Headache Medicine

ID: 10

Sleep disturbances in trigeminal autonomic cephalalgias: clinical implications and pathophysiological insights — a systematic review

Giulia Miranda Reale Lemos, Camila Lopes Lima, Carolina Veruska Rodrigues de Deus Garrido Sales

Tiradentes University, Aracaju, Sergipe, Brazil

Giulia Miranda Reale Lemos
giuliamrlemos@gmail.com

Introduction
Trigeminal autonomic cephalalgias (TACs), particularly cluster headache, are characterized by severe attacks with marked circadian patterns, frequently arising during sleep. This temporal organization reflects a close interaction between hypothalamic function, circadian regulation, and trigeminal–autonomic activation, positioning sleep and chronobiological mechanisms as central components of TAC pathophysiology.

Objective
To investigate the pathophysiological and chronobiological relevance of sleep disturbances in trigeminal autonomic cephalalgias.

Methods
Sleep-related abnormalities in trigeminal autonomic cephalalgias were evaluated through a systematic review conducted according to PRISMA 2020 guidelines. Publications indexed in PubMed/MEDLINE, SciELO, and LILACS between January 2016 and April 2026 were screened for randomized and observational studies assessing sleep through polysomnography, actigraphy, or validated questionnaires in adult patients with TACs. Studies without defined sleep outcomes, pediatric samples, or experimental models were excluded. Search terms included "trigeminal autonomic cephalalgias," "cluster headache," "sleep disturbances," "sleep architecture," and "circadian rhythm." Risk of bias was assessed qualitatively using the Newcastle-Ottawa Scale for observational studies.

Results
The included studies, predominantly involving cluster headache, demonstrated a consistent association between sleep disturbances, increased attack frequency, and greater clinical burden, with impaired sleep quality affecting more than 60% of patients across active and remission phases. From 240 identified records, 51 duplicates were removed; of the 189 records screened, fourteen studies met full inclusion criteria, comprising 1,124 patients. Polysomnographic findings included prolonged REM latency, reduced REM proportion, increased microarousals, and decreased sleep efficiency, often independent of nocturnal attacks. Circadian dysregulation was observed in approximately 70% of patients, with nocturnal clustering between 21:00 and 03:00. Neuroendocrine alterations, including reduced melatonin, altered cortisol rhythmicity, and decreased hypocretin-1 levels, suggest the presence of hypothalamic dysfunction linking circadian disruption to trigeminal–autonomic activation.

Conclusion
Sleep disturbances in trigeminal autonomic cephalalgias reflect disruption of hypothalamically regulated circadian and sleep processes, contributing to both attack generation and disease persistence. Although the available evidence is predominantly observational and methodologically heterogeneous, findings consistently support the role of circadian dysregulation in TAC pathophysiology. Prospective studies integrating standardized sleep assessment and circadian biomarkers are needed to better define causal mechanisms and evaluate sleep-targeted interventions in TACs.

Keywords:
Trigeminal autonomic cephalalgias
Cluster headache
Sleep disturbances
Circadian rhythm
Hypothalamus

© Copyright 2025