the age of 11 years with 2 years diabetes duration. Also, the feet of the diabetic patient should be examined annually for neuropathy, infections and ulcers after 2 years duration, and annually thereafter.

For the management of diabetic neuropathy, the physician should provide general foot-care (self-care) education. A multidisciplinary approach can be used for individuals with foot ulcers and high-risk feet, especially those with a history of a prior ulcer or amputation. Patients should be referred to foot care specialists for on-going preventive care or life-long surveillance. Physicians should look out for the loss of protective sensation or structural abnormalities and history of prior lower-extremity complications.

A study was carried out explore the fear of marriage and conception among youth with T1DM. The results of the study showed that 100% of the females feared that they will not have healthy children, or they will have children with diabetes while 86% feared that they would not be able to conceive or deliver children.[10]

In conclusion, a team approach is needed as diabetes is a complex condition, and different team members are needed each with a different focus varying from diabetic complications, marriage or reproduction concerns. Integrated care is needed in order to individualize care to the patient. The child with diabetes who receives limited care is more likely to develop long-term complications at an earlier age. Screening for subclinical complications is appropriate if treatment, for intervention, is available. Early intensive therapy can prevent microvascular complications. The main goals of integrated care are early diagnosis and prompt intervention.

Summary

A team approach is needed as diabetes is a complex condition and different team members are needed each with a different focus varying from diabetic complications, marriage or reproduction concerns. Integrated care is needed in order to individualize care to the patient. The child with diabetes who receives limited care is more likely to develop long-term complications at an earlier age. Screening for subclinical complications is appropriate if treatment, for intervention, is available. Early intensive therapy can prevent microvascular complications. The main goals of integrated care are early diagnosis and prompt intervention.

References

1. Tharkar S, Devarajan A, Kumpatla S, Viswanathan V. The socioeconomics of diabetes from a developing country: A population based cost of illness study. Diabetes Res Clin Pract 2010;89:334-40.
2. Kumpatla S, Kothandan H, Tharkar S, Viswanathan V. The costs of treating long-term diabetic complications in a developing country: A study from India. J Assoc Physicians India 2013;61:102-9.
3. Bluestone JA, Herold K, Eisenbarth G. Genetics, pathogenesis and clinical interventions in type 1 diabetes. Nature 2010;464:1293-300.
4. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. N Engl J Med 1993;329:977-86.
5. Chiang JL, Kirkman MS, Laffel LM, Peters AL, Type 1 Diabetes Sourcebook Authors. Type 1 diabetes through the life span: A position statement of the American Diabetes Association. Diabetes Care 2014;37:2034-54.
6. Viswanathan V, Snehalatha C, Shina K, Ramachandran A. Persistent microalbuminuria in type 1 diabetic subjects in South India. J Assoc Physicians India 2002;50:1259-61.
7. The absence of a glycemic threshold for the development of long-term complications: The perspective of the diabetes control and complications trial. Diabetes 1996;45:1289-98.
8. Chaturvedi N, Sjoelie AK, Porta M, Aldington SJ, Fuller JH, Songini M, *et al*. Markers of insulin resistance are strong risk factors for retinopathy incidence in type 1 diabetes. Diabetes Care 2001;24:284-9.
9. Klein R, Klein BE, Moss SE. Relation of glycemic control to diabetic microvascular complications in diabetes mellitus. Ann Intern Med 1996;124:90-6.
10. Shaji UK, Satyavani K, Viswanathan V. Fear about marriage and conception among youth with type 1 diabetes: An exploratory study. J Assoc Physicians India 2011;3:1-6.

Cite this article as: Viswanathan V. Preventing microvascular complications in type 1 diabetes mellitus. Indian J Endocr Metab 2015;19:36-8.
Source of Support: Nil, **Conflict of Interest:** None declared.