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The endocannabinoid system and related lipids as potential targets for the treatment of migraine-related pain

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Abstract

Background: Migraine is a complex and highly disabling neurological disease whose treatment remains challenging in many patients, even after the recent advent of the first specific-preventive drugs, namely monoclonal antibodies that target calcitonin gene-related peptide. For this reason, headache researchers are actively searching for new therapeutic targets. Cannabis has been proposed for migraine treatment, but controlled clinical studies are lacking. A major advance in cannabinoid research has been the discovery of the endocannabinoid system (ECS), which consists of receptors CB1 and CB2; their endogenous ligands, such as N-arachidonoylethanolamine; and the enzymes that catalyze endocannabinoid biosynthesis or degradation. Preclinical and clinical findings suggest a possible role for endocannabinoids and related lipids, such as palmitoylethanolamide (PEA), in migraine-related pain treatment. In animal models of migraine-related pain, endocannabinoid tone modulation via inhibition of endocannabinoid-catabolizing enzymes has been a particular focus of research.

Methods: To conduct a narrative review of available data on the possible effects of cannabis, endocannabinoids, and other lipids in migraine-related pain, relevant key words were used to search the PubMed/MEDLINE database for basic and clinical studies.

Results: Endocannabinoids and PEA seem to reduce trigeminal nociception by interacting with many pathways associated with migraine, suggesting a potential synergistic or similar effect.

Conclusions: Modulation of the metabolic pathways of the ECS may be a basis for new migraine treatments. The multiplicity of options and the wealth of data already obtained in animal models underscore the importance of further advancing research in this area. Multiple molecules related to the ECS or to allosteric modulation of CB1 receptors have emerged as potential therapeutic targets in migraine-related pain. The complexity of the ECS calls for accurate biochemical and pharmacological characterization of any new compounds undergoing testing and development.

Keywords: endocannabinoid system; migraine; palmitoylethanolamide; trigeminal pain.

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