

# Methadone overdose associated with T wave inversions

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## ABSTRACT

Methadone commonly causes QT prolongation but T wave inversion has never been reported with methadone use in clinical settings. We report a 52-year-old female admitted for methadone overdose, had deep T wave inversions in electrocardiogram (ECG) with no cardiac symptoms, negative cardiac enzymes and subsequent normal coronary and left ventricular angiogram. Follow-up ECG showed spontaneous resolution of ECG changes. Our article which is a first of its kind gives an insight into the possibility of T wave inversion with methadone use.

**Keywords:** Electrocardiogram, Methadone, Overdose, T wave inversion

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## INTRODUCTION

Methadone is a widely used medication for opioid dependence and detoxification. Methadone is known to cause QT prolongation, torsade-de-pointes and sudden cardiac death [1]. However, methadone overdose causing T wave inversion has never been reported as per our literature search.

## CASE REPORT

A 52-year-old public school female teacher was brought to the emergency department by ambulance for altered mental status noted at school. There was no loss of consciousness.

The patient's past medical history is positive for hypertension, hyperlipidemia, and documented mild coronary obstruction of less than 30%. On physical exam patient's vital signs were stable with altered mental status. The rest of the physical exam was found to be normal. The basic metabolic panel, complete blood count, thyroid function study, urinalysis, troponins I, ammonia, and head CT were normal. Urine drug screen for opiates, benzodiazepines, marijuana, ecstasy, cocaine and amphetamines revealed the presence of opiates alone. The patient's state of drowsiness and poor orientation to surroundings was attributed to methadone overdose, since this drug had been prescribed for the management of her chronic back pain. An admission, electrocardiogram (EKG) showed corrected QT interval (QTC) prolongation of 540 with heart rate of 75, QT of 480 along with deep symmetric T wave inversions in leads V1 – V6 (Figure 1). Comparison with an old

EKG confirmed these findings as new (Figure 2). Telemetry monitoring and serial cardiac enzymes were negative. The patient's mental status improved with supportive care. Echocardiogram done during the first 24 hour demonstrated ejection fraction of 55% with no contraction abnormality to suggest typical or atypical takotsubo cardiomyopathy despite persistent T wave inversion. Emergent cardiac catheterization revealed the presence of minimal irregularities 10% or less in any view with no areas of critical focal stenosis. The patient was discharged home in stable condition. A six month follow-up EKG in the absence of methadone was normal with resolution of T wave inversions (Figure 3).

## DISCUSSION

Methadone is an established cause of QT prolongation even in conventional doses [1]. However, we could not

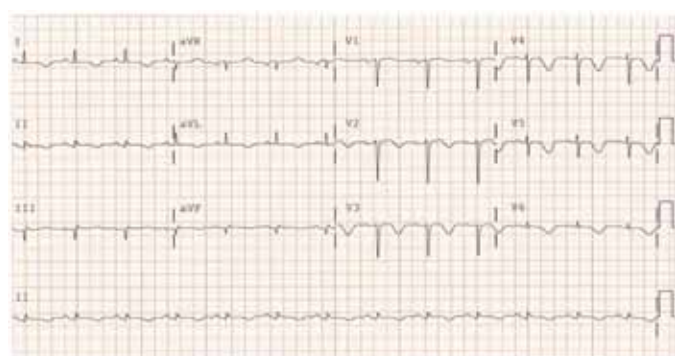


Figure 1: Electrocardiogram (EKG) showing QTC prolongation with deep symmetric T wave inversions in lead V1–V6.

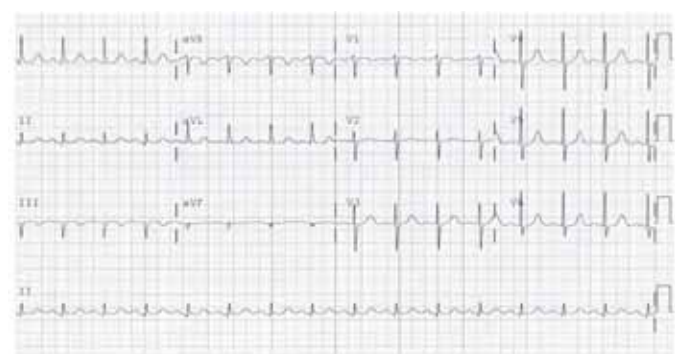


Figure 2: Baseline electrocardiogram.



Figure 3: Follow-up electrocardiogram.

find any reports of T wave inversion associated with either therapeutic or toxic doses of methadone. Thorough evaluation of the patient comorbidities and medication use suggests the possibility of methadone's contribution to the EKG changes.

Methadone is highly effective in treating opioid dependence, and it is also used as an analgesic for second-line management of chronic pain. However, recent increases in methadone-related deaths have instigated controversy about the use of this medication [2]. Early studies, largely from methadone maintenance clinics, found mortality primarily from respiratory depression. In recent years, torsade de pointes, a serious ventricular arrhythmia, has been implicated in methadone-related deaths [3, 4].

Methadone at the cellular level causes blockage of the potassium channel encoded by the HERG gene [4, 5]. This causes slowing of repolarization, induction of after-depolarization, and an increased heterogeneity of repolarization. It is through this mechanism that methadone causes QT prolongation and potentially lethal cardiac arrhythmias such as torsade de pointes [6]. HERG channel mutations that reduce potassium flow mimic the action of drugs like methadone, and are well-established causes of T wave abnormalities such as “flattening” and “notching” [7] but not inversion.

New onset T wave abnormalities are associated with certain well-described pathologies including myocardial ischemia, stroke, and both inherited and acquired cardiomyopathies. This patient has no significant coronary artery disease or serum markers indicative of myocardial damage. It is therefore unlikely that ischemia was the cause of the T wave inversions. The normal head CT and non-focal neurologic exam ruled out stroke. It is possible that the T wave abnormalities could be related to a “catecholamine storm” seen in multiple stressful conditions, but absence of tachycardia is inconsistent with excess sympathetic stimulation [8, 9]. Importantly, the echocardiogram did not indicate a cardiomyopathy, and the resolution rules out an inherited pathology such as apical hypertrophic cardiomyopathy which can be difficult to rule out with ultrasound.

Another possible cause of diffuse T wave inversion is takotsubo cardiomyopathy, which is a stress-induced event that presents similar to ST-elevation myocardial infarction and resolves spontaneously. Catecholamine surge is postulated to be the cause for this phenomenon. Recently, T wave inversions have been reported with takotsubo syndrome which was global [10]. There was no evidence of the characteristic pattern of left ventricular dysfunction that is typical of takotsubo in this case by either echo or left ventriculogram during catheterization within 24 hours of admission. We cannot rule out a purely “electrical” manifestation of this condition, perhaps induced by the stress of hypoventilation and hypoxia due to opiate suppression of respiration. The fact that unconsciousness was not noted when the event

occurred makes this explanation for the T wave inversion less likely.

It is a current practice in the state of West Virginia for emergency medical personnel responding to medication overdose to administer naloxone injection in order to reverse a presumptive opiate overdose. But careful review of records showed no documentation of naloxone being administered to our patient. Furthermore, naloxone has a half-life of approximately one hour, and the T wave inversions persisted and were slightly increased over the next three days.

## CONCLUSION

While it is never possible to conclusively establish causation *ex post facto*, the absence of other causes of T wave inversions, the known deleterious effect of methadone on cardiac repolarization, and the resolution of these changes after the presumed elimination of the drug suggests that methadone is a likely contributing factor in this case. A second similar report in literature will make the association of methadone induced T wave inversion more likely.

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## Author Contributions

Sunith Vijayakumar – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

William H. Carter – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Mark C. Haigney – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Kingsley Pudota – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

## Guarantor

The corresponding author is the guarantor of submission.

## Conflict of Interest

Authors declare no conflict of interest.

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