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Physiopathology of peripheral sensitization and mechanism of action of gabapentin in occipital neuralgia

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Introduction

Peripheral sensitization (PS) characterized by hypersensitivity of nociceptors is a key process in the pathophysiology of occipital neuralgia (ON). PS amplifies neuronal excitability and pain perception due to upregulation of ion channels and receptors. Gabapentin seems to treat ON by mitigating PS and providing analgesic relief in neuropathic pain.

Objectives

This study aims to summarize the literature regarding the physiopathology of PS in ON and to comprehend gabapentin's mechanism of action in ON.

Methods

In May 2024, three searches were conducted in MEDLINE, LILACS, and PubMed databases. Using the descriptors "peripheral sensitization" AND "Physiology" 227 results were obtained; "Gabapentin" AND "Pharmacology" OR "Neuralgia" yielded 756 results; and "Occipital Neuralgia" AND "Physiology" OR "Physiopathology" 380 results. After applying inclusion criteria for analysis, 33 articles were analyzed, resulting in 4, 14, and 15 articles for each subtheme respectively.

Results

ON is characterized by severe paroxysmal attacks of headaches, throbbing or stabbing in quality, at the suboccipital region. Other symptoms include scalp tenderness and trigger points. The pronociceptive functions involved in the pathogenesis of pain result from damage to the occipital nerves causing PS, where primary inflamed afferent neurons become hyperresponsive. Inflammatory mediators like prostaglandins and cytokines sensitize nociceptors, while nerve injuries alter ion channels, increasing neuronal excitability. The inflammatory-sensitive receptor TRPV1 upregulates, and damaged nerve fibers release nerve growth factor (NFG), further amplifying sensitivity. Underlying mechanisms of ON include the role of calcitonin gene-related peptide (CGRP) in maintaining hypersensitivity and contributing to pain perception. Gabapentin's efficacy in ON is attributed to its interaction with the 2 subunit of voltage-gated calcium channels, reducing the influx of calcium and diminishing neurotransmitter release. As a result, it reduces neuronal excitability and mitigates pain.

Conclusion

PS is crucial to understanding ON's pathophysiology. The hypersensitivity and increased pain perception are influenced by inflammatory mediators and receptors, such as TRPV1 and CGRP. Gabapentin indirectly manages ON and provides analgesic relief by modulating calcium channels and reducing neuronal excitability. Further research is needed into gabapentin's mechanisms and potential applications in ON to enhance therapeutic strategies.