



## The correlation of Osteoporosis with Trigeminal Neuralgia: a Literature Review

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### Introduction

Trigeminal neuralgia is a debilitating neuropathic pain condition that can affect one or both trigeminal nerves, causing recurrent episodes of extreme facial pain similar to electric shocks, of short duration and abrupt onset and end. The pathophysiological mechanisms of this disease, although still controversial, are limited to the vascular improvement of the trigeminal nerve, in its root entry zone, and the demyelination of the sensory fibers of this nerve. It is also known that nociceptive stimulation of the trigeminal nucleus presupposes a wave of depolarization, in which the activation of calcium channels participates. Therefore, it was conjectured, in the present study, whether structural diseases related to calcium metabolism, such as osteoporosis, related to trigeminal neuralgia.

### Objective

To review and analyze the evidence on the relation between osteoporosis and trigeminal neuralgia (TN).

### Methodology

A search was carried out using the descriptors 'Osteoporosis' and 'Trigeminal Neuralgia' in the Embase, PubMed and CAPES Periodicals Portal databases, the inclusion criteria were: articles published since 2017 in Portuguese, English or Spanish and free access. An analysis of titles and abstracts of scientific articles obtained in the selection of three scientific articles to compose this review.

### Results

It was observed that TN and osteoporosis had risk factors in common, such as hypertension and migraines. Furthermore, cohort studies found that patients with osteoporosis are approximately twice as likely to have trigeminal neuralgia compared to those without osteoporosis. An explanation for this finding would be: hypomagnesemia, which would reduce vitamin D levels, which is essential for the absorption of calcium, since the liver 25-hydroxylase and renal 1 $\alpha$ -hydroxylase enzymes require magnesium to be active, in addition this ion regulates the excitability of neuronal receptors, so that low levels of magnesium would favor the conduction and transmission of neural impulses, which represents a risk factor for TN; It was also hypothesized that the calcitonin gene-related peptide (CGRP) would be an important mediator of this investigated relation, because patients with osteoporosis had a higher plasma level of CGRP, which is an extremely important neuropeptide in sensory pathways of the trigeminal nerve and which also regulates the release of osteoblastic cytokines, therefore having an effect on bone reabsorption by osteoclasts. Thus, overexpression of CGRP would cause the development of osteoporosis and a decrease in the activation thresholds of trigeminal neuralgia.

Furthermore, hypertension was also shown to be a risk factor for both conditions, as it would cause a leak of bone calcium with subsequent hypercalciuria and increased arterial tortuosity in the brainstem.

### Conclusion

The evidence found suggests that there is an association between osteoporosis and trigeminal neuralgia, however this relation is complex and little studied, based on the hypothesis that magnesium levels and CGRP would eliminate an intermediary between these conditions. However, it is worth highlighting that, given the scarcity of literature on the subject, there is a clear need for more robust studies that directly investigate the relation between osteoporosis and trigeminal neuralgia and the mechanisms by which this would occur.

**Keywords:** Calcium; Vitamin D Deficiency; Calcitonin Gene-Related Peptide; Headache Disorders; Migraine.