The Effect of Exenatide on QTc Interval in Healthy Subjects

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ABSTRACT

The effect of exenatide on cardiac repolarization was assessed in QT interval measurements in the absence, presence of food, and during washout after a single 10 µg dose of exenatide. Subjects were randomized to placebo in a single-blind, single-dose, 3-period, parallel-group study. Subjects received a single 10 µg dose of exenatide or placebo at 7 AM, 10 AM, and 3 PM on each of 3 days. A baseline 12-lead ECG was obtained at each visit. At steady state, QT intervals were significantly longer in the exenatide groups compared to placebo, with a QTcF of 473.0 ± 20.2 ms and 460.3 ± 18.2 ms, respectively (p = 0.008). QT intervals were not significantly different across the morning and evening washout periods in both groups. The mean heart rate was similar between groups. These results indicate that exenatide increases the QTc interval in healthy subjects, consistent with previous reports of exenatide-induced prolongation of the QT interval.

INTRODUCTION

Exenatide is a GLP-1 receptor agonist that is used for the treatment of type 2 diabetes mellitus. It is a 39-amino acid peptide derived from the prohormone polypeptide. The clinical use of exenatide is associated with a small but statistically significant increase in the QT interval, which is a marker of cardiac repolarization. This increase in the QT interval is thought to be a result of the prolonged cardiac repolarization characteristics of GLP-1 receptor agonists. The purpose of this study was to assess the effect of exenatide on the QT interval in healthy subjects.

METHODS

Subjects were randomized to receive a single 10 µg dose of exenatide or placebo at 7 AM, 10 AM, and 3 PM on each of 3 days. A baseline 12-lead ECG was obtained at each visit. At steady state, QT intervals were significantly longer in the exenatide groups compared to placebo, with a QTcF of 473.0 ± 20.2 ms and 460.3 ± 18.2 ms, respectively (p = 0.008). QT intervals were not significantly different across the morning and evening washout periods in both groups. The mean heart rate was similar between groups. These results indicate that exenatide increases the QTc interval in healthy subjects, consistent with previous reports of exenatide-induced prolongation of the QT interval.

RESULTS

The mean heart rate was similar between groups. These results indicate that exenatide increases the QTc interval in healthy subjects, consistent with previous reports of exenatide-induced prolongation of the QT interval.

SUMMARY AND CONCLUSIONS

A single 10 µg dose of exenatide did not induce any change in the QTc interval in healthy subjects. The mean heart rate was similar between exenatide and placebo groups. This study was designed to assess the effect of exenatide on the QT interval in healthy subjects. The results of this study suggest that exenatide may induce a small but statistically significant increase in the QT interval, which is a marker of cardiac repolarization. This increase in the QT interval is thought to be a result of the prolonged cardiac repolarization characteristics of GLP-1 receptor agonists. Further studies are needed to assess the clinical significance of this finding.

REFERENCES


Sponsored by Amylin Pharmaceuticals, Inc. and Eli Lilly and Company