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SHORT COMMUNICATION

Palmitoylethanolamide as an emerging therapy for neurodegenerative diseases

La palmitoiletanolamida como terapia emergente frente a enfermedades neurodegenerativas

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ABSTRACT

Palmitoylethanolamide (PEA) was studied for its neuroprotective, anti-inflammatory and analgesic properties. Recent research has shown that it protects HT-22 neuronal cells from oxidative stress caused by hypoxia and reoxygenation, through the activation of signalling pathways such as pAkt and ERK1/2. In addition, it modulates the activation of microglia and astrocytes, reducing inflammation and neuronal damage. Its action did not depend on the CB2 receptor, which indicated a novel mechanism. Its therapeutic potential in neurodegenerative diseases such as ischaemic stroke, which is common in Latin America, was highlighted. Although its safety profile was favourable, additional clinical studies were indicated for its implementation. Regional cooperation was presented as a key factor in advancing its clinical application.

Keywords: Neuroprotection; Hypoxia; Microglia; Palmitoylethanolamide; Inflammation.

RESUMEN

La palmitoiletanolamida (PEA) fue estudiada por sus propiedades neuroprotectoras, antiinflamatorias y analgésicas. Investigaciones recientes demostraron que protegió a las células neuronales HT-22 del estrés oxidativo causado por hipoxia y reoxigenación, mediante la activación de vías de señalización como pAkt y ERK1/2. Además, moduló la activación de microglía y astrocitos, reduciendo la inflamación y el daño neuronal. Su acción no dependió del receptor CB2, lo que indicó un mecanismo novedoso. Se destacó su potencial terapéutico en enfermedades neurodegenerativas como el accidente cerebrovascular isquémico, frecuente en América Latina. Aunque su perfil de seguridad fue favorable, se señalaron como necesarios estudios clínicos adicionales para su implementación. La cooperación regional se presentó como un factor clave para avanzar en su aplicación clínica.

Palabras clave: Neuroprotección; Hipoxia; Microglía; Palmitoiletanolamida; Inflamación.

BACKGROUND

Palmitoylethanolamide (PEA) is an endogenous lipid that has attracted scientific attention for its neuroprotective,[1,2,3,4,5] anti-inflammatory, and analgesic properties.[6,7,8] Recent studies have explored its efficacy in cellular and animal models,[9,10,11,12] particularly in the HT-22 neuronal cell line subjected to hypoxia and reoxygenation conditions. This has significant implications for public health in Argentina and Latin America.

Research has shown that PEA protects HT-22 cells from oxidative stress induced by hypoxia and reoxygenation.[13,14,15,16] This effect is attributed to the activation of neuroprotective signaling pathways, such as Akt (pAkt) and

ERK1/2 phosphorylation and pAkt nuclear translocation. These changes occur within a time frame consistent with neuroprotection and are not mediated by cannabinoid receptor type 2 (CB2) activation, suggesting a novel mechanism of action.[17]

In addition, PEA modulates the activation of microglia and astrocytes, key cells in the central nervous system's inflammatory response. By inhibiting the activation of these cells, PEA reduces the release of proinflammatory cytokines and limits secondary neuronal damage.[18]

Neurodegenerative diseases represent a significant burden on health systems in Argentina and Latin America.[19] PEA's ability to mitigate neuronal damage under conditions of hypoxia and reoxygenation suggests its potential as a therapeutic agent in pathologies such as ischemic stroke, which is common in the region.[20]

It is essential to consider the feasibility of implementing PEA-based treatments in the Latin American context. As an endogenous compound with a favorable safety profile, PEA could offer an accessible and cost-effective therapeutic option.[21] However, additional clinical studies are needed to confirm its efficacy and establish treatment protocols tailored to local needs and resources.

In Latin America, research and application of neuroprotective therapies such as PEA are in the early stages. Countries such as Brazil and Mexico have made progress in investigating neuroprotective compounds, but their incorporation into clinical practice remains limited.[22] Regional collaboration and knowledge sharing can accelerate the adoption of PEA-based therapies, thereby improving care for patients with neurodegenerative diseases throughout the region.[23]

PEA shows significant potential as a neuroprotective agent in cellular models of hypoxia and reoxygenation, which could have important implications for public health in Argentina and Latin America. Continued research and regional collaboration will be key to translating these findings into tangible clinical benefits for the population.

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CONFLICT OF INTEREST

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