DUAL EFFECT OF CLONIDINE ON QT INTERVAL DURATION AND BODY TEMPERATURE IN CYMONOLGUS MONKEYS: QT CORRECTION FORMULA FOR CHANGES IN CORE BODY TEMPERATURE

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INTRODUCTION

QT interval lengthening produced by a drug candidate may be interrupted, in part, by the inhibition of T-type calcium currents and an increased core body temperature (20°C). The increase in body temperature can mask potential T-type calcium current inhibition and is also responsible for changes in the QT interval. To discriminate between a possible effect of a drug on QT interval lengthening in conscious non-restrained cynomolgus monkeys, we recently proposed a QT-interval correction formula for the inference of core body temperature changes based on QT bipolar (QBC) and QT Fredericia (QF) formulas. Parameters were recorded during dark and light periods over 26 hours and used for the correction of QT intervals.

MATERIALS AND METHODS

We highlighted a dual action of Clonidine on QT lengthening by acting simultaneously on body temperature and cardiac repolarization parameters, including intrinsic QT prolongation and increased heart rate. Parameters were measured using hERG potassium current (IKr) in stably transfected HEK 293 cells using an Axopatch 200 amplifier (Molecular Devices, Sunnyvale, CA). Currents were filtered at 5 kHz. All recordings were performed at near-physiology temperature (32–35°C).

DISCUSSION AND CONCLUSION

Based on physiological changes in QT, interval duration and heart rate over 26 hours and light periods in unrestrained cynomolgus monkeys, we have suggested QT-interval correction formulas for changes in core body temperature, QFBcT and QFbC, correcting for changes in core body temperature observed after Clonidine administration. We highlighted a dual action of Clonidine on QT lengthening by acting simultaneously on body temperature and cardiac repolarization parameters, including intrinsic QT prolongation and increased heart rate. Parameters were measured using hERG potassium current (IKr) in stably transfected HEK 293 cells using an Axopatch 200 amplifier (Molecular Devices, Sunnyvale, CA). Currents were filtered at 5 kHz. All recordings were performed at near-physiology temperature (32–35°C). 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