

Ultra-long-acting Recombinant Insulin Shows Promise for Use in Dogs with Diabetes Mellitus

Once-weekly subcutaneous injection with an ultra-long-acting recombinant insulin provides adequate control of diabetes mellitus in dogs.

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August 12, 2022 – Once-weekly injection of an ultra-long-acting recombinant insulin results in no significant changes in clinical signs, median body weight, fructosamine concentration, or mean interstitial glucose concentration when compared with baseline twice-daily insulin therapy.

Sean E. Hulsebosch, DVM, DACVIM, from the University of California in Davis, California, and colleagues reported their findings in the July 2022 issue of the *Journal of Veterinary Internal Medicine*.

Diabetes mellitus is estimated to have a prevalence of 0.3%-0.6% in dogs, with standard-of-care treatment currently relying upon chronic administration of exogenous subcutaneous insulin. After discussion with their veterinarian about the challenges of twice-daily insulin administration, clients elect euthanasia for their dog approximately 33% of the time within 1 hour of diagnosis. Once-weekly injections of insulin could decrease the burden on pet owners. A novel ultra-long-acting insulin construct (AKS-218d) that is injected subcutaneously once-weekly shows promise for decreasing the burden on pet owners while maintaining glycemic control in the patient.

In this prospective clinical trial, five client-owned dogs with naturally occurring diabetes mellitus were recruited from the UC Davis Veterinary Teaching Hospital and local veterinary clinics. Participating dogs were previously controlled with intermediate-acting insulin given subcutaneously every 12 hours for at least two months prior to participation in the study. Patients were transitioned to once-weekly subcutaneous injections of AKS-218d, the dose of which was titrated weekly for 8 weeks based on the patient's clinical response and continuous interstitial glucose monitoring through the use of a flash glucose monitoring system.

At the end of the study, interstitial glucose remained similar to baseline with a mean of 261 mg/dL (range 176 mg/dL to 410 mg/dL, $P = .80$). The median serum fructosamine concentration of 451 $\mu\text{mol/L}$ (range 387 $\mu\text{mol/L}$ to 634 $\mu\text{mol/L}$, $P = .43$) was not significantly changed from baseline. In comparison to baseline, owners additionally reported good control of clinical signs and body weight that was unchanged ($P = .6$). Glucose variability was also similar between patients receiving AKS-218d versus pre-study insulin (glucose variability percentage = 204% [range 134% to 304%] vs 210% [range 161% to 333%], $P = .2$). Serum AKS-218d concentrations of approximately 20 ng/mL corresponded to good glycemic control, meaning no clinical signs and a weekly interstitial glucose mean under 250 mg/dL. All five dogs achieved these concentrations after the second injection.

With the exception of infrequently low interstitial glucose, no clinical, hematological, or biochemical adverse effects were noted during the clinical trial. Patients did not develop evidence of clinical hypoglycemia. Anti-drug antibody formation, which commonly occurs with insulin therapy in dogs, developed in 1 out of 5 dogs resulting in recurrence of clinical signs of diabetes.

It is anticipated that twice-daily injection of insulin in dogs is associated with poor compliance compounded by the physical and emotional challenges of repeated injections in dogs. Dr Hulsebosch and colleagues state, "A treatment that offers an alternative to daily injections should minimize these barriers to greater treatment success, improve quality of life for the pet and owner, and increase dog survival."

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