A Retrospective Comparative Study in Patients with SUNA and SUNCT

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Abstract

Introduction: Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) and short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA) are rare primary headache disorders. **Aim:** The aim of the study is to describe and compare the clinical characteristics of patients with SUNA and SUNCT. **Methods:** Patients with SUNCT or SUNA observed in a neurology clinic of a tertiary hospital in India between January 2017 and December 2022 were evaluated. **Results:** Thirteen patients with SUNA (seven female, 54%) and 16 patients with SUNCT (nine female, 56%) were identified for the evaluation. The mean ages at the onset of SUNA and SUNCT were 36.8.5 \pm 8.1 years and 37.2 \pm 8.4 years, respectively. The age of onset in our patients was somewhat younger than that of other large series. The demographic and clinical features of SUNA patients were comparable to those of SUNCT patients. Orbital/ retro-orbital area was the most common site of pain in both types of headaches. The pattern of pain was noted as single stab (in all patients), repetitive stabs (SUNA vs. SUNCT: 77% vs. 75%), and sawtooth patterns (SUNA vs. SUNCT patients (as a part of the diagnostic criteria). The prevalence of conjunctival injection and tearing in SUNA was 46% and 31%, respectively. All patients reported spontaneous attacks. Triggers were reported in seven (54%) patients with SUNA and nine (56%) with SUNCT. Only one patient in each group had a refractory period following a trigger-induced episode. Two patients in the SUNCT group had compression of the triggenial nerve by a vascular loop. **Conclusion:** This is the largest case series from India. There were no significant differences between patients with SUNA and SUNCT.

Keywords: SUNA, SUNCT, TACs

INTRODUCTION

Short-lasting unilateral neuralgiform headache attacks (SUNHA) is a type of trigeminal autonomic cephalalgias (TACs). The third edition of the International Classification of Headache Diseases (ICHD-3) classify SUNHA into two groups: (i) short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) and (ii) short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA).^[1] SUNCT and SUNA are characterized by abrupt, brief attacks of severe unilateral orbital, periorbital, or temporal pain accompanied by ipsilateral cranial autonomic features. Pain can spread to the V2/V3 division of the trigeminal nerves and, in rare cases, to extra-trigeminal nerves as well.^[2]

The second edition of the ICHD-2 classified SUNCT as a form of TAC. The appendix section of ICHD-2 recognized SUNA and speculated that SUNCT might be a subtype of SUNA.^[2] However, SUNCT and SUNA were classified as independent disease entities in ICHD-3 and were grouped together under the umbrella term SUNHA.^[3] However, a number of recent studies suggest that both headache disorders share the same phenotype and lack significant clinical differences. It is now recommended that both disorders be classified under a single diagnostic category.^[4-6]

There are limited studies on SUCNT-SUNA in the literature. In this retrospective study, we present 13 cases with SUNA and 16 patients with SUNCT who met the ICHD-3 criteria. We also compare the characteristics of SUNA and SUNCT.

METHODS

We conducted a retrospective chart review of all patients with a putative diagnosis of SUNCT and SUNA who were seen in the neurology department of our institute between January 2017 and December 2022. The inclusion criteria were (i) a diagnosis of SUNCT or SUNA, (ii) age >18 years, and (iii) a minimum follow-up of 6 weeks. The exclusion criteria were (i) age <18 years, (ii) a possible secondary SUNCT or SUNA, (iii) patients who were never subjected for neuroimaging, and (iv) patients who refused to give consent. Our group has been

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working on strictly unilateral headaches for a number of years. So, as a departmental policy, all patients who have side-locked headaches are routinely subjected to a thorough clinical history and physical examination. So, all of the data presented here were gathered prospectively. The study protocol was approved by the institutional ethics committee. All patients provided a written informed consent for publication. The study was carried out in line with the Helsinki Declaration.

Data are presented as arithmetic means with a standard deviation or as percentages. The continuous data were compared using the Student's *t*-test. For categorical data, the Chi-square test with Yates' correction or Fisher's exact test was applied. All P values were two-tailed, and a P value of <.05 was considered statistically significant.

RESULTS

A total of 37 patients with a diagnosis of SUNCT or SUNA were observed during the study period. Eight patients were excluded for the following reasons: (i) a possibility of secondary headaches: one patient; (ii) neuroimaging was not done: two patients; (iii) incomplete data: one patient; (iv) follow-up less than 6 weeks: two patients; and (v) patients did not give consent: two patients. Finally, 29 patients were identified: 13 with a diagnosis of SUNA and 16 with SUNCT.

Table 1 summarizes the demographics of both groups of patients. The mean age of the patients was 41.5 years in SUNA and 40.6 years in SUNCT at the time of presentation. The mean duration of illness was 59.6 months in SUNA and 43.7 months in SUNCT. In both groups, there were more women than men (54% of SUNA and 56% of SUNCT). There were no discernible differences between the SUNA and SUNCT groups in terms of demographic variables. Only two patients in the SUNA group (13%) and three patients in the SUNCT group (19%) received the correct diagnosis before visiting our institute. Eleven patients (85%) in SUNA and 14 patients (81%) in the SUNCT group had received a diagnosis of trigeminal neuralgia (TN) by the previous physicians. In the diagnostic

| Table 1: Demographic profiles of patients with SUNA and SUNCT | | | | |
|---|----------------------|----------------------|-------|--|
| Parameter | SUNA (13) (n, %) | SUNCT (16) (n, %) | Р | |
| Age (years) (mean, range) | 41.5±4.6, 32-56 | 40.6±10.3, 29-67 | 0.772 | |
| Sex (F) | (7) (54%) | (9) (56%) | 0.897 | |
| Age at onset | 36.8.5±8.1, 26-54 | 37.2±8.4, 27-61 | | |
| Duration of illness | | | | |
| Mean, (months) | 59.6±40.1 | 43.7±38.1 | 0.284 | |
| Range | 6 months to 12 years | 4 months to 10 years | | |
| Residence | | | | |
| Rural | 7 (54%) | 8 (50%) | 0.836 | |
| Urban | 6 (46%) | 8 (50%) | | |
| Smoking habits | 2 (13%) | 3 (19%) | 0.811 | |
| Alcohol intake | 2 (13%) | 3 (19%) | 0.811 | |

work, two patients in the SUNCT group had a compression of the trigeminal nerve by a vascular loop.

Table 2 provides the details of the pain. Except for one patient in the SUNCT group, all patients exhibited side-locked unilateral pain. One patient in the SUNCT group reported side-shifting pain. Seven (54%) patients in the SUNA group and nine (56%) patients in the SUNCT group had side-locked pain on the left side. Eleven patients (85%) in SUNA and 14 (88%) in SUNCT had an unremitting course or chronic form of the disease. The remaining patients had episodic patterns of headache (15% in SUNA and 12% in SUNCT). Orbital/retro-orbital was the most common site of pain in both types of headaches. Other common sites for pain perception were the frontal, temporal, and parietal areas. The majority of patients (85%-87%) described their pain as extremely severe or severe. Pain severity on a visual analog scale (VAS) ranged from 6 to 10 (mean 8.3) and it hampered routine activities in all patients during attacks. The qualities of pain were mainly stabbing (SUNA: 69%; SUNCT: 75%), electric current-like (SUNA: 62%; SUNCT: 56%), and shooting (SUNA: 31%; SUNCT: 31%).

The pattern of pain was noted as single stab, repetitive stabs, and sawtooth patterns. The majority of the time, all of the patients felt a single stab. In both groups, about three-fourths of the patients also had repeated stabs. A few proportions of patients also had sawtooth-pattern pains (SUNA: 23% and SUNCT: 25%). Interictal mild pain was noted in one patient (8%) in SUNA and two patients (13%) in SUNCT. Restlessness or agitation was reported in seven (54%) patients with SUNA and nine patients (56%) with SUNCT. These patients could not lie comfortably on the bed and had to sit on the edge of the bed or in a chair.

The duration of attacks ranged from a few seconds to 600 seconds (10 minutes) (in accordance with the ICHD-3 criteria for SUNA and SUNCT). The majority of attacks, however, lasted less than 2 minutes. All patients reported at least one attack per day. About 62% of SUNA patients and 75% of SUNCT patients reported having at least 10 attacks each day on the majority of occasions. Nocturnal attacks were noted only in one patient in SUNA and in two patients in the SUNCT group.

Table 3 provides the prevalence of various cranial autonomic symptoms. Because conjunctival injection and tearing are part of the SUNCT criteria, all SUNCT patients had both features, which were statistically significant when compared to those of SUNA (P value for conjunctival injection: SUNCT vs. SUNA: 0.003, and P for tearing: SUNCT vs. SUNA: <.001). The prevalence of conjunctival injection and tearing in SUNA was 46% and 31%, respectively. In SUNA, however, both conjunctival injection and tearing were not observed in the same patient.

All patients reported spontaneous attacks. Triggers were reported in seven (54%) patients with SUNA and nine (56%) with SUNCT. Spontaneous attacks occurred without warning.

| Parameter | SUNA (n=13) n (%) | SUNCT (n=16) (n, %) | Р |
|----------------------------|----------------------|------------------------|-------|
| Laterality of pain | | | |
| Right | 6 (46%) | 7 (38%) | 0.897 |
| Left | 7 (54%) | 9 (56%) | 0.897 |
| Side-shifting | 0 (0) | 1 (6%) | 0.373 |
| Pattern or course | | | |
| Continuous | 11 (85%) | 14 (88%) | 0.822 |
| Episodic | 2 (15%) | 2 (12%) | 0.822 |
| Sites of headache, n (%) | | | |
| Orbital or retro-orbital | 10 (77%) | 13 (81%) | 0.774 |
| Frontal | 9 (70%) | 9 (56%) | 0.740 |
| Temporal | 6 (46%) | 7 (44%) | 0.897 |
| Parietal | 4 (31%) | 6 (38%) | 0.704 |
| Occipital | 3 (23%) | 3 (19%) | 0.774 |
| Infra-orbital/maxillary | 3 (23%) | 4 (25%) | 0.658 |
| Teeth | 2 (15%) | 2 (13%) | 0.822 |
| Neck | 1 (8%) | 1 (6%) | 0.878 |
| Type of pain | | | |
| Stabbing | 9 (69%) | 12 (75%) | 0.729 |
| Electric current like | 8 (62%) | 9 (56%) | 0.773 |
| Shooting | 4 (31%) | 5 (31%) | 0.680 |
| Pain intensity (VAS) | 8.3±1.0 | $8.3{\pm}0.8$ | |
| (mean±SD) | | | |
| 5-6 | 2 (15%) | 2 (13%) | 0.822 |
| 7-8 | 7 (54%) | 9 (56%) | 0.897 |
| 9-10 | 4 (31%) | 5 (31%) | 0.977 |
| Pattern of pain | | | |
| Single stab | 13 (100%) | 14 (88%) | 0.559 |
| Repetitive stabs | 10 (77%) | 12 (75%) | 0.904 |
| Sawtooth patterns | 3 (23%) | 4 (25%) | 0.668 |
| Interictal pain | 1 (8%) | 2 (13%) | 0.672 |
| Duration of attacks | | | |
| 1-10 seconds | 10 (77%) | 16 (100%) | 0.156 |
| 10 sec to 2 minutes | 8 (62%) | 12 (75%) | 0.707 |
| 2-10 minutes | 4 (31%) | 5 (31%) | 0.977 |
| >10 minutes | 1 (8%) | 0 (0%) | 0.915 |
| Frequency of attacks | | | |
| At least one attack/day | 13 (100%) | 16 (100%) | 1.000 |
| 1-10 attacks/day | 4 (31%) | 5 (31%) | 0.977 |
| >10 attacks/day | 8 (62%) | 12 (75%) | 0.707 |
| >100 attack/day | 3 (23%) | 4 (25%) | 0.668 |
| Nocturnal attacks | 1 (8%) | 2 (13%) | 0.672 |
| Refractory period | 1 (8%) | 1 (6%) | 0.878 |
| Restlessness - agitation | 7 (54%) | 9 (56%) | 0.897 |

 Table 2: Characteristics of pain in patients with SUNA and SUNCT

Eating or chewing was the most common trigger in both groups. Other common triggers were touch, cold wind, brushing teeth, shaving, and washing the face [Table 4]. There were several other triggers, but because they were not consistently documented, we decided not to include them in the analysis. The data for the refractory period after a trigger-induced attack were also not available for each patient. Only one patient in each group had a refractory period following a trigger-induced episode among the patients whose data were available. Table 5 provides an overview of the oral medications that patients received in the past before visiting to us. Carbamazepine was the most commonly prescribed drug by the previous physicians. All patients with SUNA and 94% of patients with SUNCT received either carbamazepine or oxcarbazepine. However, only one patient got a partial response. Other commonly prescribed drugs were lamotrigine, gabapentin, pregabalin, topiramate, amitriptyline, and duloxetine. Lamotrigine was administered to six patients in each cohort. Two patients in each group showed a response to lamotrigine. Six patients in the SUNCT group and five patients in the SUNA group received gabapentin. Two patients in each group showed a response to gabapentin. A response was defined as a 50% reduction in headache frequency, intensity, or duration. Only two patients in the SUNA group-one on lamotrigine and the other taking gabapentin-claimed a significant response (>90% response) to the previously used medications. Similarly, two patients in the SUNCT groupone on lamotrigine and the other taking gabapentin-claimed significant responses. The dosing schedule was not uniform for any drugs, and it was difficult to quantify the drug's response. So, it was difficult to draw any conclusions. Depending on the medications they had previously taken and the degree of response they had to those medications, we prospectively started lamotrigine, gabapentin, pregabalin, or topiramate. If the response was unsatisfactory, medications were changed or other medications were added to the previous ones. In follow-up (at least for 6 weeks), the response was satisfactory in seven patients with SUNA (four patients to lamotrigine, two patients to gabapentin, and one patient to topiramate) and eight patients with SUNCT (three patients to a combination of lamotrigine and gabapentin, two patients to gabapentin alone, two patients to lamotrigine alone, and one patient to topiramate) (not shown in the table). A 50% response to the drug was deemed satisfactory or effective here. Other patients were not satisfied with the preventive medications. None of our patients were subjected to surgery.

DISCUSSION

The first case of SUNCT was described by Sjaastad *et al.* in 1978.^[7] Initially, it was thought to be a rare headache disorder, with just 222 cases of SUNCT and SUNA recorded in the literature until 2013.^[8] However, several large case series have been published from different parts of the world in the recent past.^[4-6,9] This case series is likely the first large case series from India.

Several aspects of SUNCT and SUNA are still not known. Several changes have been made in the ICHD criteria over the years.^[4,6] Currently, SUNCT and SUNA are described as two separate diseases. However, a few large studies recently evaluated the clinical phenotypes of SUNCT and SUNA and concluded that they are the same clinical entity.^[4-6] Lambru *et al.* compared 63 patients with SUNA and 70 patients with SUNCT, and no major clinical differences were observed between SUNA and SUNCT.^[4] They suggested unified

| Parameter | SUNA (n=13) n (%) | SUNCT (<i>n</i> =16) <i>n</i> (%) | 6) <i>P</i> | |
|------------------------|----------------------|---------------------------------------|-------------|--|
| Conjunctival injection | 6 (46%) | 16 (100%) | 0.003 | |
| Tearing | 4 (31%) | 16 (100%) | < 0.001 | |
| Nasal stuffiness | 8 (62%) | 9 (56%) | 0.773 | |
| Rhinorrhea | 6 (46%) | 9 (56%) | 0.867 | |
| Facial flushing | 4 (31%) | 6 (38%) | 0.704 | |
| Facial sweating | 4 (31%) | 4 (25%) | 0.729 | |
| Aural Fullness | 2 (15%) | 2 (13%) | 0.822 | |
| Eye lid odema | 2 (15%) | 2 (13%) | 0.822 | |
| Ptosis | 2 (15%) | 2 (13%) | 0.822 | |
| Miosis | 1 (8%) | 0 (0%) | 0.915 | |

| Table 4. Attack | trianors in | n nationte | with SUNCT | AMU2 hnc |
|-----------------|-------------|------------|------------|----------|

| Table 4. Allack inggers in patients with solver and solva | | | | |
|---|--------------------------------------|-----------------------|-------|--|
| Parameter | SUNA (<i>n</i> =13) <i>n</i> (%) | SUNCT (n=16) n (%) | Р | |
| Spontaneous attacks | 13 (100%) | 16 (100%) | 1.000 | |
| Eating - chewing | 7 (54%) | 9 (56%) | 0.897 | |
| Light touch | 7 (54%) | 8 (50%) | 0.836 | |
| Cold wind | 6 (46%) | 7 (44%) | 0.897 | |
| Brushing teeth | 4 (31%) | 5 (31%) | 0.977 | |
| Washing face | 2 (15%) | 3 (19%) | 0.811 | |
| Shaving | 1 (8%) | 1 (6%) | 0.878 | |
| Talking | 1 (8%) | 1 (6%) | 0.878 | |
| No triggers | 6 (46%) | 7 (44%) | 0.897 | |

Table 5: Medications used by patients with SUNA andSUNCT before visiting us

| Drugs | SUNA | | SUNCT | |
|---------------|-----------------|-----------|-----------------|-----------|
| | No. of patients | Effective | No. of patients | Effective |
| Carbamazepine | 13 | 0 | 15 | 1 |
| Lamotrigine | 6 | 2 | 6 | 2 |
| Gabapentin | 5 | 2 | 6 | 2 |
| Pregabalin | 4 | 1 | 4 | 1 |
| Topiramate | 4 | 0 | 6 | 1 |
| Amitriptyline | 4 | 0 | 5 | 0 |
| Duloxetine | 4 | 0 | 4 | 1 |

diagnostic criteria for both diseases. Zhang *et al.* noted 31 patients with SUNA and 45 patients with SUNCT.^[5] They also noted marked similarities between the two and suggested that they represent the same clinical entity.

SUNHA often manifests between the ages of 35 and 65 years.^[2] Although no age group is exempt, it can start at any stage of life. The age range at the time of onset varies from 2 to 88 years.^[2] The mean age at onset in our cohort was 36.8 years for SUNA and 37.2 years for SUNCT. The age of onset in our patients was somewhat younger than that of other large series. The mean age at onset in Lambru *et al.*^[4] study was 45.0 years for SUNA and 42.1 years for SUNCT. The mean age at onset for SUNA and SUNCT in the case series by Zhang *et al.*^[5] was

48.6 and 41.6 years, respectively. In a review that included all patients described in the literature up to 2013, the pooled mean age at onset was 48.3 years in SUNCT patients and 42.2 years in SUNA patients.^[8]

An earlier literature review suggested that SUNHA is a disorder that primarily affects men, with SUNCT occurring more frequently in men and SUNA occurring more frequently in women.^[8] However, a few recent large case series demonstrated a female preponderance for both SUNA and SUNCT.^[4,5] Our cohort also noted a female preponderance for both disorders. Trigeminal autonomic cephalalgias, including SUNCT and SUNA, primarily involve the V1 division of the trigeminal nerve but may also spread to affect the V2 and V3 divisions.[10] Orbital, frontal, and temporal regions were three common sites in our cohort, indicating the involvement of the V1 division. In Cohen et al.[11] series, the pain was located in the orbital, supraorbital, or temporal regions in 88% of the patients with SUNCT and 78% of patients with SUNA. About one-fourth of the patients had pain in the infra-orbital areas, indicating involvement of the V2 and V3 divisions of the trigeminal nerve. Although the ICHD criteria for any TACs do not include the involvement of nerves other than the trigeminal nerves, a literature review suggests that extra-trigeminal nerve involvement is not uncommon in all TACs, including SUNA and SUNCT. Extra-trigeminal pain typically involves the C2 and C3 dermatomes. The pain may be felt in the occiput and neck areas.^[4] Pain in the occipital area was noted in about 19%-23% of the patients in our series. One patient in each group experienced neck pain as well. Approximately 20% of the cases reported by Lambru et al.[4] experienced pain in the occiput region. Similar findings were made by Cohen et al.[11] and Zhang et al.,^[5] who reported occipital pain in about 22% of SUNHA patients.

In SUNHA, attacks might take the form of a single stab, a series of stabs, or longer attacks with a saw-tooth pattern.^[2] Most of the patients experienced both a single stab and several stabs of pain. About one-fourth of the patients in both groups had saw-tooth pattern pain. Other studies have also reported more than one pattern of pain in an individual patient. Normally, SUNCT and SUNA patients experience severe or very severe pain. The pain intensity in our cohort was similar to other studies. The VAS score was between 7 and 10 in 86.7% of SUNCT and 83.9% of SUNA patients in Zhang *et al.* study.^[5] In our study, 87% of patients with SUNCT and 85% of patients with SUNA reported having a VAS score between 7 and 10.

As far as duration and frequency are concerned, the ICHD-3 criteria for SUNHA specify an attack length of 1-600 s, with at least one attack per day.^[1] Most attacks in our patients last between 1 second and 2 minutes. About 30% of patients in both groups experienced attacks lasting more than 2 minutes, and up to 10 minutes. A few authors described the duration of attacks in relation to the type of attack, such as single stab, a series of stabs, or saw-tooth patterns. The mean duration of stabs was 58 seconds, 396 seconds for a series of stabs, and

1,160 seconds for the saw-tooth pattern in Cohen *et al.*^[11] In Lambru *et al.*^[4] study, the median duration of single stabs was 10 seconds, 180 seconds for a group of repetitive stabs, and 240 seconds for the saw-tooth pattern attacks.

Cranial autonomic symptoms in our cohort were comparable to those described in other large case series. By definition, SUNCT includes both conjunctival injection and lacrimation. Therefore, they were present in all cases. Patients with SUNA can have either conjunctival injection or lacrimation, but not both. Therefore, it is obvious that SUNA will have a lower prevalence of conjunctival injection or lacrimation than SUNCT. Nevertheless, 10 of the 13 patients in our cohort (SUNA) exhibited either a conjunctival injection or lacrimation. In the studies by Cohen *et al.*,^[11] Weng *et al.*,^[9] and Lmabru *et al.*,^[4] ptosis and eyelid edema were frequent cranial autonomic symptoms, particularly in individuals with SUNCT. In our cohort, eyelid edema and ptosis were noted in only two patients in each group. Just like our observation, eyelid edema and ptosis were uncommon in the Zhang *et al.* study.^[5]

Agitation or restlessness during attacks is one of the specific features of all TACs, including SUNHA. The prevalence of agitation or restlessness in patients with SUNHA varies greatly between studies. Some studies failed to indicate the existence of restlessness in their cohorts.^[8,9] In Lambru *et al.* study,^[4] 28.6% of patients with SUNA and 30.0% of patients with SUNCT felt restless and agitated during their headaches. In Zhang *et al.* study,^[5] about 23% of the patients with SUNHA felt restlessness. In Cohen *et al.* study,^[11] 62% of patients with SUNCT and 56% of patients with SUNA were agitated or restless during an attack. All of the 15 SUNCT patients observed by Cação *et al.*^[12] had agitation. In our cohort, more than 50% of the patients in both groups had restlessness.

Just like TN, multiple triggers have been described in patients with SUNA and SUNCT. Nearly all patients with TN report attack triggers, ranging from 91% to 99% of patients.^[13] However, a significant proportion of SUNHA patientsbetween 30% and 50% of all cases-show only spontaneous attacks.^[2,4,5] In 46% of patients with SUNA and 44% of patients with SUNCT in our cohort, there were no triggers; only spontaneous attacks occurred. In Lambru et al. study,^[4] only spontaneous attacks were reported by 47.6% of patients with SUNA and 32.9% of patients with SUNCT. Similar to this, 35.6% of SUNCT patients and 51.6% of SUNA patients in the Zhang et al.^[5] study reported having exclusively spontaneous attacks. In most cases, patients who experience a trigger-induced attack do not experience a refractory period and can experience another attack right away following the previous one. Only 5%-10% of the patients with SUNHA may have a refractory period after a triggered attack.^[4-6,8] Paliwal et al. suggested that the presence of a refractory period in SUNCT or SUNA patients may be indicative of secondary SUNHA, especially a vascular loop compressing the trigeminal nerve.^[14] In our cohort, we got a vascular loop in only two patients with SUNCT (none in the SUNA group). Both patients described only spontaneous attacks; therefore, it was difficult to determine whether each had a refractory period.

Several cases with aberrant vascular loops around the ipsilateral trigeminal nerve have been reported in the literature. In a literature review, Favoni et al.[8] noted neurovascular compression in 16.9% of the patients with SUNHA. Lambru et al.^[6] evaluated the neurovascular contact in patients with SUNCT and SUNA. They evaluated 165 symptomatic and 153 asymptomatic trigeminal nerves. The symptomatic trigeminal nerves have more neurovascular contact (80.0%) than the asymptomatic trigeminal nerves (56.9%), and it was statistically significant. They also evaluated the morphological changes due to neurovascular contact. Neurovascular contact with morphological changes was much more common on the symptomatic side (61.4%) than on the asymptomatic side (31.0%). They did not, however, discover any appreciable radiological differences between SUNCT and SUNA. Neurovascular contact with morphological changes was defined as contact with distortion and/or atrophy of the nerve.^[6]

The treatments were not standardized in our patients (by previous physicians and even by our team). The dosing schedules were not uniform. Even the follow-up period was not uniform in each patient. Several patients received multiple drugs. Therefore, it was hard to draw any definite conclusions regarding treatment.

Available evidence suggests that lamotrigine is the most effective preventative drug.^[2] In a recent meta-analysis, lamotrigine showed the highest percentage of responders among all the treatments for both SUNCT and SUNA.^[15] Therefore, lamotrigine is considered as a first-line drug for the prevention of both SUNCT and SUNA. Second-line preventive therapies include oxcarbazepine, carbamazepine, topiramate, and duloxetine. Other drugs that might help are gabapentin, pregabalin, mexiletine, and zonisamide.^[2,15] About 50% of the patients showed a response to various drugs (lamotrigine, gabapentin, pregabalin, or topiramate). This response rate was comparable to the other studies. Carbamazepine was administered to all but one patient. One patient did, however, appear to respond to carbamazepine. So, most of the patients were largely refractory to carbamazepine, an important feature differentiating SUNHA from TN.

So, in this retrospective study, we compared the different aspects of SUNA and SUNCT in Indian patients. We did not discover any significant differences between the two, similar to other comparable studies. Lambru *et al.*⁽⁴⁾ recommended that these two syndromes be dropped and combined into a single diagnostic group termed SUNA. Our findings are consistent with this hypothesis.

Pathophysiology

Like other TACs, both central and peripheral processes are implicated in the generation of headache attacks in SUNCT and SUNA.^[16] Several hypothalamic nuclei and circuits, including orexinergic, somatostatinergic, opioidergic, and serotonergic, are involved in TACs. Trigeminovascular-nociceptive pathways, which include the trigeminal autonomic reflex, are the final pathways for the headaches and other symptoms of all TACs. Functional magnetic resonance imaging and positron emission tomography studies have demonstrated bilateral, contralateral, and even ipsilateral hypothalamic activation in patients with SUNHA. Dysfunctions in the hypothalamus and related circuits modify the inputs to the trigeminovascular system and the trigeminal autonomic reflex.^[16]

Limitations

There are various limitations to our study. This is a retrospective case series from a single center. It cannot, therefore, be generalized. This study may have a number of biases, including an unrecognized selection bias. The number of patients in our observation may not be enough to show the real differences between SUNA and SUNCT. For patients with SUNHA, a special standard neuroimaging approach has been recommended to screen for the presence of vascular loops compressing the trigeminal nerve. Although all of the patients included in this study had magnetic resonance imaging brain scans, only a few of them had neuroimaging according to the recommended neuroimaging protocol for such patients. Moreover, medications and dosing schedules were also not standardized.

CONCLUSION

This is the largest case series from India. There were 13 patients with SUNA and 16 patients with SUNCT. Like the recent case series, we found female predominance in SUNA and SUNCT. The demographic and clinical features of SUNA patients were comparable to those of SUNCT patients. Triggers were reported in more than half of the patients in both groups. Only one patient in each group had a refractory period following a trigger-induced episode. Two patients in the SUNCT group had compression of the triggeminal nerve by a vascular loop.

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Conflicts of interest

There are no conflicts of interest.

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