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Influence of Novel Drugs on Prophylaxis Migraine Syndromes : The Challenge Is Open

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Dear Editor,

Migraine prophylaxis represents a better choice than symptomatic drugs, both for safety and for effectiveness. Today, drugs such as calcium channel blockers, beta-blockers, gabapentin, and topiramate are still used for migraines with and without aura, with results often satisfactory; however, in some cases with adverse effects limiting the use. A new class of drugs in migraine prophylaxis concerns endocannabinoids, modulating substances the nervous mechanisms of neuroinflammation, that cause migraine pain. Anandamide (AEA) and Palmitoylethanolamide (PEA) have proved to be useful in migraine prophylaxis, suggesting their influence in neuroinflammation processes is opening the way for interesting therapeutic perspectives.

The problem for treating migraine syndromes is still debated, due to the fact that the aim is to use prophylactic drugs instead of relying on symptomatic drugs, such as painkillers and triptans. The reason is that prophylactic drugs are more manageable, effective, and have fewer adverse effects, while symptomatic drugs cause a temporary improvement in the pain and can sometimes cause serious adverse effects. Migraine prophylaxis drugs have long been known and their effects have been appreciated with considerable improvement on pain. Medications such as calcium channel blockers, beta blockers, gabapentin, and topiramate have been used over time and recognized the effectiveness.

However, these drugs have side effects, minor or major, with respect to the drug used and also taking into account comorbidity, linked to associated diseases. There are numerous studies that indicate which of these prophylactic drugs are more recommended for the best risk-benefit ratio, which leads to a choice of the appropriate drug for each patient. In the recent years, a new class of migraine prophylactic drugs emerging are so called endocannabinoids (1). They are substances that stimulate cannabinoid receptors in the central nervous system, the endocannabinoid system, consisting of neuromodulatory lipids, endogenous substances, and involved in a variety of neurophysiological processes as cognitive as well as autonomic functions (2, 3). Now, it is known that their modulation action on the migraine as well as pain has been shown to have a relationship with the endocannabinoid system. The reason can be explained in the action on mechanisms of trigeminal-vascular system, a regulating and modulating pain system, as supposed to a migraine without aura or in the implication in process of cortical spreading depression (CSD), as hypothized in migraine aura (4, 5). Anandamide, also known as N-arachidonoylethanolamide (AEA), a fatty acid neurotransmitter, for example, was deemed able to potentiate the 5-HT1A receptors, proving effective in preventive migraine treatment and its positive effects have been demonstrated also in spinal diseases, fibromyalgia, and others. Apropos, reduced levels of AEA in the cerebrospinal fluid (CSF) were found in migraineurs, confirming an impairment of the endocannabinoid system in these patients. Palmitoylethanolamide (PEA), endogenous fatty acid amide, is another substance that intervenes in the processes of neuroinflammation, used in neuropathic pain and recently, successfully, in a rare and severe type of headache, such as the nummular headache (6, 7). PEA is an aliamide or amide ALIA-effect (autacoid local inflammation antagonism) term introduced by Professor Rita Levi-Montalcini, whereby substances locally produced have a protective role to inflammation. Particularly, PEA plays an

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important role in neuroinflammation, modulating the action of glia and mastcells and mantaining cellular homeostasis. Stimulation of the trigeminal vascular system causes neuroinflammatory process with release on neuropeptides as substance P, 5-HT, calcitonine G-related peptide (CGRP). In short, PEA is an anti-inflammatory agent, in regards to the migraine syndrome is a resource not yet fully exploited. These drugs are administered in addition to prophylaxis medications already taken, the purpose is to administer them alone. Migraine is a chronic and often debilitating pathology, which needs prophylactic treatment, hence the need to find effective and safe substances. Therefore, modulate endocannabinoid system, which is considered the basis of neuroinflammation processes, can be a suggestive therapeutic option. Numerous studies are in progress, however, the prospects are encouraging, due to the fact that the data of the literature, regarding the use of endocannabinoids in several diseases of the nervous system, have demonstrated validity, effectiveness, and absence of adverse effects. Therefore it is important to follow this procedure and future studies are necessary for maximum efficency in the research and confirming their importance.

Footnote

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