Continuous subcutaneous insulin infusion (CSII) sets have been called the “Achilles heel” of infusion pump therapy, with known failure modes including leakage, occlusion alarms1-3, and “silent” occlusions4,5. Silent occlusions are characterized by in-line infusion pressure excursions that may indicate flow interruptions below insulin pump alarm thresholds.6,7 Inconsistent flow may lead to irregular blood glucose and increase the potential for hypoglycemia in some patients. Unexplained hyperglycemia is a common occurrence in T1D on pump therapy.3

A novel infusion set (BD FlowSmart™) is in development to stabilize flow. To assess flow performance, in-line infusion pressure was recorded during insulin lispro infusion in a swine model, and flow interruptions were quantified by a novel pressure/flow/rate assessment. Insulin pharmacokinetics (PK) were measured to correlate in vivo flow performance with physiological insulin uptake to establish predictive models of insulin delivery and flow fault detection.

Methods

Study Design & Data Collection:
- Insulin was delivered via commercial insulin pump over a series of infusion profiles using 2 commercial CSII sets (1 steel, 1 polymer catheter) and 1 investigational (polymer catheter) set.
- In-line infusion pressure and insulin PK were simultaneously monitored at clinically relevant infusion rates (1U/hr basal; 4U/bolus) per Table 1.
- N=11 nondiabetic Yorkshire swine during insulin lispro delivery. Each study arm was run in 1-2 replicates in every animal per Table 1.

Results

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- When comparing polymer catheter sets, BD FlowSmart™showed reduction in flow interruption frequency, duration, & 88% reduction in percent total flow interrupted (Figs. 2 & 3).
- There were no statistically significant differences in pump occlusion alarm or leakage occurrences among device types.

Study Description

- Study was designed to evaluate the PK of the investigational set FlowSmart™ vs. the commercial set Rapid-D. Two sets of studies were performed with the rapid-D set run in parallel.
- The PK studies were conducted in pigs and included 8 pigs total (6 swine, 2 boars). The PK studies were conducted by Wingate et al. (Diab Ther 2012) to validate the PK model for the devices.

Conclusions

- The consistency & reliability of subcutaneous insulin infusion is affected by multiple parameters including sub-optimal CSII set delivery with intermittent un-diagnosed silent occlusions. Stabilizing infusion pressure and reducing flow faults may enable more predictable and consistent insulin infusion.
- Insulin pressure may be a good indicator of insulin flow reliability and can provide high sensitivity occlusion detection below pump alarm thresholds. These sub-alarm events can be detected and quantified when analyzed by the proprietary pressure/flow algorithm.
- The investigational set (BD FlowSmart™) showed improved insulin flow reliability relative to the commercial polymer set. This was based on detectable silent occlusion reduction as identified by the pressure/flow algorithm.
- The use of infusion pressure input parameters into the theoretical PK prediction model improves fit to measured lispro values when flow interruption periods were >1 hour, but lacked the sensitivity to improve fit for smaller flow interruption durations.
- Additional optimization to improve sensitivity for shorter duration and more irregular flow interruptions is required. Compensation for other factors affecting PK variability (e.g. insulin absorption, assay variability, tissue site effects, animal growth variation) may improve model fitting efficiency. In addition, other methods such as population modeling or PK simulations using Artificial Pancreas simulators may enable better assessment of flow variability impact on PK.