P-952 - CANDIDATE GENES FOR PHARMACOGENETIC MANAGEMENT OF METHADONE OPTIMAL DOSE

F.Vorspan, K.Ksouda, L.Labat
Delveaux, A.Hajj, X.Decleves, V.Bloch, S.Mouly, J.Callebert, J.-M.Scherrmann, J.P.Lepine, J.-L.Laplanche, K.Peoc'h
[1]U[705], UMR[8206], INSERM, CNRS, [2]Service de Psychiatrie, APHP, Hopital Fernand Widal, [3] Pharmacie-Pharmacologie-Toxicologie, APHP, Hopital Cochin, [4]Service de Biochimie et Biologie Moléculaire, APHP, [5]Laboratoire de Pharmacocinétique, Université Paris Descartes, UFR Pharmacie, [6] Laboratoire de Biologie Cellulaire, Paris Descartes University, Paris, France

Introduction: Methadone, a Mu-opioid receptor agonist, is currently used as a maintenance treatment in opioid dependant patients. However, its therapeutic index is narrow, and side effects are life threatening. Non-optimal dosing results in withdrawal symptoms and further heroin craving and use. The optimal dose is defined as the dose necessary to obtain a stable substitution. This optimal maximal dose can then be decreased, the final goal being to stop substitution.
Objectives: To identify factors to optimize the methadone optimal daily dose.
Aims: We aimed to identify genetic variants (SNP) associated with the methadone optimal dose. In a candidate gene approach, we focused on *OPRM1*, which encodes the opioid receptor Mu, and on *DRD2/ANKK1* SNP's, implied in the reward dopaminergic signalling.
Methods: Caucasians patients (n=98) followed for methadone maintenance treatment were included in this prospective study. Candidate SNPs were genotyped (*ANKK1*: TaqI A; *DRD2*: c.957C>T; *OPRM1*: c.A118G). The plasmatic methadone level was determined using mass spectrometry in 59 patients.
Results: Two polymorphisms were significantly associated to the optimal methadone doses: *OPRM1* c.A118G (p=0.03) and *DRD2* TaqI A (p=0.035).
The TaqIA polymorphism is located within *ANKK1*, which encodes a serine threonine kinase which role remains elusive. Its molecular link to methadone pharmacodynamy remains to be established. None of these polymorphisms was associated neither to the current methadone doses, nor to the methadone plasmatic concentration.
Conclusion: This description is the first step to optimize the prescription of methadone in caucasian populations.

https://doi.org/10.1016/S0924-9338(12)75119-2 Published online by Cambridge University Press