

The Metha-do Dose Versus The Metha-don't Dose - A Case Of Methadone Induced Prolonged QT Syndrome And Torsades De Pointes

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Introduction

- Methadone is commonly prescribed to treat substance use disorder.
- Long-term exposure carries the risk of QT prolongation and, in rarer cases, can lead to torsades-de-pointes (TdP) and sudden cardiac death.
- For patients with severe opioid dependency requiring high doses of methadone, switching to alternative agents bears the challenge of acutely maintaining similar efficacy in eliminating withdrawal symptoms and risks of relapse.
- We present a case of methadone-induced TdP in a patient with heart failure with reduced ejection fraction (HFrEF) that was managed with an implantable cardioverter-defibrillator (ICD) and eventual resumption of methadone at a reduced dose.

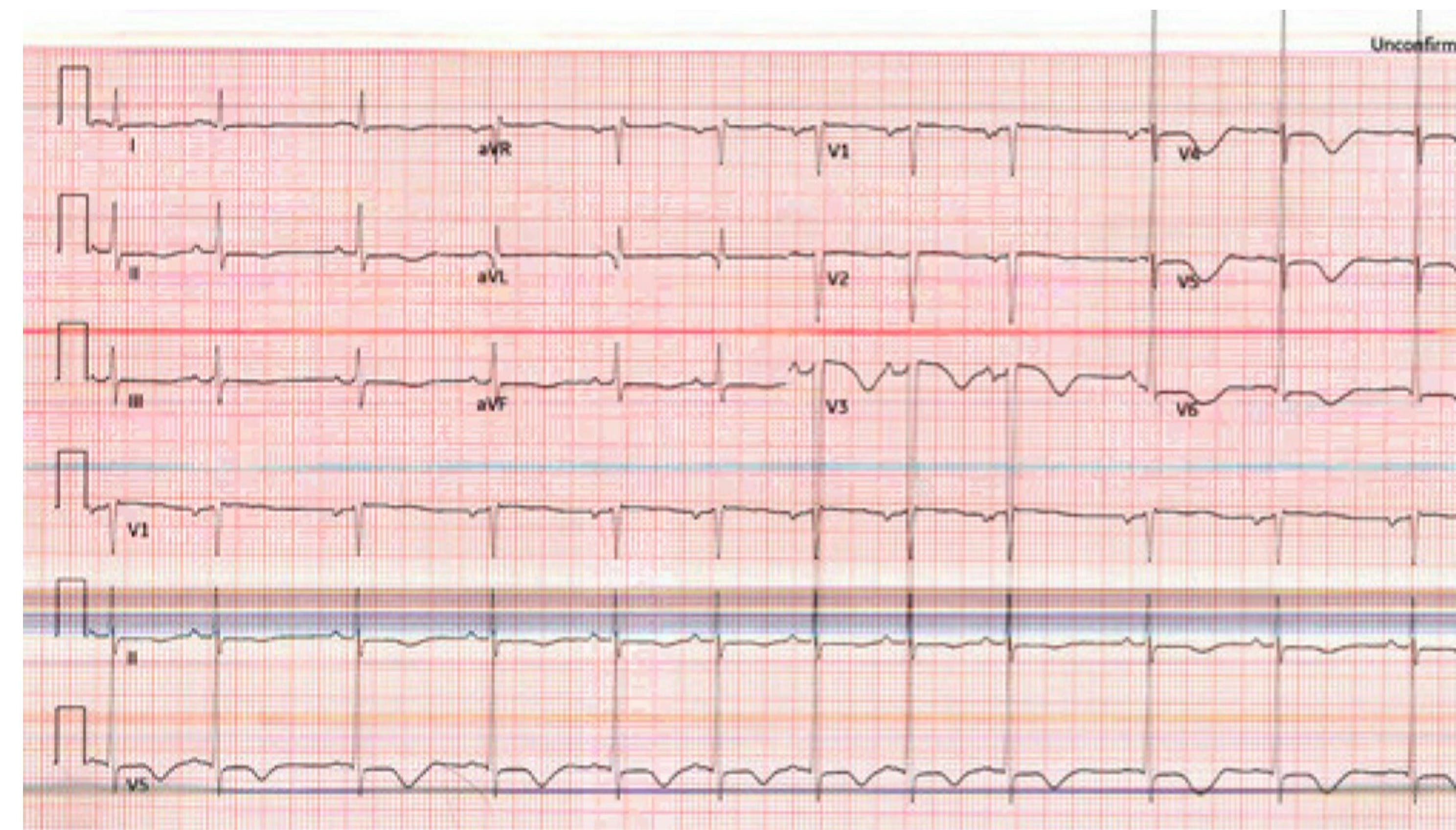


Figure 1: ECG showing prolonged QTc of 578 msec

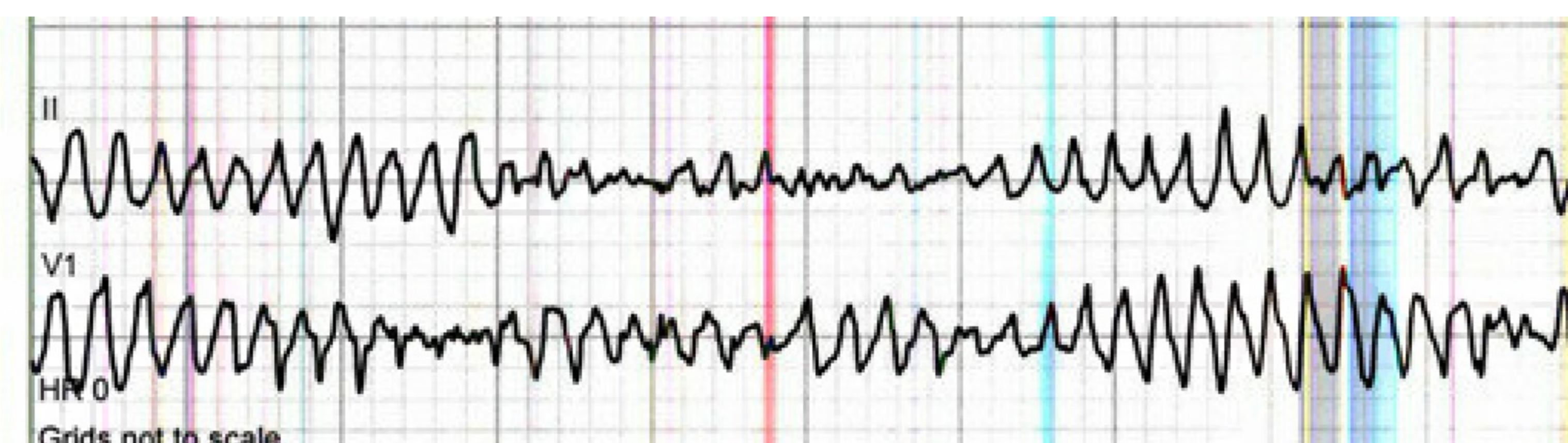


Figure 2: Telemetry reading showing torsades de pointes

Case presentation

- A 69-year-old male with hypertension, HFrEF, and opioid dependence on methadone 160mg daily presented in hypertensive emergency.
- ECG showed sinus rhythm with QTc of 578 msec.
- Shortly after presentation, he developed TdP and was initially treated with magnesium sulfate. Bedside transthoracic echocardiogram (TTE) showed an EF of 20-25% with diffuse hypokinesis.
- Left heart catheterization demonstrated no significant coronary artery disease but showed EF of 10-15% and global hypokinesis.
- A temporary transvenous pacer (TVP) was placed for overdrive pacing to suppress further TdP.

Decision-making

- His methadone was briefly suspended and later restarted at 80mg daily.
- Given continued QTc prolongment greater than 500 msec, an ICD was placed for both secondary prevention and for overdrive pacing to reduce his QTc.
- Following ICD placement, the patient was restarted on methadone at 10mg daily and monitored in the hospital for opioid withdrawal symptoms.
- He was discharged on 10 mg of methadone daily with close follow-up. Device interrogation 2 months later revealed no arrhythmias.

Discussion

- QT prolongation leading to TdP is a rare but known dose-dependent adverse effect of methadone.
- In patients with severe opioid dependency, alternative agents are not always a viable option.
- This case highlights the need to balance the risk of methadone associated cardiotoxicity in patients with known cardiomyopathy with adequate opioid addiction management.
- It offers a solution of cardiac pacing with continued use of the methadone at the lowest but most effectively tolerated dose to ensure compliance and reduce substance use related health complications.

References

1. Alinejad, Samira et al. "A systematic review of the cardiotoxicity of methadone." *EXCLI journal* vol. 14 577-600. 5 May. 2015. doi:10.17179/excli2015-553
2. Cruciani, Ricardo A. "Methadone: to ECG or not to ECG...That is still the question." *Journal of pain and symptom management* vol. 36,5 (2008): 545-52. doi:10.1016/j.jpainsymman.2007.11.003
3. Ehret GB, Voide C, Gex-Fabry M, et al. Drug-Induced Long QT Syndrome in Injection Drug Users Receiving Methadone: High Frequency in Hospitalized Patients and Risk Factors. *Arch Intern Med.* 2006;166(12):1280-1287. doi:10.1001/archinte.166.12.1280
4. Martell, Bridget A et al. "Impact of methadone treatment on cardiac repolarization and conduction in opioid users." *The American journal of cardiology* vol. 95,7 (2005): 915-8. doi:10.1016/j.amjcard.2004.11.055
5. Mujtaba, Sobia et al. "Methadone, QTc prolongation and torsades de pointes: Current concepts, management and a hidden twist in the tale?." *Journal of cardiovascular disease research* vol. 4,4 (2013): 229-35. doi:10.1016/j.jcdr.2013.10.001
6. Eap, C B et al. "Stereoselective block of hERG channel by (S)-methadone and QT interval prolongation in CYP2B6 slow metabolizers." *Clinical pharmacology and therapeutics* vol. 81,5 (2007): 719-28. doi:10.1038/sj.clpt.6100120
7. Walker, Paul W et al. "High dose methadone and ventricular arrhythmias: a report of three cases." *Pain* vol. 103,3 (2003): 321-324. doi:10.1016/S0304-3959(02)00461-X
8. Liao D-L, Chen P-C, Chen C-H, Hsieh C-J, Huang YF, Shih W-Y, et al. Higher methadone doses are associated with lower mortality in patients of opioid dependence in Taiwan. *J Psychiatr Res.* 2013;47:1530-4.
9. Russell L, Levine D. Methadone-induced Torsades de pointes. *R I Med J* (2013). 2013 Jul 30;96(8):20-1. PMID: 23923121.
10. Lamont P, Hunt SC. A twist on torsade: a prolonged QT interval on methadone. *J Gen Intern Med.* 2006 Nov;21(11):C9-C12. doi: 10.1111/j.1525-1497.2006.00588.x. PMID: 17026725; PMCID: PMC1831670.
11. Khalesi S, Shemirani H, Dehghani-Tafti F. Methadone induced torsades de pointes and ventricular fibrillation: A case review. *ARYA Atheroscler.* 2014 Nov;10(6):339-42. PMID: 25815024; PMCID: PMC4354087.

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