SUNHA: A Mystifying Cephalgia

Short-lasting unilateral neuralgiform headache attacks (SUNHA) are an important, often disabling painful syndrome encountered in neurological emergencies. It comprises two subtypes, namely short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) and short-lasting unilateral neuralgiform headache with autonomic symptoms (SUNA).

The initial record dates back to 1978 when Sjaastad *et al*.[1] described the phenomena of multiple attacks of neuralgiform unilateral headache along with conjunctival injection occurring in clusters. It was soon followed by the concept of distinct cranial autonomic features and accordingly classified into short-lasting unilateral neuralgiform headache with autonomic symptoms under the second edition of the International Classification of Headache Disorders (ICHD-2). The recent ICHD-3 combined the two into SUNHA spectrum.

With increased awareness, the literature has expanded extensively and data obtained from several case reports/series, studies, and reviews have shown its annual incidence of 1.2 per lakh population, with a mean age of 40-70 years (range 3-88 years) with a mostly male preponderance (1.5:1).[2]

The exact pathophysiology of SUNHA is unknown, however, studies have linked this entity towards dysfunction of the trigeminocervical-hypothalamic circuitry. Some recent research has also postulated the role of the ventral tegmental area (VTA) in the development of SUNHA.[3] Orexinergic pathways are also being studied in SUNHA. Lesions of the pituitary gland and posterior fossa including tumor, stroke, vascular malformation or loop, demyelinating disorders, infection, bony lesions, etc., are often associated with secondary SUNHA.

SUNHA is characterized by multiple attacks (at least 20) of short-lasting (1-600 seconds) but a moderate-severe headache (perceived as single or serial stabs or saw-toothed pattern) occurring unilaterally along the ophthalmic division of trigeminal nerve (orbital, supraorbital, temporal, and/or other trigeminal distribution) along with atleast one of the autonomic features (conjunctival injection and/or tearing/lacrimation, nasal congestion and/or rhinorrhea, eyelid edema, facial/forehead sweating, facial/forehead flushing, aural fullness, miosis and/or ptosis) occurring in the same side.[4] The differentiating point between SUNCT and SUNA is the presence of conjunctival injection and tearing/lacrimation in SUNCT, and either or none of the two in SUNA. In a study by Lambru *et al*.,[5] SUNCT has been shown to exhibit prominent cranial autonomic symptoms and a higher triggerability as compared to SUNA. The attacks in SUNHA can be either spontaneous or triggered. In 80–95% of patients, an attack can be immediately triggered after the cessation of the previous one, and the periods of refractoriness are not observed in SUNHA. In addition, there can be presence of migrainous features like photophobia, phonophobia, nausea, vomiting, or aura in 27% of patients of SUNHA.

SUNHA is further subdivided into two forms, episodic or chronic (attacks occurring for >1 year without remission or with remissions lasting <1 month). The episodic form is seen in only 10% of cases, occurring at an average of 1–4 annual attacks with events lasting for 1 week–10 months.

The diagnosis of SUNHA is distinctively clinical, based on ICHD-3, and subdivided into SUNCT and SUNA. Furthermore, the secondary causes of SUNHA are to be evaluated for possible definitive therapy. On follow-up, SUNHA can be further addressed in episodic or chronic forms.

SUNHA is considered a subtype of trigeminal autonomic cephalgia (TAC) with brief duration and a higher recurrence rate. The eminent differentials include trigeminal neuralgia, cluster headache, epicrania fugax, paroxysmal hemicranias, cluster migraine, and primary stabbing headache. The basic distribution, duration, and frequency of attacks, along with a response to pharmacotherapy can aid in vivid differentiation.

Brain magnetic resonance imaging is the most important investigation in SUNHA and sites like the hypothalamic-pituitary zone, cavernous sinus, trigeminal nerve, and posterior fossa are of prime interest.

The treatment of SUNHA (SUNCT/SUNA) remains a challenge in view of the limitation of understanding of the disease pathogenesis, short duration of the attack, clinical awareness, paucity of extensive trials, and evidence-based treatment recommendations. The management aims primarily towards abutting further attacks on a short-term/transitional basis or long-term preventive basis.

The transitional therapy rests on lidocaine (intravenous or subcutaneous) as evidenced by Baraldi *et al*.,[6] in their systematic review showing 94% effectiveness. They also assessed the use of short-course methyl prednisolone in SUNCT with variable success.

The medical preventive therapy includes first-line agents in the form of lamotrigine (up to 700 mg/day), second-line agents like oxcarbazepine (up to 2400 mg/day), duloxetine (up to 120 mg/day), carbamazepine (up to 1600 mg/day), topiramate (up to 800 mg/day) and third-line agents like gabapentin (up to 4800 mg/day), pregabalin (up to 600 mg/day), lacosamide (up to 400 mg/day) and mexiletine (up to 1200 mg/day). Lamotrigine has shown higher efficacy in treating SUNCT than SUNA, especially in reducing the frequency of further attacks, rather than the abolishment of attack.

In the largest prospective study by Lambru *et al*.[7] (n = 161), lamotrigine was observed to be the most effective

prophylactic medication (56% responder) followed by oxcarbamazepine (46%). They further extrapolated that the better response to these sodium channel blocking agents might indicate a therapeutic overlap with trigeminal neuralgia, hence suggesting that dysfunction of sodium channel might be an important pathophysiological mechanism of SUNHA. Newer therapies in the form of botulinum toxin injection and anti-calcitonin related gene peptide monoclonal antibody (galcanezumab) have also been tried with success.

However, despite most prominent medical therapy, drug refractoriness is observed in 45-55% of cases, which require further intervention in the form of occipital nerve stimulation (ONS), deep brain stimulation (DBS), pulsed radiofrequency (PRF), stereotactic radiosurgery (SRS) and microvascular decompression (MVD). In the recent review by Smit *et al*.[8] regarding interventional therapies, a better response was achieved after deep brain stimulation of the ventral tegmental area [14/16 patients (86.7%)], occipital nerve stimulation [33/41 patients (80.5%)], stereotactic radiosurgery to the sphenopalatine ganglion (SPG) [7/9 patients (77.8%)], microvascular decompression of the trigeminal nerve [56/73 patients (76.7%)] and pulsed radiofrequency of SPG [5/9 patients (55.6%)].

This retrospective study is the first study from India by Prakash *et al*.,[9] describing clinical characteristics in SUNCT and SUNA. A total of 29 patients with a relatively younger age being affected (36-38 years), higher female preponderance, with similar clinical characteristics among SUNCT and SUNA were observed in this study. In addition, the preventive medical therapy was satisfactory in 15/29 patients.

SUNHA (SUNCT and SUNA) is a distinct TAC with clinically disabling primary headache. While secondary causes unfold opportunities for specific disease-directed treatment, the management of primary SUNHA is challenging. Medical preventive therapies like lacosamide and carbamazepine have proven efficacy partially. The armamentarium of surgical interventions in drug refractory SUNHA needs exploratory implementation. Future therapeutical approaches and algorithmic guidelines can help in better outcomes in SUNHA.

Rajesh Verma, Rajarshi Chakraborty

Department of Neurology, King George's Medical University, Lucknow, Uttar Pradesh, India

Address for correspondence: Dr. Rajesh Verma, Department of Neurology, King George's Medical University, Lucknow - 226 003, Uttar Pradesh, India.
E-mail: drrajeshverma32@yahoo.com

References

1. Sjaastad O, Russel D, Horven I, Bunaes U. Multiple neuralgiform unilateral headache attacks associated with conjunctival injection and appearing in clusters. A nosological problem. Proc Scand Migraine Soc 1978;31:31.
2. Duggal AK, Chowdhury D. SUNCT and SUNA: An update. Neurol India 2021;69:144.
3. Miller S, Akram H, Lagrata S, Hariz M, Zrinzo L, Matharu M. Ventral tegmental area deep brain stimulation in refractory short-lasting unilateral neuralgiform headache attacks. Brain 2016;139:2631-40.
4. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia 2018;38:1-211. doi: 10.1177/0333102417738202.
5. Lambru G, Rantell K, Levy A, Matharu MS. A prospective comparative study and analysis of predictors of SUNA and SUNCT. Neurol 2019;93:e1127-37.
6. Baraldi C, Pellesi L, Guerzoni S, Cainazzo MM, Pini LA. Therapeutical approaches to paroxysmal hemicrania, hemicrania continua and short lasting unilateral neuralgiform headache attacks: A critical appraisal. J Headache Pain 2017;18:71.
7. Lambru G, Stubberud A, Rantell K, Lagrata S, Tronvik E, Matharu MS. Medical treatment of SUNCT and SUNA: A prospective open-label study including single-arm meta-analysis. J Neurol Neurosurg Psy 2021;92:233-41.
8. Smit RD, Mouchtouris N, Kang K, Reyes M, Sathe A, Collopy S, *et al*. Short-lasting unilateral neuralgiform headache attacks (SUNCT/SUNA): A narrative review of interventional therapies. J Neurol Neurosurg Psy 2023;94:49-56.
9. Prakash S, Vadodaria V, Patel H, Rana K, Shah C. A retrospective comparative study in patients with SUNA and SUNCT. Annals of Indian Academy of Neurology 2023;26:672-7.

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