



The CGRP receptor-associated protein RAMP1 gene variant rs3754701 determines medication use and analgesic overuse in patients with chronic migraine

Lucas Yuji de Azevedo Kayano¹, Regina Celia Poli-Frederico¹, Valéria Aparecida Bello¹, Edna Maria Vissoci Reiche¹, Aline Vitalli da Silva¹, Carlos Eduardo Coral de Oliveira¹

Pontifical Catholic University of Paraná, Londrina, Paraná, Brazil

Introduction

Migraine is a debilitating neurological illness that causes severe headaches and other unpleasant symptoms on a regular basis. Although some people are more predisposed to migraines than others, there are many variables that might bring on an episode or modify disease prognosis. Research has shed light on the fact that migraine susceptibility is influenced by gene variants. RAMP1 protein is involved in the terminal glycosylation, maturation, and presentation of the CGRP receptor into the cell surface. RAMP1 rs3754701 is a single nucleotide variant, located in the promoter region, where a change in A to T allele may impact a transcription binding site, and affect RAMP1 and CGRP receptor expression.

Objectives

Compare the allele frequencies of RAMP1 rs3754701 in migraine patients and controls and investigate the influence on clinical parameters of disease.

Methods

In a retrospective study, 177 migraine patients and 177 healthy controls were genotyped using a real-time polymerase chain reaction allelic discrimination assay. After adjusting for potential confounding variables, logistic regression analysis was used to assess the connection between gene variant and clinical parameters.

Results

No evidence of risk association was found between the RAMP1 variant and disease susceptibility nor clinical presentation, except for the presence of sensitive aura for T allele carriers (odds ratio [OR] 5.75; 95% confidence interval [CI] 1.62 – 18.7; $p=0.008$). In addition, T allele carriers were more likely of using topiramate (OR 4.6; 95%CI 1.24 – 17.3; $p=0.02$). T allele carriers with chronic migraine were more likely of using prophylactic drugs (OR 3.55; 95%CI 1.28 – 10.3; $p=0.01$), and topiramate (OR 21.3; 95%CI 1.80 – 27.1; $p=0.005$). Notably, carriers of RAMP1 rs3754701 AA genotype displayed a higher risk of analgesic overuse (vs T allele carriers, OR 3.77; 95%CI 1.06 – 13.1; $p=0.04$).

Conclusion

These findings indicate that RAMP1 rs4752701 may play an important role in drug responsiveness and medication overuse in patients with chronic migraine. Identifying patients with certain RAMP1 genotypes may improve therapy options for headache episodes. Larger population studies are required to validate these prominent results.