The World Health Organisation places diabetes amongst the top 10 causes of death in the world. World Health Statistics (2018) affirmed that non-communicable diseases accounted for 71% of all deaths with diabetes being one amongst the top 4 causes with 1.6 million deaths. The global prevalence of diabetes has reached such massive proportions that, if all the diabetic individuals were gathered together in one country, it would be the third most populous country in the world with 415 million people. According to the latest diabetes atlas from the International Diabetes Federation (8th edition, 2017), India is home to the 2nd largest population of diabetic individuals in the world. Data from the Global Burden of Disease Study further showed that enhanced prevalence of overweight adults (across all Indian states) is a key contributing factor to this increase. Diabetes also contributed to 3.1% and 2.2% of the total deaths and total disability-adjusted life-years, respectively. India’s National Health Policy (2017) has hence targeted enhanced screening and treatment of diabetic individuals and has set its 2025 goal as 25% reduction in premature deaths due to diabetes.

It is well-known that, in type 2 diabetes (T2D), 50% of β-cell function is lost at the time of diagnosis itself. Despite this, insulin sensitizers such as metformin continue to be the first choice for initiation of hypoglycaemic therapy in most patients as recommended by the 2019 guidelines from both the American Diabetes Association (ADA) and the American Association of Clinical Endocrinologists/American College of Endocrinology (AACE/AACE). Though Sulphonylureas were the preferred drugs for several decades, the accompanying debatable issues like weight gain, hypoglycaemia, cardiovascular safety, especially with older sulphonylureas, has led over time to the search for better options for treatment. To this end, since monotherapy often does not ensure adequate control, in addition to Sulphonylureas, Thiazolidinediones and Basal Insulins, newer agents such as Dipeptidyl Peptidase 4 (DPP-4) inhibitors, Sodium–Glucose Cotransporter 2 (SGLT2) inhibitors and Glucagon-Like Peptide 1 Receptor Agonists (GLP-1 RA), have gained prominence in the treatment of T2D.

DPP-4 inhibitors present with a novel mode of action (resulting in improved β cell health and suppression of glucagon, improving both fasting and post-prandial hyperglycaemia), are weight neutral, do not cause hypoglycaemia and are devoid of adverse cardiovascular effects (except Saxagliptin and Alogliptin—due to mild increase in heart failure risk). They are thus one of the preferred recommended medications for those who need to minimise hypoglycaemia and weight gain.

There are several DPP-4 inhibitors available in India, with Sitagliptin being the oldest amongst them (approved in 2006). Sitagliptin has been extensively studied across several patient groups, both as monotherapy and in combination with other antidiabetic drugs. Its efficacy coupled with a good safety profile has made it a worthy addition to the armamentarium of diabetes management. DPP-4 inhibitors (Gliptins) have been used for more than 10 years in Indian diabetic patients. There is also evidence that DPP-4 inhibitors appear to work better in Asians, (particularly Indians and Koreans where, 1.4 to 1.5% reduction in HbA1c levels have been reported compared to Non-Asians where the HbA1c reduction is more modest, (0.5–0.8%). However, one limitation is their high cost. Since diabetes is a chronic condition, the financial burden on the patient could be substantial. Grover et al. found that the direct annual costs of antidiabetic treatment in India are in the range of 14,000 rupees out of which >60% is attributed to the cost of drugs. Indian families bear the brunt of this economic burden, hence, the therapeutic focus in diabetes should ideally hinge on affordability without compromising on efficacy. In this scenario, the recent entry of a more economical option amongst gliptins has come as a welcome respite to Indian patients. Teneligliptin, the latest agent, is available in India at a price which is considerably lower than other agents of the same class. Moreover, its unique metabolic profile has enabled its use across several patient groups without the need for dosage adjustment, unlike some of the other gliptins. Oral Teneligliptin therapy was efficacious in randomised placebo-controlled trials conducted in other Asian countries, both as monotherapy or in combination with other agents. It enhanced glycaemic control, was well tolerated and was found non-inferior to Sitagliptin as part of a triple therapy regimen.

In this issue, a study by Mohan et al. compared the efficacy of two DPP-4 inhibitors in T2D patients who remained uncontrolled (HbA1c>7%) on Metformin and/or Sulphonylurea therapy. They compared Teneligliptin with Sitagliptin in A Prospective, Open-Label, Randomized Study Comparing Efficacy And Safety Of Teneligliptin Versus Sitagliptin In Indian Patients With Inadequately Controlled Type 2 Diabetes Mellitus (INSITES) Study. In India, diabetes has a younger age of onset (20-70 years) with overweight/obesity being one of the key risk factors which is in line with the T2D patients enrolled in this study (n=76; mean age 49.2 yrs; mean body mass index=27.5 kg/m²) making it a true representation...
of the Indian diabetic population. The study subjects were treated with Teneligliptin and Sitagliptin in a 1:1 ratio. The primary outcome of mean change in HbA1c at the end of the study vs baseline was similar for both agents (=1%) with a greater proportion of patients achieving the HbA1c target of <7% with Teneligliptin (33.3%) vs Sitagliptin (19.4%; post-hoc analysis). Significant and equivalent reduction in fasting and postprandial glucose levels was also observed at week 12 with both the study drugs. The lipid parameters were minimally impacted and both drugs were well-tolerated with no incidence of hypoglycaemia with either agent. Lastly, no adverse changes in electrocardiographic (ECG) parameters were observed with both the study drugs, reaffirming their safety.21

In an era where the incidence of diabetes is reaching alarming proportions, this study is heartening evidence that cost-effective therapy can be obtained without compromising on efficacy. Though the open-label design, the small sample size and the short duration of this study may be viewed as shortcomings,21 it is a step in the right direction for a country like India where optimal diabetic management without its associated economic burden is the need of the hour. After being first approved in Japan in 2012, Japanese and Korean studies of majorly 12 to 52-week duration formed the bulk of the evidence for the efficacy of Teneligliptin, with one post-marketing surveillance of 3-year duration currently underway.18 Long-term studies to accurately assess the efficacy and safety of Teneligliptin along with its impact on cardiovascular outcomes could enhance confidence in this agent and help generate data covering all aspects of its usage. Several small studies conducted in the Indian context have shown that Teneligliptin stands true on the two tenets of diabetic therapy – efficacy and economy.22 It must be emphasized that since U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) have mandated the need for Cardiovascular Outcomes Trials (CVOT) to establish their safety, longer trials on newer molecules like Teneligliptin need to be done. Since Teneligliptin has been recently introduced in India, this study can be considered a stepping stone for future longer-term trials which can further help cement its position as a good option for the treatment of T2D in our country.

References