Circadian Rhythm of Attacks – Why Does Cluster Headache "Know" When It Is Night?

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Abstract

Cluster headache is a primary headache disorder characterized by intense ipsilateral orbital pain, lacrimation, and rhinorrhea, accompanied by restlessness. Pain attacks last up to 180 minutes and may recur several times a day. The prevalence of cluster headache in the general population is approximately 0.1%, and the disorder is three times more common in men. Attacks typically occur during specific seasons, most frequently in spring or autumn, and recur annually or less frequently in clusters lasting several weeks. A characteristic feature of cluster headache is its circadian rhythm, observed in approximately 80% of patients, with most attacks occurring during the night. Studies have demonstrated functional changes in the posterior hypothalamus, which plays an important role in the regulation of wakefulness and nociception. The posterior hypothalamus is directly connected to the suprachiasmatic nucleus, which regulates the biological clock. It is also connected via parasympathetic pathways to the sphenopalatine ganglion, which is involved in the autonomic symptoms accompanying cluster headache attacks, and to the caudal trigeminal nucleus within the trigeminocervical complex, which plays an important role in nociceptive processing and the release of inflammatory neuropeptides that further promote the pain cascade. Altered circadian secretion of pituitary hormones and dysfunction of the orexinergic system are considered key mechanisms in the pathophysiology of cluster headache. Verapamil is the most effective drug for prophylactic treatment, while 100% oxygen is an effective treatment for acute attacks. These therapeutic approaches suggest the importance of central mechanisms in pain modulation. Future therapeutic strategies may include drugs acting directly on hypothalamic structures, particularly orexin receptor agonists, as well as deep brain stimulation of the hypothalamus for the prevention of cluster headache attacks. Considering these findings, a detailed understanding of the circadian rhythm of cluster headache is essential for optimizing its treatment.

Keywords: cluster headache; pathophysiology; hypothalamus; circadian rhythm; sleep

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Cirkadijani ritam napada – zašto cluster glavobolja „zna" kada je noć?

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Sažetak

Cluster glavobolja primarna je glavobolja karakterizirana intenzivnom ipsilateralnom boli u području orbite, lakrimacijom i rinorejom, uz osjećaj nemira. Napadaji boli traju do 180 minuta i mogu se ponavljati nekoliko puta dnevno. Prevalencija cluster glavobolje u općoj populaciji iznosi približno 0,1 %, a bolest je triput češća u muškaraca. Napadaji se najčešće javljaju u određenim godišnjim dobima, osobito u proljeće ili jesen, te se ponavljaju svake godine ili rjeđe, u razdobljima koja traju nekoliko tjedana. Karakteristično obilježje cluster glavobolje njezin je cirkadijani ritam, prisutan u približno 80 % bolesnika, pri čemu se većina napadaja javlja tijekom noći. Istraživanja su pokazala funkcionalne promjene u posteriornom hipotalamusu, koji ima važnu ulogu u regulaciji budnosti i nocicepcije. Posteriorni hipotalamus izravno je povezan sa suprahijazmatskom jezgrom, koja regulira biološki sat. Također je parasimpatičkim putovima povezan sa sfenopalatinalnim ganglijem, koji sudjeluje u nastanku autonomnih simptoma tijekom napadaja cluster glavobolje, te s kaudalnom jezgrom trigeminalnog živca unutar trigeminocervikalnog kompleksa, važnog za nociceptivnu obradu i otpuštanje upalnih neuropeptida koji dodatno potiču kaskadu boli. Ključni mehanizmi u patofiziologiji cluster glavobolje uključuju promijenjeno cirkadijano lučenje hipofiznih hormona i disfunkciju oreksinergičkog sustava. Verapamil je najučinkovitiji lijek u profilaktičkom liječenju, dok je primjena 100 %-tnog kisika učinkovita u liječenju akutnih napadaja. Ovi terapijski pristupi upućuju na važnost središnjih mehanizama u modulaciji boli. Buduće terapijske mogućnosti uključuju lijekove s izravnim djelovanjem na hipotalamičke strukture, osobito agoniste oreksinskih receptora, kao i duboku mozgovnu stimulaciju hipotalamusa u prevenciji napadaja cluster glavobolje. S obzirom na navedeno, detaljno poznavanje cirkadijanog ritma cluster glavobolje ključno je za optimizaciju njezina liječenja.

Ključne riječi: cluster glavobolja; patofiziologija; hipotalamus; cirkadijani ritam; spavanje

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