Message

Professor M. Zaman Shaikh (M.Sc. (Diabetes & Endocrinology) Glasgow University Ex-Director, National Institute of Diabetes & Endocrinology & Professor of Medicine, Dow University of Health Sciences, Karachi, Pakistan.)

The potential advantages of the long-acting insulin analogues are reviewed in this special supplement of Journal of Pakistan Medical Association (JPMA).

Minimizing the risk of hypoglycemia while preventing the devastating complications of T2DM is a significant challenge facing primary care providers. The frequency of hypoglycemia in T2DM is difficult to quantify due to the heterogeneity of study populations and differing definitions of hypoglycemia. It appears, however, that the frequency of hypoglycemic events is rising due to the increasing use of insulin in T2DM in order to achieve target A1C levels. Extensive clinical studies (ACCORD) have confirmed the higher risk of mortality with higher incidence of severe hypoglycemia The introduction of long-acting basal analogs, which have relatively flat and predictable time-action profiles compared with NPH, offers options for achieving glucose control with fewer episodes of hypoglycemia in the management of T2DM.

When insulin glargine was initially introduced to the market, it was shown that patients with T2DM who were newly initiated on insulin glargine had lower rates of hypoglycemic events compared with patients who were newly initiated on a premixed fixed-combination insulin.

The variability of insulin absorption and activity, known as the coefficient of variation (CV), has a major impact on glycemic control. As the CV of an insulin preparation is reduced, fewer clinically significant hypoglycemic events per patient per year are observed. A 2.7% reduction in the within-patient variation of glucose response corresponds with 3 fewer hypoglycemic events per patient-year.

Multiple studies have evaluated the efficacy and safety of adding a basal insulin to existing oral antidiabetic agents (OADs). In the Treat to Target Trial, overweight patients with T2DM who were not achieving adequate control on 1 or 2 oral agents received bedtime insulin glargine or NPH once daily. Although a majority of patients attained A1C levels less than 7% with each insulin type, nearly 25% more patients attained this goal without documented nocturnal hypoglycemia using glargine. Rates of other documented hypoglycemia were also lower with insulin glargine.

ORIGIN (Outcome Reduction with Initial Glargine Intervention), a long-term international clinical trial conducted on 12,537 people in 40 countries, over a period of six years, assessed the effect of therapy with basal insulin (glargine) on cardiovascular and other health outcomes in high risk people with dysglycemia (i.e. either pre-diabetes or type 2 diabetes).

More than 50% of participants allocated to insulin glargine achieved a FPG level below 5.3 mmol/l and 75% of these participants achieved FPG levels < 6.0 mmol/l (108 mg/dl) for most of the trial.

The development of new diabetes in people without diabetes at baseline was reduced by 28%.

Cost is a consideration in insulin therapy. Although more expensive than NPH, basal glargine is associated with 25% fewer episodes of nocturnal hypoglycemia, improved postdinner control, and slightly less weight gain. Considerable direct costs result from treatment of hypoglycemia associated with antidiabetic therapy, suggesting that therapies with less potential for inducing hypoglycemia would likely reduce these costs.

Insulin is becoming a necessary tool in the management of more and more patients with T2DM. It is necessary to be able to achieve target A1C levels and prevent long-term complications of diabetes. When considering basal insulin for initiation of therapy, NPH is clearly associated with increased risk of hypoglycemic events when compared with insulin glargine. An understanding of the pharmacodynamics of basal insulin is necessary to assist patients in obtaining glycemic control while improving safety.