Do hERG blocking agents further increase the risk of sudden cardiac death in patients with type 1 diabetes?

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Introduction

Type 1 diabetic patients have been shown to be at a higher risk of sudden cardiac death (SCD) and QTc prolongation may be a predisposing factor [1]. In diabetic patients, QT interval prolongation due to hyperglycemia has been reported [2]. Extended periods of hyperglycemia occur regularly in diabetics [3]. There is no safety warning to caution prescribers administering QT prolonging drugs to diabetic patients.

In this study, we examine the effects of hyperglycemia on QTc and its sub-intervals in type 1 diabetic patients. We also investigate the interaction between a QT prolonging medicine and the hyperglycemic state on affecting the QTc interval.

Methods

Single center, single-blinded, placebo-controlled, Phase I study in 20 type 1 diabetic patients over three days. This is an interim analysis of 15 patients (8 males, 7 females). The study was approved by the local ethics committee South Central - Berkshire B Research Ethics Committee (NCT number: NCT01984827).

Demographics: BMI 19.7 – 29.3, Age 21 – 32, 10 Caucasian, 1 black and 5 mixed race. Long term insulin therapy was maintained. Co-administration of moxifloxacin was observed to prolong the QTcF interval by a further 8 ms, leading to mean QTc prolongations of 18 ms, but maximum sustained QTc prolongations of up to 40 ms were observed in individual patients.

Results

The key findings that support this conclusion are as follows:

- The data from this study suggest that QT prolonging drugs should be administered with caution to type 1 diabetic patients.
- A hyperglycemic state was seen to prolong the QTcF interval by 10.4 ms. In the time course analysis, hyperglycemia had a greater QTc prolonging effect in female patients than males. This difference arose from an inverse glucose concentration-dependent shortening of the Tpeak-Tend interval in males during episodes of hyperglycemia that was not present in females.
- Co-administration of moxifloxacin was observed to prolong the QTcF interval by a further 8 ms, leading to mean QTc prolongations of 18 ms, but maximum sustained QTc prolongations of up to 40 ms were observed in individual patients.
- The limitations of this study are: (i) the link between long QT and arrhythmias was not explored and the resulting risk for arrhythmias is unknown, (ii) type 2 diabetic patients, a much greater patient population, were not studied.

Summary of Conclusions

References


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