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Neuromodulatory and interventional therapies in trigeminal autonomic cephalalgias: a systematic review

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Introduction
Trigeminal autonomic cephalalgias (TACs) are rare primary headache disorders characterized by severe unilateral pain and ipsilateral cranial autonomic symptoms, encompassing cluster headache, paroxysmal hemicrania, hemicrania continua, and SUNCT/SUNA.

Objective
To analyze the main therapeutic approaches used in the management of trigeminal autonomic cephalalgias, with a particular focus on neuromodulatory therapies.

Methods: A systematic literature review was conducted using the PubMed and LILACS databases. The search strategy employed was: "Trigeminal Autonomic Cephalalgias" [Title] AND "treatment", yielding an initial total of 55 articles. The research question was structured according to the PICO framework, considering: population (patients with trigeminal autonomic cephalalgias), intervention (neuromodulatory and interventional therapies), comparison (conventional pharmacological treatment or no intervention), and outcomes (reduction in attack frequency and severity, clinical improvement, and treatment tolerability). Studies published between 2021 and 2026, available in full text, free of charge, and written in English were included. After applying the eligibility criteria, five studies were selected for full-text analysis.

Results
Based on the analyzed studies, the management of trigeminal autonomic cephalalgias remains challenging. Corticosteroids, triptans, and verapamil were widely used for cluster headache, whereas indomethacin remained the standard treatment for hemicrania continua and paroxysmal hemicrania, despite limitations related to poor tolerability and gastrointestinal adverse effects. In refractory cases, interventional approaches demonstrated promising outcomes. Occipital, supraorbital, and supratrochlear nerve blocks significantly reduced attack frequency and severity, with near-complete symptom resolution reported in some patients with post-traumatic headaches presenting TAC-like features. Peripheral nerve decompression surgery also showed sustained benefits in patients intolerant to indomethacin, achieving pain reductions of up to 90% with long-term maintenance of clinical improvement. Furthermore, non-invasive vagus nerve stimulation (nVNS) demonstrated clinical benefit in approximately 65% of patients, particularly as a preventive therapy, with more than a 50% reduction in attack frequency among most responders and a low incidence of serious adverse events. These findings highlight the potential of neuromodulatory and interventional therapies as effective alternatives for refractory TACs or for patients with contraindications to conventional pharmacological treatment.

Conclusion
The treatment of trigeminal autonomic cephalalgias remains challenging, particularly in refractory cases. However, neuromodulatory therapies and peripheral interventions have shown promising results in reducing attack frequency and severity, representing effective therapeutic alternatives for patients with intolerance or inadequate response to conventional pharmacological management.

Keywords:
Neuromodulation
Vagus nerve stimulation
Trigeminal autonomic cephalalgias
Treatment outcome
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