

Diurnal Variations Analysis of the Cardiovascular Parameters in Cynomolgus Monkeys of Stand-Alone Safety Pharmacology Studies

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Introduction

Cynomolgus monkey (*Macaca fascicularis*) is one of standard non-rodent species for evaluating and determining the effects of test articles on the cardiovascular (CV) system in nonclinical safety pharmacology studies. Telemetry technology is considered the “gold standard” approach for monitoring CV parameters. With the frequent use of cynomolgus monkeys to monitor CV parameters using telemetry technology in stand-alone safety pharmacology studies, the objective of this study was to establish the in-house reference background data for this species and analyze diurnal variations in CV parameters by comparing daytime (07:00–19:00) and nighttime (19:00–07:00) measurements. In the stand-alone safety pharmacology studies, electrocardiograms (ECG), blood pressure and body temperature were recorded from at least 2 hours prior each dose to approximately 24 hours after dosing using DSI/Ponemah software. The data were collected from 106 cynomolgus monkeys that were previously instrumented with DSI L11-F4 transmitters via surgery.

Results

The study results indicated no apparent variations between daytime and nighttime values in systolic blood pressure (SBP, 113 vs. 107 mmHg), diastolic blood pressure (DBP, 78 vs. 74 mmHg), mean arterial pressure (MAP, 90 vs. 85 mmHg), pulse pressure (PP, 36 vs. 34 mmHg), or the PR (82 vs. 87 msec), QRS (35 vs. 36 msec), and RR-corrected QTc (248 vs. 253 msec) intervals. However, diurnal rhythm was observed in heart rate (HR, 159 vs. 125 bpm) and body temperature (BT, 38.1 vs. 37.2 °C), with HR fluctuations consequently influencing QT interval (213 vs. 250 msec) (Comparative approach: daytime values vs. nighttime values). Furthermore, the data comparison between this study and published literature revealed a favorable concordance. (Xiefan Fang, Stephen D. Tichenor, 2023).

Conclusion

In conclusion, the background data of CV parameters in this study can provide a valuable reference for the cardiovascular evaluation of vivo safety pharmacology studies in cynomolgus monkeys with telemetry technology.