Article: 1644
Topic: 38 - Addictive Behaviours

GENETIC VARIABILITY AND HEROIN DOSAGE REQUIREMENTS IN OPIOID-DEPENDENT INDIVIDUALS

D. González[1,2], *M. Cañadas*[1], *M. Aguilera*[3], *J.A. Reyes*[2], *A. Plaza*[2], *M.Á. Calleja*[1]

[1]Pharmacogenetics Unit. Pharmacy Service, [2]PSP-PEPSA, Hospital Universitario Virgen de las Nieves, [3]Microbiology Deparment, Universidad de Granada, Granada, Spain

Introduction: Effective and safe prescription of individualized opioid-doses for opioid-dependent is a complicated task for the clinician, due inter-individual differences in dosage requirements and narrow therapeutic range.
Mu-opioid receptor gene (OPRM1) plays a key role in addiction. A118G-rs1799971 polymorphism in OPRM1 is probably the most promising biomarker of better response in opioid-dependents.
Gene polymorphisms in CYP450-isoenzymes (CYP3A5, CYP3A4, CYP2D6, CYP2B6, CYP1A2, CYP2C9 and CYP2C19) also significantly influence pharmacokinetics and effects of opioids and concomitant treatments.
Objectives and aims: Association of heroin-dose requirements to OPRM1-rs1799971, CYP3A4-rs2740574 and CYP3A5-rs776746 gene polymorphisms in patients from a Heroin Prescription Program (PPH) in Andalusia.
Methods: Series of cases: 15 patients with opioid-addiction. Collection of heroin-doses/patient administered for a year. Genotyping of A118G, CYP3A4 and CYP3A5 polymorphisms was performed by Polymerase Chain Reaction and Restriction Fragment Length Polymorphism.
Results: Eleven patients were AA homozygous (11/15;73.33%) and four heterozygous AG (4/15;26.67%) for A118G-OPRM1; median doses: 179.57[157.85,225.49] and 271.38[145.11,288.88]mg/day respectively were no statistically different (p=0.240). Four subjects presented doses>250mg/day, showing an association of AG-OPRM1 genotype with higher doses, OR:30.00(CI95%:1.41,638.15);p=0.033.
Fourteen patients were homozygous AA and GG for CYP3A4 and CYP3A5 respectively (14/15;93.33%), and one patient was heterozygous AG(1/15;6.66%) for both isoenzymes and presented a high dose(280 mg/day).
Conclusions: Higher heroin-doses (>250mg/day) were associated to AG genotype for OPRM1-A118G, despite the great variability in the dose prescription avoided to find an association between OPRM1 genotype and the specific administered dose.
Pharmacogenetic analysis, focused on OPRM1-A118G, may be a useful tool to adjust the pharmacotherapeutic dose in each case.

https://doi.org/10.1016/S0924-9338(13)76635-5 Published online by Cambridge University Press