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Background

Wilford Hall Ambulatory and Surgical Center is the Department of Defense's largest outpatient ambulatory surgical center serving over 55,000 patients, and is the U.S. Air Force's flagship medical facility for outpatient care.

As with the measurement of any medication concentration or lab value, there is some reasonable expectation that there may be some variability between the reported value and the objective measurement. However, expectations are that variability should be minimal in order to ensure reliable doses of medication. In the case of diabetes management, insulin concentration variability should be kept to a minimum for both its life-saving and stress-mitigating effects. Insulin in the correct doses is lifesaving for type 1 Diabetes, so understandably, the impact of degraded insulin is catastrophic. In both type I and type II diabetes, "diabetes distress" can lead to poor self management and is linked to higher A1C levels. A study published in 2017 testing insulin after receipt from their cold supply chain found shockingly low concentrations of insulin. Recent literature published in the Journal of Diabetes Science and Technology reported that insulin concentrations in randomly tested vials not only failed to meet a pre-established concentration standard per unit of insulin, but also had concerning variability. The prevalence of Diabetes in the Department of Defense population is approaching 20%, making the impact of degraded insulin concerning. There are expectations of variability in any medications prescribed, but the FDA states that the expected insulin concentration should be 95% or greater.

Methods

Overall, 40 vials representing two different types of insulin (20 vials of Novolog and 20 vials of Lantus) were collecting from the military pharmacy and transported to the clinical research laboratory for analysis. Following baseline analysis, half of the vials were stored in refrigerated conditions of 2-8 degrees Celsius; the other half were stored at room temperature according to manufacturer's directions.

Results

At the laboratory, all vials underwent initial analysis to determine concentration at baseline. The Novolog insulin was found to have a concentration range of 105.1% to 107.7% and the Lantus insulin concentration was 99.0% to 103.9%. Thus, all vials met the minimum concentration of 95 U/ml at time of baseline testing. Vials will be tested weekly to determine if degradation occurs under refrigeration and at room temperature.

Discussion

Given the high cost of insulin and the high impact on the health of the person with diabetes, assurance of a minimum of 95 U/ml must be met. If this is not met, investigation of the cold supply chain should identify the source of the problem and address it. Our study demonstrates that Novolog and Lantus were meeting the minimum concentration upon receipt at the pharmacy.

Neuroendocrinology and Pituitary

ADVANCES IN NEUROENDOCRINOLOGY

Deletion of Hepatic Kisspeptin Results in Abnormal Glucose Metabolism in Female Mice

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Kisspeptin is a hypothalamic protein critical for neuroendocrine control of pubertal development and fertility and is modulated by nutritional signals. Kisspeptin has been localized to specific neurons located in the arcuate and anteroventral periventricular (AVPV) nuclei of the hypothalamus and is secreted to control GnRH mediated pubertal maturation and reproduction. Kisspeptin has also been localized to peripheral tissues including the liver, fat, gonads, intestine and placenta, although its role in these tissues is unclear. The objective of current study is to define the role of hepatic kisspeptin as a metabolic sensor. A floxed *Kiss1* mouse has been developed, and ablation of liver-specific *Kiss1* was achieved in two to three month old $Kiss1^{f/f}$ male and female mice given a single tail vein injection of thyroid hormone-binding globulin (TBG) promoter-driven Cre recombinase adeno-associated virus (AAV-CRE). A control group of $Kiss1^{f/f}$ male and female mice received an injection of AAV-GFP, expressing green fluorescent protein. Two weeks after injection, a glucose tolerance test (GTT) was performed followed by an insulin tolerance test. To determine whether changes had occurred in the reproductive axis, estrous cyclicity was assessed by daily vaginal smears and estrous cycle phases determined by vaginal cytology. Mice were euthanized four weeks post-injection and tissues were collected for RNA extraction and gene expression analysis via qRT-PCR. As expected, qRT-PCR data showed absence of *Kiss1* expression in the liver of AAV-CRE mice compared to AAV-GFP mice with no changes in kisspeptin gene expression were noted in the ovary, testes, spleen, pancreas, arcuate or AVPV. Estrous cyclicity was also not affected by viral ablation of hepatic *Kiss1*. Elevated fasting glucose and glucose intolerance in the GTT were found in AAV-CRE compared to AAV-GFP females ($P < 0.05$). No differences in AAV-CRE and AAV-GFP male mice were found, indicating the importance of *Kiss1* in glucose homeostasis in females. The insulin tolerance test was not statistically different between groups or treatments. Further research is required to elucidate the mechanism by which hepatic kisspeptin alters glucose metabolism in mice in a sexually-dimorphic fashion.

Diabetes Mellitus and Glucose Metabolism

GESTATIONAL DIABETES, DIABETES IN PREGNANCY, AND IN UTERO EXPOSURES

Sex-Specific Difference in REG3G Expression Directs the Maintenance of Islet Function in Offspring of Obese Mice

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