

# Paranasal Sinusal Congestion in Cluster Type Headache Küme Bas Ağrısında Paranazal Sinüs Konjesvonu

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#### Abstract

**Objective:** Cluster headache (CH) is a primary headache syndrome accompanied by parasympathetic autonomic symptoms. Our main objective is to put forth that radiological paranasal sinus congestion, frequently encountered in this syndrome, results from autonomic dysfunction, such as conjunctival injection, lacrimation, nasal congestion, and rhinorrhea rather than being of incidental appearance.

Materials and Methods: The radiological data of the patients who met the diagnostic criteria, had negative infectious markers, did not receive any antibiotics, and whose symptoms were under control by standard CH management were evaluated. Positive imaging was considered to show ipsilateral sinus congestion. Negative imaging showed no congestion, sinus retention cysts, or contralateral or bilateral congestion.

**Results:** Of the 38 subjects, 42% had positive sinus congestion, and 57.9% were negative.

**Conclusion:** We found that 42% of patients with CH had ipsilateral paranasal sinus congestion, and this feature was a part of autonomic dysfunction. However, further studies are needed to support these findings.

Keywords: Cluster headache, sinusal congestion, parasympathetic nervous system

## Öz

Amaç: Küme baş ağrısı (KBA), otonomik belirtilerin eşlik ettiği primer bir baş ağrısı sendromudur. Temel amacımız, bu sendromda sıklıkla karşılaşılan radyolojik paranazal sinüzal konjesyonun, konjonktival enjeksiyon, artan gözyaşı, nazal konjesyon ya da burun tıkanıklığı gibi, insidental bir görünüm değil otonom bir bulgu olduğunu ortaya koymaktır.

Gereç ve Yöntem: Tanı kriterlerini karşılayan, enfeksiyon belirteçleri negatif olan ve antibiyotik almaksızın KBA belirtileri standart tedaviler ile kontrol altına alınan hastaların tanı anındaki beyin görüntüleri paranazal sinüs konjesyonu açısından değerlendirildi. Pozitif görüntüleme, KBA'ya ipsilateral paranazal sinüsün konjesyonu olarak ele alındı. Negatif görüntüleme ise, radyolojide konjesyonun olmaması, sinüs retansiyon kistleri, kontralateral konjesyon veya bilateral konjesyon bulunması olarak ele alındı.

**Bulgular:** Otuz sekiz hastanın %42,1'inde ipsilateral pozitif sinüs konjesyonu saptanmıştır. %57,9'unda ise radyolojik görüntüler sinüs konjesyonu açısından negatif olarak değerlendirilmiştir.

**Sonuç:** Araştırma popülasyonunda, KBA'da ipsilateral paranazal sinüs konjesyonunun %42 oranında geliştiğini ve bunun otonom disfonksiyonun bir sonucu olduğunu ortaya koyduk. Ancak bulgularımızı desteklemek için daha ilerideki çalışmalara da ihtiyaç vardır.

Anahtar Kelimeler: Küme baş ağrısı, sinüs konjesyonu, parasempatik sinir sistemi





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# Introduction

Cluster headache (CH) is a primary headache syndrome accompanied by autonomic symptoms in short-term attacks around the unilateral orbit (1). According to the Headache Classification Committee of the International Headache Society, if left untreated, CH is characterized by at least five (maybe up to eight) attacks of severe or very severe orbital or temporal pain lasting 15–180 minutes and is accompanied by at least one of the following autonomic symptoms: ipsilateral conjunctival injection or increased lacrimation, nasal congestion or runny nose, eyelid edema, sweating on the forehead or face, miosis and/or ptosis, and/ or restlessness or agitation (2).

In the literature, some radiological findings in patients who meet the diagnostic criteria for CH are not the result of cluster pathophysiology but have been evaluated as rare primary causes that may lead to CH. For example, Balgetir et al. (3) published a series of 7 patients with radiologically acute rhinosinusitis underlying symptomatic CH. In addition, Edvardsson (4) presented a case report suggesting that maxillary sinusitis was the underlying cause of CH (4).

Incidental paranasal sinus findings encountered radiologically in CH, such as congestion or serous discharge in the ipsilateral frontal, maxillary, sphenoid, or ethmoid sinuses, have not been interpreted as a sign of autonomic dysfunction to date. However, it is known that the posterior hypothalamus has an activating role in CH episodes (1), and parasympathetic hyperactivity and sympathetic dysfunction develop during attacks (5). Furthermore, it is well known that parasympathetic cholinergic reflexes increase nasal blood flow and trigger sinuses to fill with secretions and mucosal thickening (6).

The authors' aim to show in a large population that paranasal sinus congestion (or sinus inflammation, as it was erroneously called) is not a primary factor causing CH but rather an autonomic symptom, such as conjunctival injection, increased tears, and nasal congestion, that develops secondary to the pathophysiology of cluster pain, presenting the first research study on this subject.

### Materials and Methods

Ethical approval was obtained from the Ankara Bilkent City Hospital 2<sup>nd</sup> Ethics Committee (approval no: E2-23-4737, date: 09.08.2023). The study took place in accordance with the latest version of the Declaration of Helsinki and Good Clinical Practice guidelines. Patients who were admitted to the Neurology Outpatient Clinic of the VM Medicalpark Ankara Hospital during 2022 and 2023 who were in the ictal period and met the criteria for CH based on the diagnostic standards determined by the International Headache Association were included in the study, having signed a voluntary consent form.

At the time of diagnosis, all patients underwent magnetic resonance imaging or computed tomography. C-reactive protein (CRP) and hemogram findings of all patients were recorded, and body temperature was measured.

Patients with parenchymal diseases such as an intracranial mass, demyelinating pathology, meningoencephalitis, acute ischemia, or intracerebral hemorrhage, patients with vascular diseases such as an intracerebral aneurysm, subarachnoid hemorrhage, or subdural hematoma, patients with a CRP level and white blood cell count deviating from the normal range suggesting an infection, and patients with hypothermia (<36°C) or hyperthermia (>37.4°C) were excluded. Patients who did not benefit from common evidence-based CH treatments, such as a steroid and verapamil or a steroid and lithium (combined or not with indomethacin), were also excluded based on information collected at the 15-day follow-up visit. This was to prevent the patients who did not benefit from standard treatments and those with a possible infection causing sinus congestion at the time of diagnosis from affecting the results.

Patients whose brain images at the time of diagnosis met the diagnostic criteria, whose infection markers were negative, and whose CH symptoms were controlled with the treatments listed above without using antibiotics were evaluated as "positive" or "negative" in terms of paranasal sinus congestion at the 15-day follow-up visit. The evaluation was made by a radiologist with 5 years of experience in cranial imaging. Positive imaging was considered as frontal, maxillary, ethmoid, or sphenoid sinus congestion ipsilateral to CH or congestion of more than one ipsilateral paranasal sinus. Negative imaging was defined as the absence of congestion, the presence of sinus retention cysts, contralateral congestion, or bilateral congestion on radiological examination. The evaluation of patients with contralateral or bilateral congestion as negative was because the diagnostic criteria state that autonomic symptoms develop ipsilaterally.

#### Statistical Analysis

The SPSS 23.0 was used as the statistical program. A descriptive study was conducted to summarize the data collected. While frequency tables were used to present the distribution of different categories, the mean and standard deviation, along with the observed minimum (min) and maximum (max) values, were used to present continuous variables, such as the age of the patients.

#### Results

Of the 38 patients who met the diagnostic criteria for CH and benefited from the evidence-based standard treatments recommended and whose radiological imaging results at the time of diagnosis were evaluated at the second visit for paranasal sinus congestion, 32 were men (84%), and 6 were women (16%). The average age of the patients was  $36.8 \pm 17.1$  years (min: 21, max: 62). Of the patients, 63% had right-sided CH, and 37% had left-sided CH.

Ipsilateral positive sinus congestion was detected in 42.1% of the patients. In 57.9% of the patients, radiological images were evaluated as negative for sinus congestion. The rate of paranasal sinus congestion was 16.6% in females and 46.8% in males. However, the number of female patients was insufficient to make a comparison.

## Discussion

This study found that ipsilateral sinus congestion was observed in 42% of the patients with CH. This observation should be seen as a natural result when the basic pathophysiological processes of the autonomic nervous system are examined closely. This is because, under the influence of acetylcholine and substance P released due to parasympathetic activation, glandular secretion and plasma extravasation develop, and congestion is observed in the nasal and sinus cavities (7). Considering that the basic pathophysiological mechanism in CH is cranial parasympathetic hyperactivation (8), fluid flow into the nasal and sinus cavities is consistent with this basic physiological knowledge.

However, in the case reports published to date in the literature (there have been no research studies), the opposite view of this basic pathophysiological mechanism has prevailed. It has generally been thought that sinus congestion or inflammation is the primary factor, and CH is a consequence. For example, Yang and Huang (9) reported that CH was accompanied by chronic nasosinusitis. In another study, CH-like symptoms due to sinusitis were reported (10). Taking this claim even further, Nellis and Payne (11) reported a patient in whom episodic parasympathetic hyperactivation and CH-like findings developed due to chronic rhinosinusitis.

### Study Limitations

To the authors' knowledge, this is the first study investigating the frequency of paranasal sinus congestion in CH, and, unlike case reports or case series published to date, it shows that paranasal congestion is a result, not a cause of CH, linking it to objective diagnostic criteria and basic physiopathological mechanisms. The limitation of this study is that, although it looked at a wider population than the case reports, it still examined a relatively small number of patients.

#### Conclusion

In this study, it was found that paranasal sinus congestion developed in 42% of patients with CH and that this was the result of autonomic dysfunction. However, further studies are needed to support these findings.

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#### Ethics

Ethics Committee Approval: Ethical approval was obtained from the Ankara Bilkent City Hospital 2<sup>nd</sup> Ethics Committee (approval no: E2-23-4737, date: 09.08.2023). Informed Consent: Obtained.

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