Post-Prandial Glucose Following a Bolus with Inhaled Insulin Versus Usual Care

Results from the INHALE-3 Randomized Trial

Irl B. Hirsch[1], MD for the INHALE-3 Investigator Group

[1]University of Washington, Seattle, WA USA

OBJECTIVE

To assess efficacy and safety of a higher dose of Technosphere® Insulin (TI) compared to United States Prescribing Information (USPI) by using a modified dose conversion in patients with usual care rapid acting insulin analogue (RAA) therapy comprising of Automated Insulin Delivery (AID), Non-Automated Pumps, and Multiple Daily Injections (MDI)

CONCLUSIONS

- Post-meal hyperglycemia was significantly reduced with TI compared to subcutaneous RAA
  - Area under the curve (AUC 180) reduced by 20%
  - Peak glucose reduced by 20 mg/dL
- Post-meal hypoglycemia infrequent with both insulins

INTRODUCTION

Inhaled Technosphere Insulin (TI) has an ultra-rapid acting profile, due to its unique pharmacokinetic and pharmacodynamic properties, resulting in a much faster time-to-peak effect and clearance compared to subcutaneously (SC) administered RAA.

A significant proportion of individuals with type 1 diabetes are not achieving their glycemic targets including those on AID with SC RAA infusion[1]. RAA mealtime insulin has a longer action that potentially limits the ability to achieve 2-hour postprandial glucose targets without causing hypoglycemia 3-4 hours after the meal.

INHALE-3 is a 17-week randomized controlled trial comparing efficacy and safety of TI combined with insulin degludec versus usual care (AID, nonautomated pump, or MDI) in adult subjects with T1D. This first meal analysis uses a higher modified TI dose conversion compared to the USPI, shown in other proof of concept studies to improve postprandial glucose without any new safety concerns[2].

TI is approved for use in adults with diabetes and is available in three color-coded dosage cartridges: 4U (blue), 8U (green), and 12U (yellow)[2].

METHODS

Study Population

One hundred and twenty-three adult participants with T1D on either AID, MDI, or non-automated pumps were randomized one-to-one to TI or stay on their usual care.

Study Design

Participants were provided identical amounts of a nutritional shake (one 37g bottle of Boost® [Nestlé, Leeds, England]) for the standardized meal. Participants were requested to fast and avoid an insulin bolus for four hours prior to the meal.

Participants in the TI group converted from RAA to TI using a modified dose conversion described in Table 1. TI was inhaled at the start of the meal (t=0) and RAA was administered 5-15 minutes prior to the start of the meal per their individual insulin's instructions.

Participants with insulin pumps continued to receive their basal insulin through the pump.

Glucose was monitored through fingersticks taken at 15-30 minute intervals across the two hour post-prandial period and Dexcom G6 Pro (Dexcom, San Diego, CA).

Table 1. TI Dose Conversion

Injected Mealtime Insulin Dose (RAA)	Converted Inhaled Insulin Dose (TI)
up to 3 units	4 units
4-5 units	8 units
6-7 units	12 units
8-9 units	16 units
10-11 units	20 units
12+ units	24 units

RESULTS

One participant withdrew consent leading to 122 participants continuing through the standardized meal. Demographic characteristics are summarized in Table 2. The distribution of usual care modalities and AID systems is summarized in Figure 1.

Area under the curve (AUC) 180 mg/dL, peak glucose, time to peak glucose, and glucose excursion were all favorable to TI in the two-hour post-prandial period ($p<0.05$). AUC was reduced by 20% and peak glucose was reduced by 20 mg/dL.

Table 2. Participant Demographics

Baseline Characteristics	N=122
Mean Age	45 yrs (range 18-77)
Female	57%
HbA1c	7.6% (range 5.4-10.5)

Figure 1. Insulin Delivery Modalities

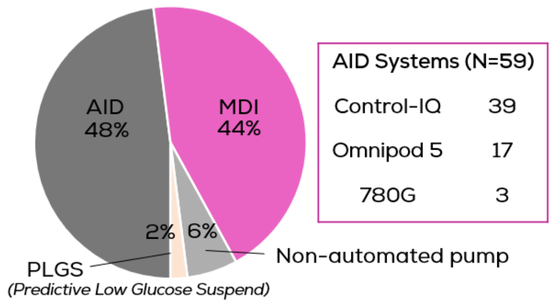
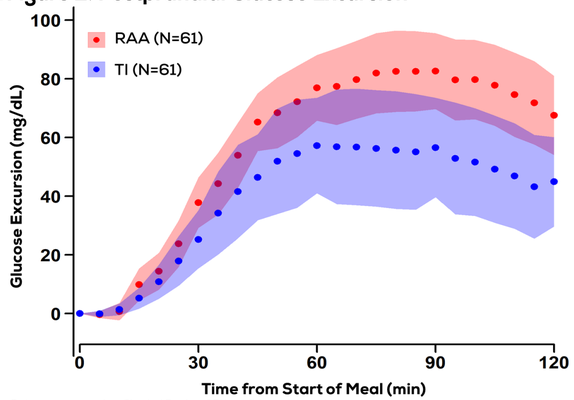


Table 3. RAA Group Distribution

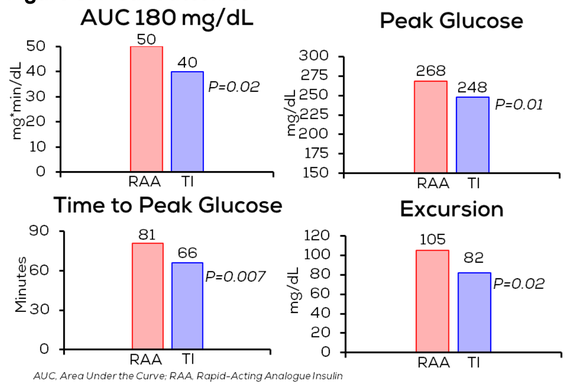
Insulin Delivery		Type of RAA Insulin	
AID	48%	Lispro	32
MDI	43%	Aspart	23
Non-Automated Pump	5%	Fact-Acting Aspart	3
PLGS Pump	5%	Glulisine	1
		Ultra-Rapid Lispro	1
		Regular Insulin	1

Figure 2. Postprandial Glucose Excursion



Dots: mean excursion; Shaded Region: 95% confidence interval

Figure 3. Meal Outcomes



AUC, Area Under the Curve; RAA, Rapid-Acting Analogue Insulin

Safety

One participant in the RAA group and one participant in the TI group were treated for hypoglycemia during the 2-hour meal challenge. One participant in the RAA group required additional insulin due to hyperglycemia.

1. Ebekozien O et al. Diabetes Technol Ther. 2023;25:765-773. 2. Afrezza (insulin human) Inhalation Powder Prescribing Information. MannKind Corporation. Danbury, CT; February 2023.

mannkind

Children With Diabetes Friends for Life • July 9-14, 2024 • Presenting: Kevin Kaiserman, MD; Joanne Rinker MS, RDN, BC-ADM, CDCES, FADCES