Altasciences, 562 State Road DD, Auxvasse, MO 65231, United States
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An Examination of the Effects of Body Temperature on QT Interval in Non-Naïve Telemetered Göttingen Minipigs®

Miri K Pannu[1], Joel Baublits[2], Rebecca M Smith[1], Emily M Griffith[1], and Theodore J Baird[1].
[1]Altasciences Preclinical Columbia, Auxvasse, MO, United States, [2]Cardiovascular Analytics, Newbury Park, CA, United States

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ABSTRACT

Body temperature (BT) changes have been shown to affect the QT/QTcH interval. Given the known inverse relationship in other species (e.g., dog and human), the study objective was designed to propose a correction formula for routine application in miniature swine. Eight male telemetered Göttingen Minipigs® were used to determine the relationship between QT/QTcH interval and BT. The study was conducted in two phases. In Phase 1, the animals received a singular intramuscular (IM) injection of Zoletil (tiletamine and zolazepam for injection) (9 mg/kg) due to known effects on heart rate and BT. In Phase 2, the same animals were anesthetized, and manual cooling and heating procedures were applied to investigate further the relationship between BT and QT/QTcH interval. After administration of Zoletil, significant ($p< 0.05$) increases in the QT/QTcH interval with concomitant ($p< 0.05$) decreases in BT were observed. Peak differences for QT/QTcH occurred at 2 hours post-dose, with values returning to baseline by approximately 4 hours post-dose. Peak differences for BT occurred at 2 hours post-dose, with values returning to baseline by approximately 4 hours post-dose. Given the known inverse relationship between BT and QT/QTcH, these changes were to be expected. The relationship between BT and the QTcH interval was established in Göttingen Minipigs® in both conscious and anesthetized states. This study provided evidence of an inverse, apparent linear relationship between the two parameters. A QTcH formula with a correction factor for BT changes (QTcHcT) was derived for both conscious and anesthetized states.

METHODS

Animals were instrumented with telemetry implants, and continuous data collection was conducted using Ponemah® software during both study phases.

Phase 1:
- Animals received a singular IM injection of Zoletil.

Phase 2:
- Animals were anesthetized with isoflurane via mask, then intubated to provide consistent oxygen levels, and maintained in a constant anesthetic plane with isoflurane.
- At least 10 minutes of continuous readings were collected at normal BT.
- BT was cooled to a target of 34 ºC
- BT was then warmed to a target of 41 ºC

The resulting data was analyzed post-acquisition on a validated system with EMKA ecgAUTO.

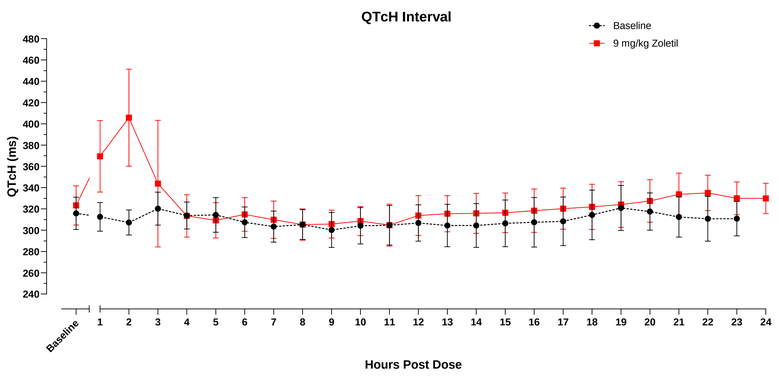

Figure 1. QTcH interval observed following administration of Zoletil

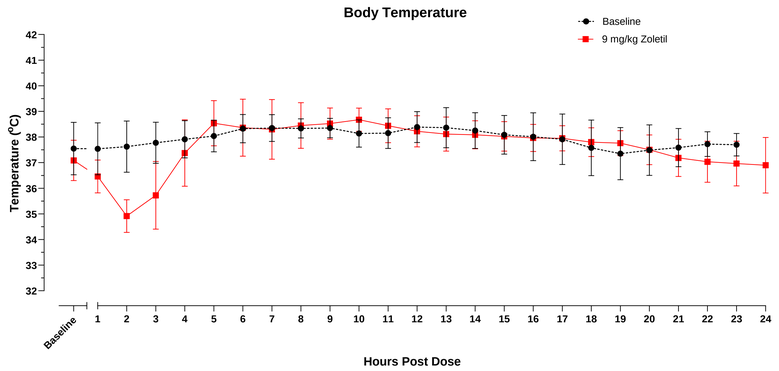

Figure 2. Body Temperature observed following administration of Zoletil

RESULTS

ECG:
Significant ($p<0.05$) increases in the QT and QTcH interval were observed following administration of Zoletil (**Figure 1**). Peak difference in covariate-adjusted mean for QT and QTcH occurred at 2 hours post-dose (+106.3 ms, 34.4%, and +86.8 ms, +27.7%, respectively) with values returning to normal by approximately 4 hours post-dose.

BT:
Significant ($p<0.05$) decreases in BT were observed following administration of Zoletil (**Figure 2**). Peak difference in covariate-adjusted mean occurred at 2 hours post-dose (-2.3 ºC , -6.2%), with values returning to normal by approximately 4 hours post-dose. Given the known suppression of thermoregulation following administration of injectable anesthesia, these changes were expected. The duration of change was consistent with the known pharmacokinetic properties of Zoletil.

CONCLUSIONS

The applied correction formula (below) produced slopes of 0.00 and 0.00 ms/ ºC , respectively, indicating adequate correction for body temperature:

$$QTcHcT = QTcH + CF(37.5 – Tc)$$

Tc: Core body temperature; CF: Slope of QTcH against BT

Zoletil administered via intramuscular (IM) injection at 9 mg/kg produced expected physiological changes, further outlining the relationship between body temperature and the QTcH interval in Göttingen Minipigs® in both conscious (Phase 1) and anesthetized (Phase 2) states. The study provided evidence of an inverse, apparent linear relationship between the two parameters. A QTcH formula with a correction factor for body temperature changes (QTcHcT) was derived for both conscious and anesthetized states.

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