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Relationship between ABCB1 polymorphisms and serum methadone concentration in patients undergoing methadone maintenance therapy (MMT).

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Abstract

BACKGROUND: Methadone is a substrate of the permeability glycoprotein (P-gp) efflux transporter, which is encoded by the ABCB1 (MDR1) gene. Large interindividual variability in serum methadone levels for therapeutic response has been reported. Genetic variations in ABCB1 gene may be responsible for the variability in observed methadone concentrations.

OBJECTIVE: This study investigated the associations of ABCB1 polymorphisms and serum methadone concentration over the 24-hour dosing interval in opioid-dependent patients on methadone maintenance therapy (MMT).

METHODS: One hundred and forty-eight male opioid-dependent patients receiving MMT were recruited. Genomic deoxyribonucleic acid (DNA) was extracted from whole blood and genotyped for ABCB1 polymorphisms [i.e. 1236C>T (dbSNP rs1128503), 2677G>T/A (dbSNP rs2032582), and 3435C>T (dbSNP rs1045642)] using the allelic discrimination real-time polymerase chain reaction (PCR). Blood samples were collected at 0, 0.5, 1, 2, 4, 8, 12, and 24 hours after the dose. Serum methadone concentrations were measured using the Methadone ELISA Kit.

RESULTS: Our results revealed an association of CGC/TTT diplotype (1236C>T, 2677G>T/A, and 3435C>T) with dose-adjusted serum methadone concentration over the 24-hour dosing interval. Patients with CGC/TTT diplotype had 32.9% higher dose-adjusted serum methadone concentration over the 24-hour dosing interval when compared with those without the diplotype [mean (SD) = 8.12 (0.84) and 6.11 (0.41) ng ml⁻¹ mg⁻¹, respectively; p = 0.033].

CONCLUSION: There was an association between the CGC/TTT diplotype of ABCB1 polymorphisms and serum methadone concentration over the 24-hour dosing interval among patients on MMT. Genotyping of ABCB1 among opioid-dependent patients on MMT may help individualize and optimize methadone substitution treatment.

KEYWORDS: ABCB1; MDR1; P-glycoprotein (P-gp); methadone maintenance therapy (MMT); opioid dependence; serum methadone concentration

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