

Controlling Diabetes Mellitus: Struggle Continued

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Diabetes remains a challenge for the treating physicians today despite all the advances in pharmacotherapy and treating devices and the increasing emphasis on the preventive measures. Not long ago, it was thought to be a disease of the affluent segments of the society, but statistics have proved that the growing problem is striking the mankind from slums of Africa to the palaces of Beverley Hills without any socio-economic discrimination. It is not a disease of the modern era either. Even in the ancient times, physicians had recognized Diabetes mellitus and were looking for possible remedies.

Dating back to 1552 BC, it was the physician Hesy-Ra of the Egyptian Papyrus dynasty who first described polyuria as the symptom of Diabetes. Following him in the 600 BC, an Indian physician Sushruta who advocated exercise to maintain equilibrium between the humors and minimize the consequences of obesity and diabetes. He also noted 'sweet' urine in Diabetes.¹ Later in the 2nd century AD, the first complete description was given by the Greek physician Aretaeus who described it as "melting down of flesh and limbs into urine". Muslim scientists of the 9th century also made significant contribution towards the recognition of Diabetes. It was Al Razi who mentioned remedies for treatment of polyuria and obesity. Following him was Ibn-e-Sina who described Diabetes as a water wheel or diarrhea of the kidneys, the abnormal appetite and collapse of sexual function in his book "Al Qanun" that remained a standard medical text in many European Universities for over five centuries.²

Few developments were made in the next few centuries and the real clinical breakthrough was the development of "Insulin" in 1921 by Friedrich Banting and Charles Best. This revolution actually changed the lives of people with Diabetes. This gift of life has prolonged the life of countless number of people but at the same time, it is again a heart rendering reality that millions of children worldwide do not have access to this blessing which was made available about 90 years ago.

Today, according to the figures of International Diabetes Federation (IDF), some 285 million people worldwide are affected with diabetes and it is estimated that the figures will reach new height of 438.4 million by 2030 which would mean an increase of about 54%.³ In the MENA (Middle East and North Africa) region, which includes Pakistan as well, the number of people living with Diabetes is about 26.4 million and the forecast for 2030 is 51.7 million which would mean an increase of

94%. Coming to Pakistan, the situation is alarming and with a current diabetic population of 7.1 million, she ranks 7th in the world in terms of the number of people with Diabetes. With an estimated prevalence of 7.6% at present and the rising growth rate, it is estimated that by 2030, she will have the 4th largest diabetic population in the world (about 13.8 million) and, therefore, it would be wise to develop a preventive strategy to combat the problem.³ There are about 88000 deaths per annum in our country due to Diabetes. The mean health expenditure on diabetes is only 24 USD per person in contrast to 55 USD per person in India. Even in Afghanistan it is 33 USD, 47 USD in Nigeria, 52 USD in Sudan and in Turkey the expenditure is as high as 571 USD per person.³

The condition is preventable and can even be treated as well with the lifestyle modification and proper therapeutic regimen. Proper control of Diabetes can prevent and delay the long-term complications which improves both the duration and the quality of life and reduces the overall health expenditure which can multiply many times in complications like renal or cardiac failure.

One of the largest clinical research studies available so far is the "United Kingdom Prospective Diabetes Study" (UKPDS). It has provided conclusive evidence that the life threatening complications of type 2 Diabetes can be significantly reduced by appropriate treatment. The initial investment of 2 million sterling pounds proved to be very cost effective as all the results provided evidence that the effective use of existing treatments reduces the risk of complications, mainly macrovascular.⁴ Similar conclusions were drawn from the Diabetes Control and Complication Trial (DCCT) which was conducted on patients with type 1 Diabetes in USA.⁵

Another striking observation made in the UKPDS was the progressive nature of the disease despite of using the best therapeutic options which makes it clear that type 2 should never be considered as a mild form of Diabetes. The objective of treatment is to achieve near normal blood glucose levels and now the American Diabetes Association has recommended the use of metformin along with lifestyle modification from the first day of diagnosis.⁶

Following UKPDS, a famous trial was ACCORD (Action to Control Cardiovascular Risk in Diabetes) that randomized 10251 participants who either had a history of cardiovascular events or were at increased risk of developing cardiovascular disease. It was observed that there was an increased mortality in the arm that included patients who were on intensive control. This striking observation actually made the researchers stop the trial after a mean follow up period of 3.5 years in the intensive regimen, 17 months before the scheduled end

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Received December 22, 2009; accepted March 22, 2010.

of the study. Later, certain downstream effects were identified in the study like higher rates of hypoglycemia, more frequent use of insulin, use of glitazones etc. and, therefore, the findings were not supportive enough. Following it was the ADVANCE (Action in Diabetes and Vascular Disease) trial that randomized 11,140 participants who also produced results that were in favour of intensive control.⁶

Studies like Da-Qing, Finnish Diabetes Prevention Study, Malmo study and the Diabetes Prevention Program have all shown that lifestyle modifications have very favourable outcomes. Diabetes Prevention Program conducted in the United States, found that the incidence of Diabetes was reduced by up to 58% in people who were following the diet and lifestyle recommendations. In contrast, metformin could achieve the target in only about 31% of the patients.⁷ This is now one of the reasons that experts across the globe are now stressing on advocating the masses to adopt a healthy lifestyle. The International Diabetes Federation has also declared "Understand Diabetes" as its theme for the years 2009-2013 focused on conveying the message of knowing the risk factors and decreasing the risk factors by changing eating habits and lifestyle.

Treating Diabetes has remained a challenge for physicians, particularly, the insulin analogs and the incretins have served as novel therapeutic agents. The guidelines are continuously in a process of revision and it is best to remain in touch with the advancements. IDF recently released new guidelines to improve Diabetes care. These guidelines cover the essential, but often neglected areas of care such as pregnancy, self-monitoring blood glucose and oral health.

The pregnancy guidelines for example now includes oral hypoglycemic agents like glibenclamide and metformin with some reservations for use during pregnancy.⁸ The focus is ofcourse to achieve the desired outcome of a healthy mother and a baby while minimize the incidence of malformations and other metabolic complications. These are the first IDF guidelines on pregnancy.

The IDF guidelines on oral health recommend focus on integrating oral health professionals. Poor oral health can negatively impact the quality of lives of people with Diabetes who need to be educated on oral health as well.

The IDF guidelines on self-monitoring of blood glucose (SMBG) in type 2 diabetes recommend that SMBG should be considered an ongoing integral part of Diabetes self-management education. SMBG protocols should be individualized to address each individual's specific educational and behavioural requirements to identify, prevent and treat glycemic metabolic disturbances to monitor the impact of treatment on decision-making.

Insulin-phobia is a global phenomenon. Attractive alternate route of administration of insulin now seems possible, after failure of the first-generation inhaled insulin (Exubera). Recent trials demonstrate that insulin oral spray is a simple, effective and safe treatment, especially for reducing post-prandial hyperglycemia with least risk of hypoglycemic events. This seems to normalize the first

phase insulin response, especially to treat hyperglycemia which is associated with co-morbidities, such as central obesity, endothelial dysfunction, hypertension, dyslipidemia and micro-albuminuria.

Regulatory approval of insulin oral-spray by the Ecuadorian Ministry of Public Health in 2005 for clinical use in type 2 diabetes was based on data from clinical trials conducted in Ecuador which involved more than 250 patients with type 2 Diabetes. Plans are underway for Phase III trials in Canada, Europe, Ukraine and North America and it is likely to be launched by early 2011.

Since publication of Edmonton protocol by researchers at the University of Alberta in Edmonton, Canada, many advances in islet cell transplantation and novel immunomodulatory agents are in pipeline, which will revolutionize this field. New drug regimens are directed towards causing selective and specific immunosuppression with least toxicity, which will allow recipients to maintain their B-cell graft.

New insulin pumps about the size of small pager will soon be in market with novel features such as insulin on board, bolus calculators, custom alarms, touch bolus, interface to personal computers, integration with blood glucose meters, full featured remote and tubeless pod. They can be programmed to deliver insulin based on individual's life style. Moreover, when this technology is combined with a continuous blood glucose monitoring system, dream of real-time control of the blood sugar level will come true. This may function as an artificial pancreas when the loop is closed.

In short, adopting a healthy lifestyle and use of proper therapeutic regimen can actually reduce the burden of Diabetes manifolds and can stop people from dying of this incurable but treatable disease.

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