Tissue Histology Surrounding Continuous Subcutaneous Insulin Infusion (CSII) Catheters Implanted in Canines for 7 Days


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Introduction

- We are trying to understand the mechanisms that cause variable insulin absorption when infused through a commercial CSII catheter into the subcutaneous tissue.
- A pilot observational canine study was performed to evaluate the PK-PD of insulin lispro absorption and the tissue histology surrounding CSII catheters implanted for 7 days.
- Insulin absorption into the circulation may be affected by variable capillary blood flow, insulin transport across the endothelium, lymph flow, insulin sequestration within the wound, degradation by proteases, and transport upward along the cannula onto the skin surface.
- Manufacturers and clinicians recommend insertion of a new CSII catheter at an alternate location every 2 to 3 days to minimize the risk for hyperglycemia, hypoglycemia, DKA and infection.

Methods

- IACUC approval
- 13 adult mongrel female non-diabetic canine ~ 30 kg
- Two Teflon CSII catheters (Quickset, Medtronic MiniMed) and 3 L-CGM (Guardian L4, DexCom) were inserted into the soft underbelly of each canine using general anesthesia.
- One CSII catheter was continuously infused with insulin lispro (basal rate 0.1 unit/hour), while the other catheter was filled with saline and capped.
- Glucose clamp experiments were performed days 1, 3, 6, & 7 after implantation (hyperinsulinemic-euglycemic clamp).
- Glucose clamps used a bolus of insulin lispro (0.1 unit/kg) only (n=5), insulin lispro plus tissue plasminogen activator (tPA) (n=3), insulin lispro plus streptokinase (n=3), insulin lispro plus streptokinase plus mechanical vibration (n=1), and insulin lispro plus tissue plasminogen activator plus mechanical vibration (n=1).
- The skin and subcutaneous tissue surrounding the CSII catheters were excised, fixed with 10% formalin, sectioned, and stained.
- A surgical pathologist is currently analyzing the slides to determine the degree of tissue damage, inflammation, and thrombus in relation to adjacent vascular adipose tissue.

Results

- The layer of inflammatory tissue that surrounds a CSII cannula may inhibit or slow the flow of insulin into adjacent vascular subcutaneous tissue.
- There was a variable degree of tissue damage and variable amount of inflammatory tissue.
- The layer of inflammatory tissue was variable in thickness, density, composition, and continuity.
- The tissue histology surrounding the CSII cannula was grossly similar when infused with insulin lispro only, lispro plus tPA, lispro plus streptokinase, and filled only with saline.
- A detailed analysis of the tissue histology is currently being completed by a surgical pathologist.

Discussion

- CSII catheters implanted for 7 days produced a variable amount of damage to adipose cells, connective tissue, capillaries, lymphatic vessels and skeletal muscle cells.
- All of the CSII cannulas were partially or completely surrounded by a layer of inflammatory tissue (containing neutrophils, macrophages, cellular debris, and fibrous tissue).
- Canine subcutaneous tissue had layers of skeletal muscle and mammary tissue mixed within the adipose tissue.
- The layer of inflammatory tissue surrounding CSII catheters infused with insulin lispro only, insulin lispro plus streptokinase, and insulin lispro plus tPA varied in thickness, composition, density, and continuity.
- The tissue surrounding the CSII catheters infused with lispro only (control group), tissue plasminogen activator, or streptokinase had minimal thrombus.

References