Diabetology

Extended Abstract

Continuous Glucose Monitoring Guided Assessment of Concentrated 200 IU/Ml rDNA Human Premix 30/70 Insulin in Type 2 Diabetes Mellitus Patients - Hemant Thacker - Bhatia Hospital, India

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Abstract

Of the worldwide 415 million people with diabetes, India is home to 69.1 million cases, representing approximately 6% of the global population with diabetes [1]. Association between body weight and type 2 diabetes mellitus (T2DM) is well known. Higher levels of free fatty acids in patients with central obesity increase the need of more insulin production and predisposes patient to insulin resistance [2]. Thus, obesity and its associated insulin resistance have contributed not only to increased prevalence of T2DM but also to a rise in the insulin needs of insulin requiring patients with T2DM. Despite the availability of several anti-diabetic agents, most patients with T2DM need addition of insulin in their treatment regimen [2]. Thus, insulin is an indispensable treatment option for diabetes management. Several and long acting insulin analogues are available for the treatment of diabetes mellitus. The traditional insulin formulations (U-100) provide 100 units per milliliter. Apart from some endocrine disorders like polycystic ovarian diseases, Cushing syndrome, and temporary conditions like pregnancy, severe infection, and intake of steroid that cause high insulin resistance thereby increasing total daily insulin requirement, diabetes with obesity has been a common observation in outpatient clinics. Such patients in long run eventually develop high resistance and require ≥ 2 units of insulin per kilogram of body weight daily or > 200 units of insulin daily to meet their insulin needs. Such patients require high volume of insulin, in multiple doses which is painful thus leading to adherence issues.

Therefore, a need of insulin formulations providing high dose at the lower volume was felt [2,3]. In order to fulfill this unmet need, concentrated insulin formulations are prepared. U-200 i.e. r-DNA human insulin premix 30/70, a concentrated insulin formulation which provides 200 IU per milliliter is marketed in India. U-200 is a rapid-acting insulin analog which differs from human insulin in its amino acid profile [2]. The advantages of U-200 insulin include less intra-individual variability as well as reduced injection burden in individuals requiring high-dose and large volume insulin therapy with lower or

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similar risk of hypoglycemia like U-100 insulin [4]. Data on 24 hour glycemic control with concentrated insulin in Indian T2DM patients are limited. Thus the study was planned to study the 24 hour glycemic variability with use of r-DNA Human insulin premix 30/70 at concentration of 200 IU/mL in patients with T2DM.

This was a prospective, open label, single arm, two center, observational study conducted at 2 centers of India; Jothydev's Diabetes Research Centre, Trivandrum, Kerala and Bhatia Hospital, Mumbai during October 2016 to December 2016. Adult T2DM patients between 18-70 years of age treated with regular/NPH or premixed human insulin levels were included. Adult patients between 18-70 years of age having T2DM for minimum six months and on treatment with human insulin (regular/NPH/Premix) on stable insulin dose since last eight weeks were enrolled. Patients with body mass index (BMI) less than 18 kg/m^2 and more than 30 kg/m^2, those with HbA1c > 9.5% or receiving any insulin other than regular/NPH r-DNA human insulin or on any insulin analogues in last one month were excluded. Patients with modification of concomitant oral anti-diabetic (OAD) medicines regimens or insulin dose in past three months, patients treated with Sulfonylureas, Meglitinide derivatives in last 1 month, history of recurrent hypoglycemic episodes or event of severe hypoglycemia or diabetic ketoacidosis/hyperglycemic hyperosmolar coma in past three months, diabetes related moderate to severe complications, history of surgery, severe trauma, infection or hospitalization in past six months, pregnant and lactating women were also excluded from the study. Before enrollment, informed consent was obtained from eligible patients. The study was initiated after receiving approval from the Independent Ethics Committee.

The demographics, medical history, dietary history, current insulin regimen, concomitant OADs and treatment history were recorded. Variability in 24-hour blood glucose profile was measured by a CGMS device. For this, all study participants were educated about use of CGM device (iPro2, Medtronic, USA). The sensor was deployed under medical supervision at study site and the iPro2 recording device was connected to sensor. All patients were trained on operating procedure of glucometer for self-monitoring of blood glucose (SMBG) and U-200 pen.

All enrolled patients were treated with U-200 (r-DNA Human Insulin Premix 30/70 - 200 IU/mL) pre-filled disposable pens and cartridges for six days. The dose and regimen was continued as per ongoing regimen of patient. Existing dietary habits and physical activity were continued during study period. They were also be informed about possible adverse events/signs of hypoglycemia and advised to inform the investigator in event of adverse event/CGM device malfunctioning. Time of meals, time and dose of insulin administration and blood glucose levels at different time points were reported in patient diary by the patients till the next study visit. Minimum three readings i.e. pre-breakfast, pre-lunch, pre-dinner were taken at eight hour intervals for proper calibration of device.

The CGM device was removed on day seven (Visit 2) and CGM readings were recorded. The evaluation

parameters included percentage of patients within acceptable glycemic range, Mean Amplitude of Glucose Excursions (MAGE) [5] and duration and frequency of hypoglycemic (< 70 mg/dL) and hyperglycemic (> 150 mg/dL) episodes. Patients were educated about the CGMS device as the part of informed consent process and study procedure by the Investigator or the person designated by the Investigator. Used/unused cartridges and pen device were collected to ensure appropriate insulin doses during entire study period and adverse events if any were recorded.

This work is partly presented at 52th Annual Congress on Neuroscience and stroke 2020, December 14, 2020

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