

Impact of CYP2B6 Genetic Polymorphisms on Methadone Dose and Withdrawal Symptoms

Ryan Low, Dr Ana Alfirevic

Introduction

Methadone is the most widely used drug treatment for the 200,000 individuals addicted to opioids in the United Kingdom. However, one of the major challenges when prescribing methadone is the wide inter-individual variability in dose requirement that exists amongst patients. Genetic variation in cytochrome P450 enzymes has been reported to explain this variability. Methadone is metabolised in the liver by a range of P450 enzymes including CYP3A4, CYP2B6, CYP2D6 and CYP1A2. CYP2B6 is known to have single nucleotide polymorphisms with reduced function (rs2279343, c785A>G and rs3745274, c516G>T), which can lead to raised plasma methadone levels. Therefore it is hypothesised that these polymorphisms known as CYP2B6*4 and CYP2B6*9 may potentially decrease the dose of methadone required by an individual.

Methods

250 Caucasian participants that have been on a stable dose of methadone for over 2 weeks were selected for the study, a sample of blood or saliva was collected for DNA. Real time PCR was used with Taqman® probes to determine the genotype of the samples for each SNP.

Results

The range of daily methadone dose ranged from 12-200mg/day. The average dose of methadone for rare homozygotes of both SNPs (rs2279343 and rs3745274) was lower (47.78, 48.57mg/day) when compared to the dose required for the wild-type individuals for both SNPs, although not statistically significant ($p=0.462, 0.664$). When comparing genotypes of those requiring doses greater and less than 90mg/day, those requiring ≥ 90 mg/day were more

likely (OR 2.77, 3.36) to be wild-type homozygotes than those requiring less than 90mg/day. The results show potential to genotype individuals before commencing methadone, with the aim of reducing risk of adverse drug reactions. Further research requires larger sample sizes and a focus on pharmacodynamic factors.

Keywords: methadone, CYP2B6, Real-time PCR, Caucasian, Taqman