INTRODUCTION

- >1 million people with diabetes on CSII therapy
- CSII set needs to be replaced every 2-3 days due to insulin absorption variability
- Variable and unreliable glucose control increases risk of developing hyper-hypoglycemia, and diabetic ketoacidosis
- Previous studies from this group identified a layer of inflammatory tissue surrounding CSII cannulas which increases in thickness and density over time
- Layer = coagulated blood, edema fluid, damaged connective tissue, cellular debris, neutrophils, macrophages, and fibroblasts
- Layer = mechanical barrier; slowing or inhibiting the movement of insulin into adjacent subcutaneous tissue containing capillary and lymph vessels
- Repeated trauma of insertion contributes to scar tissue formation and may result in infusion site loss

The dose-to-dose/site-to-site variability of insulin absorption over CSI set wear-time may be related to:

- Location of functionning capillary and lymph vessels in the vicinity of cannula
- Variable capillary blood and lymph flow
- Variable rate of insulin transport across the endothelium
- Insulin degradation by proteases within the wound and/or lymph nodes
- Insulin movement upward onto the skin surface (path of least resistance)

Capillary Biomedical, Inc. (CapBio) has developed a prototype kink-resistant infusion set cannula using a soft polymer material with coil reinforcement and multiple ports.

PURPOSE OF THE STUDY

To compare the CapBio investigational CSII set with a coil-reinforced soft polymer cannula to a commercially available Teflon CSII set (Upmedical).

HYPOTHESIS

The use of the investigational soft, flexible cannula (CapBio) produces less tissue inflammation compared to a standard Teflon set over a 14 day period.

METHODS

- Large farm swine, n=16, t=14 days
- CapBio (13 mm, 30°) and 1 commercial set (Teflon, 6 mm, 90°) were inserted every other day for 14 days; indwelling duration: t=10 minutes, and t=2, 4, 6, 8, 10, 12, 14 days
- U-5 insulin was continuously infused (commercial insulin pumps)
- 7U bolus 1-2x/day with meals.
- Day 14: infusion of 7U bolus U-100 insulin; excision.
- Transfer of tissue to formalin for subsequent histopathological staining and analysis of:
  o Thickness of the inflammatory layer along the cannula channel
  o Total surface area of inflammation around the cannula channel
- Statistics (Systat software, ver. 13): ANOVA – GLM and Linear Mixed Models performed Post hoc analyses were performed using Bonferroni correction A p<0.05 was set for statistical significance.

Note: Only cannulas with ≥50% view of the channel were included in this analysis; measurements were repeated 5 times separately by 2 analysts and averaged.

RESULTS

1. Thickness of the Inflammatory Layer

- Statistically significant difference (p<0.001) between the 2 groups in the mean inflammatory layer’s thickness over the 14-day period.
- Statistically significant (p<0.001) thinner inflammatory tissue layer around the CapBio CSII cannulas compared with the commercial CSITeflon cannulas for Days 4–14 post insertion.
- Thickness and area of inflammatory tissue around the CapBio cannulas stabilized after 2 days, but continued to increase around the commercial CSII cannulas until Day 6. The observed difference persisted to from Days 8–14.

2. Total Surface Area of Inflammation

- Statistically significant difference (p<0.0001) between the 2 groups in the total surface area of inflammation over the 14-day period.
- Area of inflammation was significantly (p<0.05) higher around commercial catheters compared with CapBio for days 10–14 post insertion.

DISCUSSION

- Compared with the commercial CSII set, the CapBio with a soft, flexible polymer cannula and wire-reinforced wall and multiple ports resulted in less tissue inflammation over 14 days.
- A thick inflammatory layer around the infusion catheter presents a mechanical and chemical barrier to insulin flow into the tissue.
- The CapBio may produce greater reliability of insulin delivery due to the wire-reinforced cannula that resists kinking and the multiple orifices that produce redundancy.
- The CapBio may produce greater reliability of insulin delivery over extended wear-time due to better tolerability and less elicited inflammation.

OUTLOOK/CONCLUSION

- There is great clinical need for an insulin infusion set that functions reliably for more than 3-4 days with improved consistency of absorption (PK).
- PK/ID studies in humans will determine whether this lower inflammatory response results in more consistent insulin absorption from dose-to-dose.

REFERENCES