



Do paroxysmal hemicrania and hemicrania continua represent different headaches? A retrospective study

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Abstract

Objective Hemicrania continua and paroxysmal hemicrania are considered different headaches belonging to a group of trigeminal autonomic cephalalgias. However, they share many clinical features. Both headaches also show complete response to indomethacin, which is a mandatory criterion for their diagnosis. Are they really different headaches? To answer this question, we compared the pain characteristics and autonomic features between two headaches. We also determined whether paroxysmal hemicrania transforms into hemicrania continua or vice versa in their natural history.

Methods The patients with hemicrania continua and paroxysmal hemicrania were compared for severity, location, character, and mean effective indomethacin dose. The number of autonomic features and their severity was also compared. The natural history of headache was looked into to see the evolution of hemicrania continua and paroxysmal hemicrania from episodic and chronic pains, respectively.

Results We included 35 patients with hemicrania continua and 27 patients with paroxysmal hemicrania from July 2015 to March 2017. The mean age of patients with paroxysmal hemicrania was 34.42 years, and hemicrania continua was 37 years. Both groups were similar for majority of pain characteristics and number/severity of autonomic features. However, paroxysmal hemicrania had higher pain severity. Five patients transformed from paroxysmal hemicrania to hemicrania continua, and 3 patients transformed from hemicrania continua to paroxysmal hemicrania.

Conclusion Paroxysmal hemicrania and hemicrania continua were similar on majority of pain characteristics and autonomic features. The paroxysmal hemicrania and hemicrania continua are not exclusive headaches and can transform into each other.

Keywords Trigeminal autonomic cephalalgia · Migraine · Chronic daily headache · Paroxysmal hemicrania · Hemicrania continua

Background

Hemicrania continua (HC) and paroxysmal hemicrania (PH) are considered different headache types belonging to a group of trigeminal autonomic cephalalgias [1, 2]. Both the headaches are characterized by side-locked frontal-periorbital pain with varying severity of ipsilateral autonomic symptoms like conjunctival injection, lacrimation, rhinorrhea, stuffed nose, or forehead sweating. Pain of HC and PH completely subsides with the therapeutic doses of indomethacin [3, 4]. HC and PH clearly differ from each other by the duration of pain. HC produces a continuous daily headache with overlying exacerbations of pain, whereas PH produces repetitive attacks of short-lasting pain attacks lasting up to 30 min [1, 5, 6]. Some experts believe that the pain and autonomic symptoms in PH are more severe as compared with HC [7–9]. However, they also admit that PH with background continuous interictal pain is indistinguishable from HC [7, 9].

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The posterior hypothalamus is thought to be central in the pathophysiology of trigeminal autonomic cephalalgias. The stimulation of trigeminal afferents results in autonomic outflow, and hypothalamus is thought to have modulatory role in pain and autonomic pathways. The brain areas that brighten up due to pain on functional MRI in patients with HC and PH are posterior hypothalamus and ventrolateral midbrain [10]. The rostral dorsal pons additionally brightens up during pain in HC [11]. The pathophysiology of PH and HC is poorly understood. The current literature proposes a common central disinhibition of a trigeminal autonomic reflex model to explain pain and autonomic symptoms in TACs [11].

Do HC and PH represent different headaches? There are no clear answers. The differences in the characteristics/severity of pain and autonomic features between HC and PH have never been compared. Headache experts do believe that one form of headache listed under “trigeminal autonomic cephalalgias” may sometimes transform into other, but we did not find reports of PH and HC transforming into each other in their natural history. Therefore, we conducted this study to compare the severity, character, distribution, and other characteristics of pain, autonomic symptoms, and mean effective indomethacin dose in patients with HC and PH. We also tried to determine whether the patients with PH transform to HC or vice versa in their natural history. We propose a null hypothesis that HC and PH will have significant difference in characteristics of pain and autonomic features.

Methods

This was a retrospective study. We reviewed the clinical data of patients with the diagnosis of HC and PH that visited the out-patient department between July 2015 and March 2017. In 2015, we generated the patient’s performance for documentation of pain characteristics, autonomic features, and other clinical characteristics of patients with new daily persistent headache (NDPH), chronic migraine, chronic tension type headache, and hemicrania continua. This patient’s performa was

meant for another cross-sectional study. Since 2015, we have been using the same performance for routine evaluation and documentation of clinical features of patients with TACs. A neurologist expert in the headache field made the diagnosis. All consecutive patients with HC and PH were evaluated and documented in the patient’s performa. After obtaining the ethical clearance from the institutional ethics committee in November 2017, we retrospectively evaluated the patients with hemicrania continua and paroxysmal hemicrania for inclusion in this study. Patients fulfilling the ICHD 3 beta criteria for PH and HC were included in the study [2]. Patients with any presumed secondary causes of PH and HC were excluded. We compared the severity of autonomic features, severity, and duration of pain and other headache characteristics between the two groups. We graded the severity of autonomic features and migrainous characteristics into mild, moderate, and severe (Table 1). We classified autonomic symptoms like forehead sweating, nasal congestion, and ptosis as present or absent. Similarly, we classified migrainous symptoms like irritability, neck pain, nausea, and vertigo/sense of motion as present or absent. We identified patients of HC with preceding history of paroxysmal unilateral headaches. Their clinical details and treatment history regarding the previous paroxysmal headaches were reviewed. Similarly, we identified patients of PH with preceding continuous unilateral headaches and reviewed the clinical details and treatment history of their continuous headaches. Sample size was calculated using a free online calculator (OpenEpi, version 3) (<http://www.openepi.com/SampleSize/SSMean.htm>). By considering mean difference in the effective dose of indomethacin for both kinds of headaches as 14 mg, 80% power, and 95% confidence interval, the sample size for each group was estimated to be 23 [12].

Statistical methods

The categorical variables were compared by using the chi-square test. Wherever needed, the Fisher exact test was used.

Table 1 Severity grading of autonomic and migrainous symptoms

Clinical features	Mild	Moderate	Severe
Autonomic symptoms			
Lacrimation	Not requiring wiping	Requiring intermittent wiping	Necessitating frequent wiping
Redness	In one quadrant	In 2–4 quadrants (but not severe)	Marked congestion/bilateral (with asymmetry)
Nasal discharge	Mild and occasional	Moderate and noticeable	Severe to warrant medications/measures, affecting work
Migrainous symptoms			
Photophobia	Only in bright light	In daylight	In dim light/no light
Phonophobia	Only with loud noise (horns, heavy traffic)	With ambient sound (someone talking)	Bothered by noises in the next room

The continuous variables were compared by independent *t* test. The Kruskal-Wallis test or Mann-Whitney *U* test was used to compare the non-parametric data.

Results

We included 35 patients with HC and 27 patients with PH. All the patients fulfilled the ICHD 3 beta criteria for HC and PH, respectively. The mean age of patients with PH was 34.42 years and those with HC was 37 years. The male:female ratio was 2:3 in the either group. The demographic profile and characteristics of pain in patients with PH and HC are compared in Table 2, and characteristics of autonomic features are compared in Table 3. None of the patients with PH had background continuous interictal pain. Patients with PH and HC were comparable in age, male:female ratio, majority of pain characteristics, number of autonomic symptoms, severity of autonomic symptoms, and median effective dose of indomethacin to relieve headache. However, higher pain severity (visual analogue scale) and higher prevalence of photophobia were found in more patients with paroxysmal hemicrania. Majority of patients with HC and PH had frontal-periorbital location of headache. The additional involvement of temporal and parietal areas was seen in more patients with HC as compared with PH.

Five patients with HC had preceding ipsilateral paroxysmal headache attacks with autonomic symptoms. Their paroxysmal headache lasted for 3 to 6 months (Table 4). One patient transformed from paroxysmal attacks of pain into continuous pain of HC directly without any time gap, whereas four patients had spontaneous resolution of their paroxysmal attacks for 6 to 18 months prior to the new onset of HC. None of these 5 patients were ever prescribed indomethacin for their paroxysmal headaches.

Three patients with PH had history of continuous mild/moderate pain lasting 3 to 6 months (Table 5). One patient transformed directly into PH, whereas 2 patients had resolution of this continuous headache for 18 months and 3 years, respectively, prior to the appearance of the pain of PH. Only one patient had history of intake of indomethacin for 1 week following which his continuous headache disappeared. Location of continuous headache was similar to that of their recent pain of PH.

Discussion

HC and PH appear to be different headaches based only on the duration of headache. However, they share many other clinical features. We could not find any significant difference in most of the headache characteristics and the number/severity of autonomic features between HC and PH. Though, the pain

Table 2 Comparison of demographic profile, characteristics of pain, and mean effective dose of indomethacin in patients with paroxysmal hemicrania and hemicrania continua

Clinical features	Paroxysmal hemicranias (<i>n</i> = 27)	Hemicranias continua (<i>n</i> = 35)	<i>P</i> value
Age (mean ± SD)	34.42 ± 12.56	37.00 ± 11.00	0.39
Age at headache onset	31.62 ± 12.57	33.91 ± 11.48	0.45
M:F ratio	10:17 (≅2:3)	14:21 (≅2:3)	0.81
Duration (median with range) (months)	12 (3–240)	18 (3–216)	0.51
Side (right:left)	10:17 (≅2:3)	18:17 (≅1:1)	0.25
Location			
Frontal-periorbital	17 (62.9%)	23 (65.7%)	0.82
Temporal	9 (33.3%)	24 (68.6%)	0.006
Parietal	1 (3.7%)	12 (34.28%)	0.003
Occipital	1 (3.7%)	2 (5.7%)	0.71
Character			0.17
Throbbing:nonthrobbing	17:10 (62.9%)	16:19 (45.7%)	
Sharp	1 (3.7%)	4 (11.4%)	
Heaviness	7 (25.9%)	19 (54.3%)	
Bursting	9 (33.3%)	11 (31.4%)	
Band like	9 (33.3%)	0	
Median VAS score (range)	8 (5–10)	5 (2–10)	< 0.001
Median number of autonomic symptoms (range)	3 (1–8)	2 (1–5)	0.36
Median indomethacin dose (range)	75 (50–150)	75 (50–225)	0.80

Table 3 Comparison of severity of cranial autonomic features and migrainous features in patients with paroxysmal hemicrania and hemicrania continua

Clinical features	Paroxysmal hemicranias (<i>n</i> = 27)	Hemicranias continua (<i>n</i> = 35)	<i>P</i> value
Ptosis	7 (25.9%)	6 (17.1%)	0.40
Lacrimation			
No	6 (22.2%)	8 (22.9%)	0.95
Mild	5 (18.5%)	13 (37.1%)	0.10
Mod	12 (44.4%)	9 (25.7%)	0.12
Severe	4 (14.8%)	5 (14.3%)	0.95
Eye redness			
No	5 (18.5%)	9 (25.7%)	0.75
Mild	7 (25.9%)	14 (40%)	0.24
Mod	11 (40.7%)	8 (22.9%)	0.13
Severe	4 (14.8%)	4 (11.4%)	0.10
Nasal congestion			
No	13 (48.1%)	21 (60%)	0.35
Mild	6 (22.2%)	8 (22.9%)	0.95
Mod	8 (29.6%)	6 (17.1%)	0.24
Nasal drip			
No	25 (92.6%)	35 (100%)	0.69
Mild	2 (7.4%)	0 (0%)	0.00
Forehead sweating	2 (7.4%)	2 (5.7%)	0.79
Forehead flushing	5 (18.5%)	4 (11.4%)	0.43
Photophobia			
No	7 (25.9%)	20 (57.1%)	0.01
Mild	11 (40.7%)	9 (25.7%)	0.21
Mod	7 (25.9%)	5 (14.3%)	0.25
Severe	2 (7.4%)	1 (2.9%)	0.40
Phonophobia			
No	20 (74.1%)	30 (85.7%)	0.25
Mild	6 (22.2%)	5 (14.3%)	0.41
Mod	1 (3.7%)	0 (0%)	0.25
Nausea/vomit			
No	17 (62.9%)	23 (65.7%)	0.82
Nausea	5 (18.5%)	11 (31.4%)	0.25
Vomiting	5 (18.5%)	1 (2.9%)	0.39
Irritability/agitation	4 (14.8%)	13 (37.1%)	0.05
Sense of motion	5 (18.5%)	8 (22.9%)	0.68
Neck pain	6 (22.2%)	10 (28.6%)	0.57

severity was higher in PH, the difference in the median visual analogue scale score was of only 2 points. Many experts believe that pain in PH is more severe. Their observation is also validated by our study. It is perhaps due to more severe pain that PH was considered closer to cluster headache [13].

In our study, more patients with HC had extension of headache into the parietal and temporal areas in addition to their usual location in the frontal-periorbital region. This could be related to the continuous nature of pain. Similar phenomenon is also seen in chronic (transformed) migraine whereby the chronic, daily, and continuous headache is more holocranial as compared with hemicranial

pains in episodic migraine [14]. The number and severity of autonomic features were comparable between two headaches. The autonomic features in trigeminal autonomic cephalalgias are postulated to be due to hypothalamic activation [10, 15]. Some people believe that the hypothalamic activation is related to the severity of pain attacks as seen in patients with episodic migraine and SUNCT syndrome [16, 17]. Despite higher severity of pain in PH, we did not find any significant difference in the severity of autonomic features in our patients with PH. Both headaches also required similar doses of indomethacin for effective prophylaxes.

Table 4 Clinical details of paroxysmal hemicrania (PH) like pains that preceded the hemicrania continua (HC)

Age (years)/sex	Side/location of HC	Characteristics of PH-like pain	Duration of PH	Time gap between PH and HC	Treatment for PH ^a
48 Y/F	Left temporal	Paroxysmal pain lasting 10 min in left supra-orbital region with nasal congestion and conjunctival injection	4 months	1 year	Spontaneous remission
26 Y/F	Right fronto-temporal	Paroxysmal burning pain lasting 4–5 min in right fronto-temporal region with forehead and facial sweating	4 months	6 months	Spontaneous remission
28 Y/M	Left fronto-temporal	Paroxysmal pain lasting 30 min in left temporal region with conjunctival injection	6 months	6 months	NSAIDs, spontaneous remission
42 Y/F	Right temporal	Paroxysmal pain in right fronto-temporal region lasting 5 min with forehead sweating	3 months	No gap	NSAIDs
32 Y/F	Left temporal	Paroxysmal pain in left temporal region lasting 10 min with agitation	6 months	18 months	Spontaneous remission

^a None of the patients received indomethacin

ICHD 3 beta considers restless/agitation as a variable for diagnosis of HC [2]. We found higher prevalence of agitation/restlessness in HC as compared with PH. However, the difference in the prevalence of agitation/restlessness in PH and HC was not statistically significant. The recent ICHD 3 criteria changed its stance and suggested that restlessness/agitation as one of the diagnostic variables for both HC and PH [1]. This recent change in ICHD 3 is also supported by our study.

We found 5 patients of HC, who suffered from paroxysmal headaches in the past. None of them received indomethacin. However, they had paroxysmal headaches with characteristics similar to that of PH. Similarly, three patients with PH had preceding continuous ipsilateral headaches with autonomic features similar to HC. One of the three patients showed response to indomethacin. Many experts do believe that one type of trigeminal autonomic cephalgia (TAC) may transform into other, but we were able to observe and document this phenomenon in our study. Therefore, we can say that PH and HC are not exclusive headaches, and a subgroup of patients with HC may transform into PH or vice versa.

Our study suffered from the usual limitations of a retrospective study. Despite the fact that we quantified autonomic features and other pain characteristics in order to be more objective in comparing the two groups, we could not define definite end points so as to call two headaches similar or different. However, we believe that our study will convince people to agree that there are more similarities than differences between HC and PH. We also had a small sample size to compare a large number of variables between the two headaches.

Conclusion

Except for the episodic nature and higher pain severity in PH, most other pain characteristics and autonomic features in PH are similar to HC. PH and HC may transform from one to another in a subset of patients. Our study raises an important question that whether HC and PH represent the episodic and chronic variants of same headache type. A prospective long-term study that determines the natural history of HC and PH

Table 5 Clinical details of hemicrania continua (HC) like pains that preceded paroxysmal hemicrania (PH)

Age/sex	Side/location of PH	Characteristics of HC-like pain	Duration	Time gap between HC and PH	Treatment for HC
47 Y/F	Left supra-orbital and temporal region	Continuous moderate pain in left supra-orbital and temporal region with occasional forehead sweating and agitation	3 months	18 months	Indomethacin 75 mg twice a day for 1-week produced remission
20 Y/F	Right fronto-temporal region	Continuous mild to moderate pain in right fronto-temporal region with occasional nasal congestion	3 months	3 years	Spontaneous remission
46 Y/F	Left orbital region lasting	Continuous mild pain in left orbital and supra-orbital region, intermittent worsening of pain with agitation and forehead sweating	6 months	No gap	NSAIDs

and also compares the clinical characteristics, therapeutic response to indomethacin and functional imaging between HC and PH may give some answers.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interests.

Ethical standards The study was conducted after obtaining the ethical clearance from our Institute's Ethics Committee.

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