Headache Medicine

Genetic Biomakers: the Promising Tools in the Diagnosis and Manage of Headache Cases

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Categoria: Genética e Biomarcadores em Cefaleia

Introduction
Headaches are any painful process of the nervous system that reaches a certain cephalic segment. Enhanced by the speed of contemporary life, they, in addition to being one of the most disabling pains, have become even more prevalent, affecting more than half of the world's population. Given this, science sought to find ways to mitigate this situation. It is known that one of the promising and usable tools in such pain conditions are genetic biomarkers. Thus, since this work is relevant due to the need for more and more studies that address the theme of headaches, its justification is given by the intention of better understanding how genetic biomarkers can participate in the diagnosis and management of headache occurrences.

Objective
To analyze genetic biomarkers as tools in the diagnosis and management of headache cases.

Methods
This is an integrative review based on research in the MEDLINE, EMBASE, LILACS and SciELO databases, using the descriptors "Biomarkers", "Genetics" and "Headache Disorders", combined using the Boolean operator "AND". We selected studies available in their full versions, published in English, Portuguese or Spanish, between 2019 and 2023. After screening in stages, excluding studies of the review type and those that were not directly related to the aforementioned descriptors, 11 articles were selected that addressed the usefulness of genetic biomarkers in the diagnosis and management of headache occurrences.

Results
We found data that contemplated the intention of this study. A priori, it was found that headaches due to excessive use of medication were likely to be analyzed by genetic biomarkers, due to the high methylation of the three genes (CORIN, CCKBR and CLDN9) in cells of patients affected by this condition, compared to control individuals. It was also found that the smaller T allele of the rs3782218 of the NOS1 gene, together with rs2779249 and rs2297518 of the NOS2gene, represents an important genetic biomarker of high relevance for, in hypertensive patients, the overlapping of this comorbidity by tension headache. In addition, research conducted with Finnish families has shown that there are biomarkers associated with polygenic effects that signal increased susceptibility to migraine. In fact, miRNA activities have been highlighted as signaling this type of headache. In addition, a case-control study pointed out that the analysis of epigenetic biomarkers, such as the methylation status of the Long Intercalated Nuclear Element-1 and the Short Intercalated Nuclear Element, in peripheral blood mononuclear cells (PBMCs) can help identify patients at higher risk of developing migraine. Finally, in addition to helping in the diagnosis of headaches, genetic biomarkers were presented as potential therapeutic factors, assisting in the management of patients affected by such pain conditions. Gene therapies based on the genes MEF2D, TSPAN2, PHACTR1, TRPM8 and PRDM16, being related to migraine susceptibility, have the potential to contribute to the treatment and prevention of migraine. The CHRNA7 gene can be controlled by hsa-miR-3158-5p, via copy number variations, to modulate the mechanism of pain associated with this pain condition. Effects associated with altering tryptophan degradation via kynurenine may also have therapeutic action, so that, together with the regulation of miRNA correlated to this, it has the potential to greatly enhance the management of headache cases.

Conclusion
It can be stated, therefore, that genetic biomarkers are promising tools, not only in the diagnosis, but also in the management of the various cases of these pain conditions. Thus, more and more studies are needed to reach and improve their therapeutic potential, so that it is possible to reduce the considerable impacts of headaches on society.

Keywords: Genetic Biomakers; Headache Disorders; Diagnosis; Manage of Headache cases.