The Importance of Preventing Diabetes

The diabetes epidemic statistics hide another pandemic that grows in parallel with it. Just as the world houses — million people with diabetes, it is also home to a further — million with impaired glucose (IGT), or pre diabetes.  

The current definitions for diabetes are based upon a statistical analysis of the glucose levels at which chronic microvascular complications, specifically retinopathy, begin increasing in incidence. Retinopathy was chosen because of the objectively associated diagnosis and grading. Other chronic complications are also traditionally thought to occur with glycaemic levels commensurable with the diagnosis of diabetes. Gradually, however, researchers have begun to uncover enhanced occurrence of both macrovascular and microvascular complications with IGT as well. 

IGT, or prediabetes, is an important clinical entity, therefore, not only it is a risk factor for chronic complications, it also contributes to a diagnosis of metabolic syndrome. Pre diabetes may be symptomatic in its own right, presenting with complaints similar to those observed in people with diabetes. Hence, prediabetes must be managed. Management of prediabetes is a synonym for prevention of diabetes.

Pharmacological Management

Till recently, lifestyle modification was thought to be the only treatment for prediabetes. Data from seminal studies such as the Diabetes Prevention Programme trial and well-conducted modelling studies have reinforced this opinion. Recent developments, however, have forced a relook at this issue. 

The American Association of Clinical Endocrinologists (AACE) has come out with an algorithm for management of prediabetes. The AACE promotes use of low risk antihyperglycaemic therapies if fasting plasma glucose (FPG) exceeds 100mg% or 2 hour plasma glucose is more than 140mg%. Irrespective of number of pre-diabetes criteria present (e.g. family history of diabetes, prior h/o gestational diabetes mellitus), metformin and acarbose are suggested as low risk drugs. It is recommended that life style modification (including medically assisted weight loss) be instituted prior to, or in parallel, with pharmacotherapy. The American Diabetes Association also recommends use of metformin as preventive strategy in “very high risk” individuals at high risk of developing diabetes. A quantitative approach to determination of risk in such persons has recently been published. 

Metformin is approved for use as preventive therapy for type 2 diabetes in many countries of the world. Acarbose, the only drug approved for this indication in Pakistan, has approval status in over 50 countries. Voglibose, approved in Japan as a preventive drug in 2009, also has approval in a few nations.

Caution

This, does not, however, mean that we automatically begin prescribing drugs (acarbose as per label; metformin and voglibose as alternatives) to all persons with IGT. Drug therapy comes with a risk of side effects such as gastro-intestinal intolerance, albeit mild and self limiting. Drug prescriptions carry with them a social stigma for the person with diabetes: extending these drugs to people with prediabetes will imply exposing them to societal discrimination. Diabetes diagnosis is linked with psychological morbidity, including depression; ‘medicalization’ of prediabetes can put people at risk of significant psychological stress.

Quaternary Prevention

The concept of prevention has undergone significant change in recent years. The definition and onomastics of prevention are being modified gradually. Earlier used for infectious disease, prevention is now utilized for chronic diseases as well. The line between disease and risk factors is also blurred at times. Prediabetes, for example, can be considered a disease entity on its own and a risk factor for diabetes as well.

A relatively new concept in this field is that of quaternary prevention. Proposed by Jamouille, the original statement defines quaternary prevention as “action taken to identify patient at risk of overmedicalisation, to prevent him from new medical invasion, and to suggest to him interventions ethically acceptable”. Does pharmacotherapy of prediabetes live up to the standards set by quaternary prevention? The person with prediabetes is certainly at risk of over-medicalization, just as he or she is at risk of diabetes. Protecting him or her, by any means possible, from diabetes,
means preventing or postponing various life-threatening and organ — threatening complications. Avoiding these illnesses will reduce “new medical invasion” rather than enhance it. The interventions proposed as preventive pharmacotherapy of prediabetes are ethically acceptable: they are approved by various national regulatory authorities and leading professional organizations.

Moving Ahead

It stands to reason therefore, that prediabetes must be prevented. As lifestyle modification does not control progression in all persons with IGT, and is associated with a high discontinuation rate, it needs to be supplemented. It is not enough just to “look ahead”, we need to move ahead.

No South Asian guidelines are currently available to guide the choice of prediabetes-modifying drug therapy, help decide their doses, or choose appropriate persons for pharmacological intervention.

The best persons for intervention will be those at a relatively higher risk of diabetes, such as those with a family history of diabetes, or with prior history of gestational diabetes mellitus. Bio-psychosocial constraints which limit a person’s ability to follow appropriate dietary or physical activity patterns will be another indication. Yet another robust indication for drug-based prevention is the concomitant presence of other components of metabolic syndrome with prediabetes, viz, obesity/overweight, hypertension and dyslipidaemia. Comorbid coronary artery disease may be another indication for preventive therapy (Table).

In Pakistan and in India, the only drug approved for this purpose is acarbose. However, other alpha glucosidase inhibitors such as voglibose, and the time tested metformin are approved for use in other countries. In the Indian Diabetes Prevention study, metformin was used in a dose of 250 mg twice daily.10 The AACE Prediabetes algorithm also lists thiazolidinediones and glucagon-like peptide 1 (GLP 1) receptor agonists as possible alternatives for the management of pre-diabetes. It is probable that the coming years may see the approval of liraglutide not only as an anti-obesity agent, but an evidence-backed therapy for prediabetes as well.11

Conclusion

Science is ever changing, ever dynamic. So is diabetology. Newer research continues to challenge, and change, our understanding of this syndrome, as well as our response to it. As we gather evidence of the potential long term outcomes of prediabetes, we must move to prevent it. A pragmatic approach, using available non-drug as well as pharmacological resources, will help us achieve the best for people with prediabetes in our care.

References


Table: Suggested indications for pharmacotherapy in pre-diabetes.

A. High risk of progression to diabetes
   ◆ Family history of diabetes
   ◆ Prior history of gestational diabetes mellitus
   ◆ Use of glycaemia - modifying drugs, eg, glucocorticoids
B. Presence of chronic comorbid conditions
   ◆ Comorbid artery disease
   ◆ Hypertension
   ◆ Obesity/overweight
   ◆ Dyslipidaemia
C. Presence of acute comorbid conditions which require euglycaemia for optimal resolution
   ◆ Acute trauma, eg, fracture
   ◆ Acute infection, eg, tuberculosis, skin and soft tissue infections, genitourinary infections.

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