**The pharmacogenetics of the response to triptans in patients affected by migraine without aura**

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**Background**. Migraine is a disabling neurovascular disease affecting more than 10% of worldwide population, with a female-to-male prevalence ratio of about 3:1.1 Migraine without aura (MwoA) is the most common clinical subtype of migraine and it is characterized by unilateral and throbbing headache pain, typically accompanied by nausea, vomiting, photophobia and phonophobia.2 Although triptans represent the gold standard therapy for MwoA patients with mild-to-moderate attacks, up to 40% of treated patients do not respond to triptan treatment.3 Genetic factors have been postulated to modulate the interindividual variability in terms of therapeutic effects of triptans. However, little information is currently available concerning the role of polymorphisms in genes implicated in migraine pathophysiology or triptans pharmacokinetics/dinamics as pharmacogenetic determinants of triptans efficacy. 4

**Aim**. We herein investigated the role of 7 polymorphic gene variants (COMT rs4680, COMT rs6269, PRDM16 rs2651899, FAAH rs324420, SLC6A4 Stin2 VNTR, SLC6A4 rs1042173 and CYP1A2 rs762551) as predictors of the clinical response to triptans in patients affected by migraine without aura.

**Methods**. Genotyping was conducted retrospectively by real-time polymerase chain reaction (real-time PCR) or by restriction fragment length polymorphism-polymerase chain reaction (RFLP-PCR) in MwoA patients treated with triptans. Gene variants association was evaluated by logistic regression analysis adjusted by confounding clinical factors. For all the selected polymorphisms, we considered a log-additive mode of inheritance. The threshold of statistical significance was set according to the False Discovery Rate (FDR) correction for multiple comparisons.

**Results**. This study included a total of 221 MwoA patients (79.6% of women, mean age: 38.5 ± 10.5 years), of which the 37.1% (N=82) experienced a poor response to triptans. Multivariate logistic regression analysis showed a statistically significant correlation between triptan response and the following genetic variants: CYP1A2 rs762551 (OR 0.56, 95% CI 0.35-0.91, Qvalue=0.03), SLC6A4 rs1042173 (OR 0.59, 95% CI 0.39-0.89, Qvalue=0.03) and COMT rs6269 - rs4680, analyzed as single markers or in haplotype combination (rs6269: OR 0.55, 95% CI 0.35-0.86, Qvalue=0.03; rs4680: OR 1.76, 95% CI 1.12-2.75, Qvalue=0.03; global association of rs6269-rs4680 haplotype: Qvalue=0.05). Conversely, no evidence of association was detected with SLC6A4 STin2 VNTR, PRDM16 rs2651899 and FAAH rs324420.

**Conclusions**. Our results indicate that genotyping for CYP1A2 rs762551, SLC6A4 rs1042173, COMT rs4680 and COMT rs6269 may be useful for the identification of MwoA patients at higher risk of having a poor response to triptans.

**References**

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