**BACKGROUND**

- Hyperglycemia is associated with increased risk of diabetic complications and mortality
- Post-prandial hyperglycemia and late post-prandial hypoglycemia are common problems due to insulin stacking with rapid-acting insulin analogs
- Technosphere insulin (TI, Afrezza® Mannkind Corporation, Westlake Village, CA) is a dry powder formulation of regular human insulin adsorbed onto Technosphere microparticles for oral inhalation (Figure 1)
- TI has a faster onset and shorter duration of action that allows more rapid post-prandial insulin action

**STUDY OBJECTIVE**

- In this pilot investigator-led, collaborative open-label multi-center randomized pilot clinical trial, we evaluated the efficacy of TI for post-prandial glucose control (PPBG) measured by time-in-range (TIR) on continuous glucose monitor (CGM) and post-prandial glucose excursions (PPGE) over a 4-week treatment period.

**METHODS AND MATERIALS**

**Study Participants:** Adults 18-70 years old with T1D for at least 6 months and HbA1c 6.5-10.0% (48.0-86.0 mmol/mol) participated at 5 clinical centers in the US between June 2017 and December 2017.

**Inclusion Criteria:** Non-smoking adults, BMI ≤ 35 kg/m², forced expiratory volume in 1 s (FEV₁) and forced vital capacity (FVC) ≥ 70% predicted, on multiple daily injections (MDI), with stable insulin dose ≥ 3 months, and use of insulin degludec or glargine as a basal insulin.

**Withdrawal Criteria:** A decrease ≥ 20% of FEV₁ was a withdrawal criteria, but no patients met this criteria.

**Randomization:** Patients were randomized 1:1 to TI or insulin aspart, stratified by screening HbA1c (≤ 8% or > 8%).

**Insulin Dosing:** Patients randomized to insulin aspart continued the same bolus dose as used prior to randomization; Patients randomized to TI converted to a starting pre-meal TI dose according to a conversion table based on the label (Table 1). Patients in the TI group were advised to take additional injections at 1 and 2 hours after meals based on PPBG per protocol (Table 1).

**Compliance:** At least 80% compliance with TI doses was considered ‘compliant’, and a per protocol analysis was conducted to examine compliant use of TI vs. insulin aspart.

**RESULTS**

**Use of TI Improved PPBG and PPGE (Table 4, Figure 4, 6 and 8)**

- TIR was significantly increased in Compliant patients (Figure 3)
- There was no increase in time in hypoglycemia (Table 4)

**SUMMARY OF RESULTS**

In summary, TI improved PPG as well as all day glucose time-in-range with additional post-prandial TI dose as needed. Further, TI decreased daytime glucose variability and reduced time spent in hypoglycemia.

**CONCLUSION**

The faster action with shorter duration profile of TI when compared to rapid-acting insulin analogs may provide a flexible approach for patients to optimize post-prandial glucose control without increasing risk of hypoglycemia.

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