



Expression of the CGRP gene (*calca*) and its influence on the clinical phenotypes of migraine

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Background

Migraine is a disabling primary headache characterized by pulsatile and recurrent unilateral pain, whose pathophysiological mechanism involves the activation of the trigeminovascular system by calcitonin gene-related peptide (CGRP). The expression of the CGRP (*CALCA*) gene is influenced by epigenetic factors and genetic variation, playing a crucial role in promoting vasodilation of meningeal vessels and the release of inflammatory factors.

Objective

To evaluate the expression of mRNA transcripts from the CGRP gene in participants with and without migraine, as well as its association with clinical phenotypes of migraine.

Materials and Methods

This case-control study comprised 45 participants, including 31 migraine patients and 14 healthy controls, seen at the academic outpatient clinic of PUC-PR, Londrina-PR, Brazil. Clinical, demographic, and anthropometric data were collected. Participants also completed validated questionnaires on disability (MIDAS), migraine impact (HIT-6), and the presence of allodynia (ASC-12). For molecular analysis, RNA was extracted from peripheral blood, followed by cDNA synthesis using 1.5 µg of total RNA. Quantitative real-time polymerase chain reaction (RT-qPCR) was performed with SYBR Green and 200 nM of each primer for the two specific mRNA targets and normalized with the 18S ribosomal RNA as the reference gene. The relative expression of CGRP was evaluated using the $2^{-\Delta\Delta Ct}$ method.

Results

The migraine and control groups were comparable in terms of sex, age, ethnicity, and BMI ($p > 0.05$). Among migraine patients, 51.6% had the episodic form and 67.7% presented with aura. The gene transcripts of the CGRP gene was identified in the peripheral blood leukocytes of 3/14 patients (21.4%) in the control group and 6/31 (19.3%) in the migraine group. The control group had a median of 2 (1.5-4.8) Relative Quantification - RQ compared to the migraine group with 9 (1-20) RQ; $p = 0.548$. There was no association between CGRP mRNA expression and migraine phenotype or correlation with headache days, disabling pain days, MIDAS, HIT-6, and ASC-12 scores.

Conclusion

There was a low yield in the quantification of CGRP mRNA expression in leukocytes from peripheral blood samples. Increasing the sample size and controlling for the presence or absence of pain at the time of collection are necessary.