▪ Headache Medicine 2026, Supplement ▪ p-ISSN 2178-7468, e-ISSN 2763-6178

Headache Medicine

ID: 343

Cluster headache and circadian dysregulation: hypothalamic mechanisms, sleep alterations and clinical implications

Rhaissa Soledade Couto[1], Igor Alves de Lucena Maciel Chacon[1], Isabelly Furtado Ramalho[2], Lais Claudia Seixas Cruz[1], Luize Daniel Bandeira Castelo Branco[1], Maria Luiza Fragoso Pereira Neta[1], Márcio Santos Cortez[1]

[1]Afya School of Medical Sciences of Jaboatão dos Guararapes, Jaboatão dos Guararapes, Pernambuco, Brazil
[2]Olinda School of Medicine, Olinda, Pernambuco, Brazil

Rhaissa Soledade Couto
rhaissacouto@gmail.com

Introduction
Cluster headache (CH) is one of the most disabling primary headache disorders, characterized by excruciating unilateral orbitotemporal pain associated with cranial autonomic symptoms. Unlike other headache syndromes, CH exhibits marked circadian and circannual periodicity, with attacks frequently occurring at fixed times, particularly during sleep. Evidence supports hypothalamic involvement, especially dysfunction of the suprachiasmatic nucleus, alongside altered melatonin secretion and disturbances in REM sleep, suggesting an important neurocircadian component in disease pathophysiology.
Objective: To evaluate the relationship between cluster headache and circadian rhythm, discussing underlying neurobiological mechanisms, temporal attack patterns, and clinical implications.

Methods
A systematic review with meta-analysis was conducted according to PRISMA 2020 guidelines. Searches were performed in PubMed, MEDLINE, Embase, Cochrane Library, and SciELO for studies published between 2010 and 2026. Clinical trials, observational studies, systematic reviews, and neuroimaging investigations addressing circadian aspects of CH were included. Data focused on pathophysiology, sleep alterations, hormonal findings, and clinical outcomes.

Results
Most patients demonstrated attacks occurring at predictable circadian intervals, predominantly during nighttime periods. Functional neuroimaging studies revealed activation of the inferior posterior hypothalamic gray matter during painful episodes, supporting a central role of hypothalamic dysregulation. Reduced melatonin levels, altered cortisol rhythmicity, and decreased REM sleep were recurrent findings, indicating disruption of biological clock regulation. Recognition of these chronobiological patterns may improve diagnostic accuracy and support therapeutic approaches involving chronomodulation and melatonin use.

Conclusion
Cluster headache is strongly associated with circadian dysfunction involving hypothalamic activation, neuroendocrine alterations, and sleep disturbances. Understanding brain–clock interaction may refine diagnosis and contribute to more effective therapeutic strategies and improved patient outcomes.

Keywords:
Cluster headache
Circadian rhythm
Hypothalamus
Melatonin

© Copyright 2025