

#7_Periooperative intravenous methadone and QTc interval: An observational study.

Presenting Author: Vijay K Ramaiah MD

Co-Author: Evan D. Kharasch MD PhD

Department of Anesthesiology, Duke University School of Medicine, Durham NC 27710

Background:

A single dose of intravenous (IV) methadone (0.2-0.3 mg/kg) in patients undergoing surgery under general anesthesia provides excellent intraoperative antinociception and superior postoperative analgesia with significant opioid sparing up to 72 hours postoperatively. Chronic oral methadone can cause prolonged corrected QT interval (QTc), and carries a black box warning, but QTc effects usually occurs at higher doses for prolonged duration (months). QTc effects of low-dose perioperative IV methadone may be a potential safety concern to practitioners. QTc effects of low-dose perioperative IV methadone are unknown.

Purpose:

The research goal is to identify the effects of intraoperative intravenous methadone on the cardiac QTc interval, and to compare QTc intervals in patients receiving and not receiving methadone for induction of anesthesia.

Methods:

We conducted an observational study of QTc intervals in patients receiving intraoperative opioid (methadone, fentanyl or other, and dose, chosen at the discretion of the anesthesia care team). QTc interval (corrected using Fridericia's formula) was evaluated at baseline and 1, 5, 10, 15, 30, 45, and 60 min after dosing.

Outcome measurements:

Primary outcome: QTcF (Fridericia's formula) > 500 msec.

Secondary outcomes: QTcF increase > 60 msec from baseline, QTcF >450 msec in males or QTcF >470 msec in females.

Results:

QTcF data were analyzed from 282 patients receiving methadone and 144 patients receiving other opioids (non-methadone) during induction of anesthesia. Demographic data and outcome measurements are described in the table below. Methadone dose (mean±SD) was 19±6 mg and fentanyl dose in non-methadone group was 277±165 µg. Baseline QTcF was 412±16 msec in methadone group and 418±22 msec non-methadone group.

Primary outcome: New onset QTcF >500 msec were observed in 7 patients (2.5%) with methadone, compared to 15 patients (10.4%) in the non-methadone group.

Secondary outcomes:

Any QTcF >60 msec were observed in 12 patients (4.3%) after methadone vs 22 patients (15.3%) in the non-methadone group. Peak 1-60 min QTcF with methadone was 442±29 msec vs 460±28 msec in non-methadone group. Peak 1-60 min QTcF change from baseline with

methadone was 30±15 msec vs 42±19 msec in the non-methadone group. Any QTcF >450 msec (male) or >470 msec (female) were observed in 59 patients (21%) with methadone vs 65 patients (45%) in non-methadone group. No adverse cardiac events were observed in any patient.

Conclusions: IV methadone (0.2-0.3 mg/kg at induction) was found to cause no clinically meaningful changes in QTc, particularly at peak plasma concentrations. QTc changes were not greater after methadone compared with no methadone. No adverse cardiac events were noted. Current results provide clinical assurance regarding methadone and QTc. Routine preoperative QTc assessment and postoperative ECG telemetry monitoring do not appear warranted.

Table:

	Methadone (N=282)*	Non-methadone (N=144)**
Demographics		
Age, mean (SD)	55 ± 16	58 ± 16
Sex, M:F (n, %)	148:134 (52%:48%)	61:83 (43%:57%)
Weight (Kg), mean±SD	86±20	85 ± 24
Baseline QTcF (msec), mean±SD	412±16	418±22
QT interval (Fridericia correction)		
new onset QTcF>500 msec, n (%)	7 (2.5%)	15 (10.4%)
Peak 1-60 min QTcF (msec), mean±SD	442±29	460±28
Peak 1-60 min QTcF change from baseline (msec), mean±SD	30±15	42±19
Any QTcF>60 msec, n (%)	12 (4.3%)	22 (15.3%)
Any QTcF >450 msec (male) or >470 msec (female), n (%)	59 (21%)	65 (45%)

Induction opioid administered at time zero. ECG (II, V5) obtained 1, 5, 10, 15, 30, 45, 60 min after opioid

* Induction dose methadone 19±6 mg

**Induction dose fentanyl 277±165 µg