Study of cluster headache: A hospital-based study

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ABSTRACT

Introduction: Cluster headache (CH) is uncommon and most painful of all primary headaches, and continues to be managed suboptimally because of wrong diagnosis. It needs to be diagnosed correctly and specifically treated. There are few studies and none from this region on CH. **Materials and Methods:** To study the detailed clinical profile of CH patients and to compare them among both the genders. Study was conducted at Mahatma Gandhi hospital, Jodhpur (from January 2011 to December 2013). Study comprises 30 CH patients diagnosed according to International Headache Society guidelines (ICHD-II). Routine investigations and MRI brain was done in all patients. All measurements were reported as mean $\pm$ SD. Categorical variables were compared using the Chi-square test, and continuous variables were compared using Student's *t*-test. SPSS for Windows, Version 16.0, was used for statistical analyses with the significance level set at $P = 0.05$. **Results:** M: F ratio was 9:1. Age at presentation was from 22-60 years (mean - 38 years). Latency before diagnosis was 3 months-12 years (mean - 3.5 years). All suffered from episodic CH and aura was found in none. Pain was strictly unilateral (right-19, left-11), predominantly over temporal region-18 (60%). Pain intensity was severe in 27 (90%) and moderate in 3 (10%). Pain quality was throbbing in 12 (40%). Peak intensity was reached in 5 minutes-30 minutes and attack duration varied from 30 minutes to 3 hours (mean - 2.45 hours). Among autonomic features, conjunctival injection-23 (76.6%) and lacrimation-25 (83.3%) were most common. Restlessness during episode was found in 80%. CH duration varied from 10 days to 12 weeks. Circadian periodicity for attacks was noted in 24 (80%). **Conclusion:** Results are consistent with other studies on many accounts, but is different from Western studies with respect to low frequency of family history, chronic CH, restlessness and aura preceding the attack. Detailed elicitation of history is paramount as misdiagnosis is common.

Key words: Autonomic, cluster headache, trigeminal

Introduction

Cluster headache (CH) is an excruciating primary headache syndrome, which is strictly unilateral pain usually involving the orbital or periorbital region innervated by the first (ophthalmic) division of the trigeminal nerve and is accompanied by ipsilateral autonomic features, including lacrimation, conjunctival injection, nasal congestion and/or rhinorrhea, ptosis and/or miosis, and periorbital edema. CH show male predominance, and striking circannual and circadian periodicity.^[1,2] The prevalence of CH is estimated to be 0.1-0.4%. Most of the literature about CH is derived from Western studies.^[3,4] This study is done to know the

detailed clinical characteristics of CH patients in this part of the India.

Materials and Methods

It is a hospital-based prospective study conducted at department of Neurology, M G hospital, Dr S N Medical college, Jodhpur, Rajasthan, between January 2011 and December 2013. The study population consisted of Patients diagnosed with CH, as defined by the second edition of the International Classification of Headache Disorders (ICHD-II),^[5] attending neurology unit.

All patients underwent detailed clinical evaluation by two consultants. Data was recorded with respect to disease course, location, laterality, quality, intensity and radiation of pain, frequency, duration, periodicity of attacks, duration of clusters. Possible trigger factors, autonomic features, additional features (e.g. nausea, vomiting, photophobia, phonophobia, behaviors during attacks), family history of headache, history of smoking and drinking were all noted. Patients were classified as

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episodic or chronic CH types. Brain imaging (MRI), with routine hematological and biochemical investigations were done in all patients. MRI brain was done to rule out underlying intracranial or neck structural lesions such as neoplasms, vascular malformations, and cervicocephalic arterial aneurysms/dissections which can present as cluster-like headaches.

Treatment was individualized. Subcutaneous and intranasal sumatriptan was not routinely prescribed in view of its cost, except for few urban literate patients. Corticosteroids and ergotamine were used as emergency measures. For those with longer bouts, verapamil was given for appropriate period of time.

Results

Study population

A total of 33 consecutive CH patients were evaluated during the study period. Three patients were excluded as one of the patients also had the features of trigeminal neuralgia, other had features of paroxysmal hemicrania, and in third case it was his first presentation which didn't fulfill the criteria of ICHD-II. Out of remaining 30 patients, 27 (90%) were males and 3 (10%) were females, giving a male-to-female (M: F) ratio of 9:1. All our patients had episodic CH (100%). Mean age at presentation was 38.8 ± 13.5 years (range 22-68 years) (males, 39.5 ± 13.93 years vs. females, 32.3 ± 8.02 years). The mean age at onset was 35.14 ± 14 years (range 20-67 years) (males 35.8 ± 14.6 years vs. females 31.3 ± 8.08 years, $P = 0.607$) [Table 1]. Two patients (6.6%, 2 M) also had tension-type headache and one had migraine headache (1 F). Time lag before diagnosis was 3 months to 12 years (3.5 years) [Table 2]. All our patients had consulted other medical clinics and had been referred from other doctors, and none of them had previously been diagnosed with CH.

Sites and laterality of headache

Pain was strictly unilateral right-19 (63.3%), left-11 (36.6%) and was predominantly over temporal region-18 (60%) followed by orbital-16 (53.3%), forehead-2 (6.6%), and parietal-2 (6.6%). Pain intensity was severe in 27 (90%) and moderate in 3 (10%). Pain quality was throbbing in 12 (40%), followed by stabbing-10 (33.3%), burning-6 (20%), and boring in 2 (6.6%). Peak intensity of pain was reached within 5 to 30 minutes (mean = 18.8 minutes) [Table 3].

Cranial autonomic and additional features in patients with CH

None of our patients experienced any kind of aura prior to attacks. Among autonomic features,

lacrimation-25 (83.3%) was most common followed by conjunctival injection-23 (76.6%), rhinorrhea-11 (36.6%), nasal congestion-7 (23.3%), and less commonly, facial sweating-2 (6.6%), Ptosis-5 (16.7%). Other associated features during the attacks were nausea/vomiting-9 (30%), photophobia-10 (33.3%), phonophobia-12 (40%) and restlessness (80%). There was no statistically significant difference in any of the clinical characteristics between male and female patients [Table 4].

Periodicity of Cluster headache

Regarding frequency of cluster periods we observed that majority had <1 cluster period/year-20 (66.6%), followed

Table 1: Demographic profile

Patient characteristics	Total (n=30)	Males (n=27)	Females (n=03)	P value
Type of cluster headache				
Episodic	30	27	03	1.00
Chronic	0	0	0	0
Age at presentation in years (mean±SD)	38.8±13.5	39.5±13.93	32.3±8.02	0.393
Age at onset in years (mean±SD)	35.4±14.0	35.8±14.6	31.3±8.08	0.607
Family history	0	0	0	0

SD - Standard deviation

Table 2: Latency before diagnosis

	Total (N=30)	Male (N=27)	Female (N=03)
Time before diagnosis			
Less than 1 year	6 (20)	4 (14.8)	2 (66.6)
From 1 to 5 years	17 (56.6)	16 (59.2)	1 (33.3)
From 6 to 10 years	5 (16.6)	4 (14.8)	0
More than 10 years	2 (6.6)	2 (7.4)	0

Results are reported as number of patients (percent)

Table 3: Characteristics of pain

	Total (n=30)	Males (n=27)	Females (n=03)	P value
Sites of pain				
Temporal	18 (60)	15 (55.5)	3 (100)	0.497
Orbital	16 (53.3)	14 (51.8)	2 (66.6)	1
Parietal	2 (6.6)	2 (7.4)	0	1
forehead	2 (6.6)	2 (7.4)	0	1
Laterality of pain				
Right side	19 (63.3)	17 (62.96)	2 (66.6)	1
Left side	11 (36.6)	10 (37.03)	1 (33.3)	
Quality of pain				
Stabbing	10 (33.3)	9 (33.3)	1 (33.3)	1
Throbbing	12 (40)	11 (40.7)	1 (33.3)	1
Burning	6 (20)	6 (22.2)	0	1
Boring	2 (6.6)	1 (3.7)	1 (33.3)	0.1871
Pain intensity				
Mild	0	0	0	
Moderate	3 (10)	3 (11.1)	0	1
Severe	27 (90)	24 (88.8)	3 (100)	1

Results are reported as number of patients (percent)

by irregular clusters-7 (23.3%), 1-2 cluster periods/year-2 (6.6%) and 3.3% had >2 cluster periods per year. The duration of cluster periods were 2 weeks to less than 1 month in 12 (40%), 1-2 months in 11 (36.6%) of patients, less than 2 weeks in 4 (13.3%) and more than 2 months in 10%. Attacks occurred 1-2 times per day in 19 (63.3%) of patients, >2 times/day in 10 (33.3%) and <1 time per day in 3.3%. We observed that each attack ranged in duration from 1 h to less than 2 h in 12 (40%) and from 2 to 3 h in 16 (53.2%) of patients. Other 6.6% patients comment on the attack duration as less than 1 h [Table 4]. Circadian periodicity for attacks was noted in 25 (83.3%) with (2 PM-5 PM, 12 AM-4 AM) as most common.

Table 4: Associated autonomic features

	Total (n=30)	Males (n=27)	Females (n=03)	P value
Autonomic features				
Lacrimation	25 (83.3)	22 (81.4)	3 (100)	1
Conjunctival injection	23 (76.6)	20 (74.07)	3 (100)	1
Rhinorrhea	11 (36.6)	10 (37.03)	1 (33.3)	1
Nasal congestion	7 (23.3)	6 (22.2)	1 (33.3)	1
Ptosis/miosis	5 (16.6)	5 (18.51)	0	1
Facial sweating	2 (6.6)	2 (7.40)	0	1
Blepharedema	0	0	0	
Additional features				
Nausea	9 (30)	9 (33.3)	0	1
Vomiting	9 (30)	9 (33.3)	0	1
Photophobia	10 (33.3)	9 (33.3)	1 (33.3)	0.49
Phonophobia	12 (40)	10 (37.03)	2 (66.6)	0.13
Restlessness	24 (80)	22 (81.4)	2 (66.6)	
Aura	0			

Results are reported as number of patients (percent)

Table 5: Characteristics of cluster episodes

	Total (n=30)	Males (n=27)	Females (n=03)
Frequency of clusters			
More than 2 times/year	1 (3.3)	1 (3.7)	0
1-2 times/year	2 (6.6)	2 (7.4)	0
Less than 1 time/year	20 (66.6)	17 (62.9)	3 (100)
Irregular	7 (23.3)	7 (25.9)	
Duration of clusters			
Less than 2 weeks	4 (13.3)	3 (11.1)	1 (33.3)
2 weeks-1 month	12 (40)	10 (37.03)	2 (66.6)
From 1 to 2 months	11 (36.6)	11 (40.74)	0
More than 2 months	3 (10)	3 (11.1)	0
Frequency of attacks			
More than 2 times/day	10 (33.3)	8 (29.6)	2 (66.6)
1-2 times/day	19 (63.3)	18 (66.6)	1 (33.3)
Less than 1/day	1 (3.3)	1 (3.7)	0
Duration of attacks			
Less than 1 hour	2 (6.6)	2 (7.4)	0
From 1-2 hour	12 (40)	11 (40.74)	1 (33.3)
From 2-3 hour	16 (53.3)	14 (51.8)	2 (66.6)
More than 3 hour	0		

Results are reported as number of patients (percent)

In 19 (63.3%) patients attacks were seen both during nocturnal and day time, only during day in 9 (30%) and only nocturnal in 2 (6.6%) [Table 5].

Other features

Seasonal predilection was seen in 46% of patients, summer (30%), winter (16%). Sixteen (53.4%) patients were smokers, 8 (27%) were tobacco chewers and 3 (10%) were alcoholics [Table 6].

Discussion

Though patients of headache form the main bulk of outpatient clinics in hospitals, the time it receives by the clinicians is often less leading to misdiagnosis and prolonged suffering to the patient. Keen observation and extra dedication may prevent trigeminal autonomic cephalalgias being dismissed as tension type or migrainous headache. There are very few studies on CH in India. Over a period of 3 years we came across 30 patients of CH in a busy outpatient clinic of a medical college hospital. There are many similarities and few dissimilarities in clinical characteristics of our patients with that of other Asian and western studies.

In our study CH was mainly seen in males than in females with a ratio of 9:1. This was almost similar to that seen from other Asian studies (Dong Z *et al.*,^[6] 7:1, Lin KH *et al.*,^[7] 6.4:1) and much higher than western studies.^[8] Decreasing trend for M/F ratio is observed in western studies possibly because of life style changes adopted by females. Majority (46.6%) of our patients had their onset of CH in the third decade of life, which was also found in other studies.^[6-8] Although positive family history has been reported in 1.9% to 6.7% of patients with CH by Bharar *et al.*,^[8] we didn't find that in any of our patients. But the time lag prior to correct diagnosis was between 3 months and 12 years (mean = 3.5 years), which highlights the fact about the lack of awareness of this condition and the need to educate clinicians to prevent the suffering of the patients.

Though aura preceding the CH had been described in western studies,^[8-10] none of our patients experienced this phenomenon which was similar to Chinese study.^[6] This difference may be due to genetic and racial factors.

Most of the literature on CH mentions orbital/retroorbital region as the predominant site of pain which was found only in 53.3% of our patients. In our study temporal region (60%) was the predominant site of pain which was also found in Japanese^[11] and Chinese^[6] patients. Western studies^[8,9,12] also describe jaw, teeth and maxilla as other sites of pain which was seldom seen in our patients.

Table 6: Other associated features

	Total (n=30)	Males (n=27)	Females (n=03)
Periodicity of CH			
Nocturnal and day	19 (63.3)	16 (59.25)	3 (100)
Day only	9 (30)	9 (33.3)	0
Nocturnal only	2 (6.6)	2 (7.4)	0
Seasonal specificity			
Only summer	9 (30)	9 (33.3)	0
Only winter	5 (16.6)	5 (18.5)	0
Irregular	16 (53.3)	13 (48)	3 (100)
Association with habits			
With smoking	16 (53.3)	16 (59.2%)	0
With tobacco	8 (27%)	8 (26%)	0
With alcohol	3 (10%)	3 (11%)	0
No habits	6 (33.3)	3 (11%)	3 (100)

Results are reported as number of patients (percent)

It's a well-known fact that CH is one of the worst forms of headache, and was agreed upon by 90% of our patients. As majority of patients were rural folks we found it difficult to use VAS (visual analog scale) for defining pain. But quality of pain was described as throbbing (40%) and stabbing (33.3%) in our patients in contrast to earlier Indian studies by Chakravarty^[13] and Ravishankar,^[14] where burning and boring quality was predominant. As intensity and quality of pain is a subjective phenomenon, these differences could be due to the cultural and educational background of the patients. The associated autonomic symptoms which is the defining feature of these headaches was found in our patients as similar to that of other Indian^[13] and Asian studies.^[6,7]

Feeling of restlessness and manifesting as restless behavior, as two separate entities was described by Imai *et al.*^[11] in their Japanese patients. True to his description we found that though 80% patients had feeling of restlessness, felt as sense of agitation and anxiety, only 46% showed restless behavior in the form of pacing around. Cultural differences, where in patience is emphasized by eastern culture was explained as one of the reasons for patients remaining still despite feelings of restlessness.

The clock-like rhythmicity and periodicity which is the characteristic feature of CH had been attributed to biological clock in suprachiasmatic nucleus of hypothalamus, the evidence for which comes from functional and morphometric imaging using PET scans by May *et al.*^[15] Though many studies describe attacks to be common during nocturnal hours, we found that 63.5% of our patients had attacks both during day and nocturnal hours which is similar to other Indian^[13] and

Chinese study.^[6] In 80% of patients attacks commonly occurred from 2 PM to 5 PM and from 12 AM to 4 AM.

Seasonal Predilection- CH is considered a circadian-based syndrome, and its seasonal occurrence was first noted by Ekbom^[16] and Kudrow.^[17] This pattern was seen in around 46% of our patients, where recurrence was only in summers in 30%, and only during winters in the remaining.

Lifestyle factors and Cluster Headache- It has received much attention from western studies (Rozen,^[9] Manzoni^[18]) who have observed association of CH and smoking in around 70% of their patients, alcohol and coffee abuse in lesser number of patients. Smoking was seen in 53.3% of our patients, smoking and tobacco combined was observed in 10%. Majority of our patients continued to smoke and consume alcohol even during clusters.

Limitations of our study are the small sample size and the data of which cannot be extrapolated to general population. Recall bias while recording history of previous episodes of clusters. We didn't study the impact of CH on patient's occupation and quality of life. Further studies with large number of patients, ideally from headache clinics could give better insight about this disease.

Our study is an attempt to describe detailed clinical characteristics of CH in Indian patients. Results of our study are consistent with those of other Western and Asian studies regarding various demographic and clinical profile, but is different from Western studies with respect to low frequency of family history, chronic CH, restless behavior and aura preceding the attack. These differences could be explained by different genetic, racial, cultural and lifestyle factors between Indian and Western patients. CH still remains misdiagnosed for years. Increasing the knowledge of CH among referring clinicians could improve the recognition and treatment of cluster headache.

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