

## Comparison of ECG and Holter monitoring QTc interval measurements in patients with increased risk for QTc prolongation

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### Purpose

Methadone is a potent opioid that has been used for many years as substitution therapy in Methadone Maintenance Treatment Programs (MMTP) to treat patients with opioid addiction. In the last decade due to its low cost, long duration of action, and analgesic efficacy, its use to treat chronic pain patients became more common. As a result higher doses of methadone are being prescribed. Recently it has been observed a rise in deaths in patients taking methadone and was attributed to cardiac toxicity. Several studies were performed that reported a variety of observations, in some cases contradictory, on the effect of methadone on the QTc interval duration. Indeed, Eap et al and Cruciani et al reported a correlation between the QTc duration and the dose of methadone while other investigators did not find such correlation. In this study we are presenting data of single ECG studies on patients on methadone and its correlate with 24-hour Holter monitoring on detection of QTc interval prolongation.

### Method

Chronic pain patients on methadone and over 50 years old each had an EKG, a 24-hour Holter and electrolytes (K, Ca, Mg) drawn during visit #1. This was repeated 8 weeks later during visit #2 (completers=20/36). Participants were grouped based on their methadone dose: 0, 10 to 40, 41 to 120, and >121 mg. All data were analyzed by an experienced cardiologist. The data from visit #1 will be presented here. A QTc prolongation >500 msec was considered as definite risk for TdP. QTc >430 and 450 in males, >450 and >470 in females was considered increased and high risk respectively.

### Results

To this day 39 patients completed visit #1. A single EKG detected QTcP (males >430; females >450) in 15/39 patients (5/15 >500 ms). Of those 15 patients 12 had at least one Holter reading and showed QTcP in 11 (5/11 >500 ms). Of the 5 patients with QTc >500 ms by EKG, 3 had correlative Holter that detected two. Of the 36 patients that had at least one Holter reading, 21 showed QTcP. EKG detected it in 11 of these patients. We then compared QTcP detected at 4 different times of the day by Holter monitoring single with a single EKG. The results were as follows: 12 am=12/10; 6 am=17/9; 12 noon 15/7, and 6 pm 13/9). The QTc prolongation is dose dependent. At baseline, the highest dose group (>120 mg) showed significantly higher QTc intervals than the lower 3 dose groups (479.3±82.5 vs 439.8±32.4, P=.01). The 3 lowest dose groups did not differ from each other. The QTc prolongation was dose dependent. The >120 mg group showed significantly higher QTcP than the lower 3 groups (467.3±42.6 vs 422.8±34.0, P=.003).

### Conclusions

- A single ECG detected fewer patients with QTc interval prolongation (15 vs 20) as compared to a 24-hour Holter monitoring but detected the same number of patients with QTc >500 ms.

- Twenty-four h Holter monitoring detected twice as many patients with QTc interval prolongation than ECG at 12 noon, suggesting that one ECG might not sufficient to identify patients at risk.
- There is a dose dependent effect on QTc interval prolongation in patients taking > 120 mg/day as compared to pulled lower doses.