Misdiagnosis of Trigeminal Neuralgia and Misuse of Carbamazepine and Its Derivatives in Headache Disorders

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INTRODUCTION

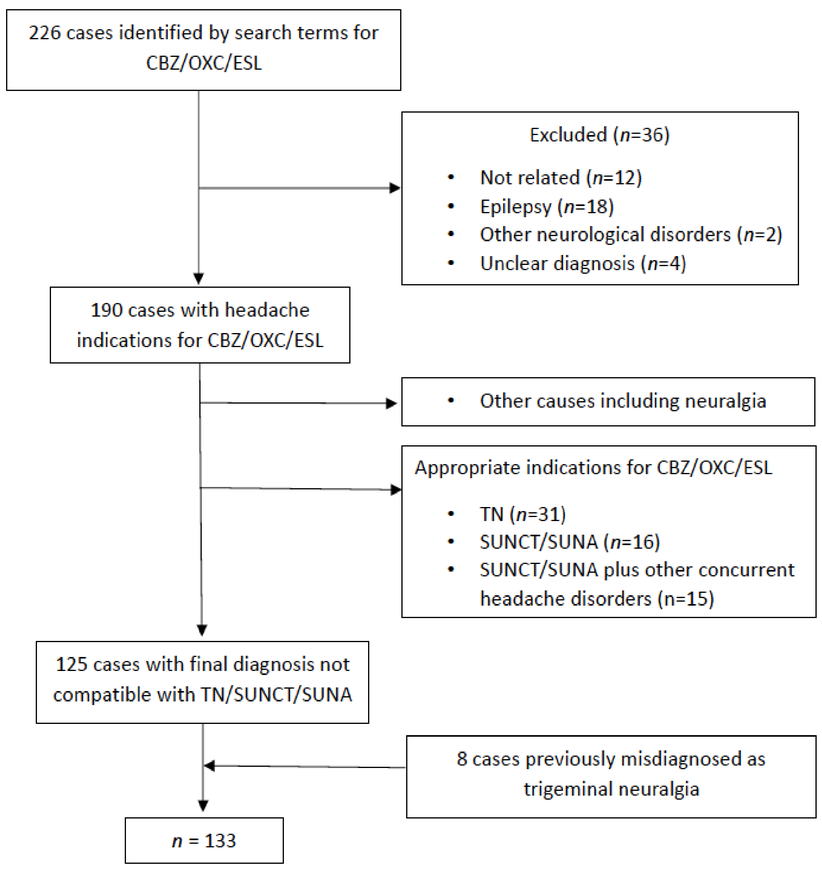
- Carbamazepine (CBZ) and oxcarbazepine (OXC) are first-line therapies in trigeminal neuralgia.
- CBZ and OXC are useful in short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) or with cranial autonomic symptoms (SUNA).
- We have consistently seen patients mis-diagnosed with trigeminal neuralgia and thus inappropriately treated with CBZ or OXC

➢ We aimed to investigate the rate of facial pain misdiagnosis leading to the use of CBZ, OXC or eslicarbazepine (ESL), along with the clinical features associated with the misdiagnosis.

METHODS

- We conducted a service evaluation of patients seen in a single tertiary-care headache centre to identify patients with any exposure to CBZ, OXC, or ESL from June 2014 to April 2024.
- All patients who were prescribed these medications for headache where the final diagnosis was not trigeminal neuralgia, neuralgia or SUNCT/SUNA, were included and reviewed. Additional patients with previous misdiagnosis of trigeminal neuralgia were also considered.

FIGURE 1: Flowchart for case identification



RESULTS (1)

- Of 133 patients, 79 % (*n* = 105) had migrainous components: 44% with migraine and 35% with other types of headache plus migraine, of these 16% had new daily persistent headache (NDPH). Thirty-six percent had a trigeminal autonomic cephalalgia (TACs).
- Facial pain was common in these patients (75%, 97/130), and two-thirds (68%, 89/130) had unilateral headache. Common pain characteristics were throbbing (55%), stabbing (34%), and sharp (32%) pain.

RESULTS (2)

TABLE 1: Patient characteristics and final diagnosis

All *n* = 133 patients	
Male: female	47:86 (1:1.8)
Age of headache onset, years, median (IQR)	39 (24,53)
Final Diagnosis, (%)	
• **Migraine**	58 (44%)
• **Paroxysmal hemicrania**	1 (1%)
• **Cluster headache**	8 (6%)
• **Hemicrania continua**	11 (8%)
• **TACs NOS**	2 (2%)
• **Post-traumatic trigeminal neuropathy**	1 (1%)
• **Other headache types**	4 (3%)[a]
• **Mixed components including migraine**	48 (36%)[b]
Medication overuse headache	34 (26%)

a. 1 orthostatic headache (spontaneous intracranial hypotension), 1 cardiac cephalalgia, 1 hemicrania alternans, 1 temporomandibular joint dysfunction

b. 47 had a migrainous background (3 SUNCT/SUNA, 3 paroxysmal hemicrania, 7 cluster headache, 6 hemicrania continua, 1 cluster headache/ NDPH with migrainous features and stabbing headaches, 4 TACs NOS, 1 TACs NOS/ NDPH with migrainous features and post-traumatic trigeminal neuropathy and 1 had cluster headache with hypnic headache

- Of mis-diagnosed patients, up to 63% had at least one of stabbing, sharp, shooting or electric pain, and two-thirds had allodynia (66%).
- In 58 patients with only migraine, 53% had at least one of stabbing, sharp, shooting or electric component to the pain phenotype and 57% had allodynia.

TABLE 2: Headache characteristics

Headache features	
Headache days/month, median (IQR)	30 (30,30)
Facial pain	97/130 (75%)
Sides of headache (*n* =131)	
• **Only unilateral side**	89 (68%)
• **Alternate side**	8 (6%)
• **Both sides**	14 (11%)
• **Both unilateral and bilateral**	27 (21%)
Most painful score, median (IQR) (*n* =116)	10 (9,10)
Pain characteristics (*n* =126)	
• **Throbbing**	69 (55%)
• **Stabbing**	43 (34%)
• **Sharp**	41 (32%)
• **Dull**	33 (26%)
• **Pressure**	29 (23%)
• **Burning**	24 (19%)
• **Nagging/constant**	19 (15%)
• **Electric**	17 (14%)
• **Shooting**	12 (10%)
• **Squeezing**	9 (7%)
• **Stabbing/ sharp/ shooting or electric**	79 (63%)
Allodynia	70/106 (66%)
Refractory period	4/15 (27%)
Cutaneous trigger	15/120 (12%)
Associated symptoms	
• **Photophobia**	80/125 (64%)
• **Photic allodynia**	21/125 (17%)
• **Phonophobia**	74/125 (59%)
Side of associated photophobia or phonophobia	29/107 (27%)
- **Unilateral**	45/107 (42%)
- **Bilateral**	33/107 (31%)
- **No**	
Restless/agitated	44/58 (76%)
Aura	25/121 (21%)
Cranial autonomic symptoms	
• **Ipsilateral to headache**	73/124 (60%)
• **Bilateral**	29/124 (23%)
• **Contralateral to headache**	1/124 (1%)
• **None**	21/124 (17%)

Treatments

- Of those mistreated or misdiagnosed with TN, 89% had previous CBZ prescription, none had a good, persistent effect.
- Some (58%) had adverse effects, with drowsiness and concentration difficulty or cognitive problems being the two most common. OXC was previously prescribed in 10% of patients and none had a complete response. Side effects were reported in 54%.

CONCLUSIONS

- Migraine with lateralised facial pain or short-lasting pain characteristics can sometimes be misdiagnosed as trigeminal neuralgia.
- Overdiagnosis of trigeminal neuralgia can lead to unwarranted prescription of carbamazepine and its derivatives, resulting in avoidable side effects.

DISCUSSION

- CBZ is very effective in certain conditions such as trigeminal neuralgia but side effects are common, roughly 30%.[1]
- Our data showed that patients were appropriately prescribed one of CBZ/OXC/ESL in only 33% for correctly diagnosed trigeminal neuralgia and SUNCT/SUNA. Two-thirds of patients exposed to CBZ/OXC should not have had the drug, with the most common misdiagnosis being migraine.
- The misdiagnosis is likely based on facial distribution of the pain and mis-interpreting the patients' use of the term "stabbing" to trigger a neuralgia diagnosis. Stabbing can be regular in cadence as in migraine, in contrast to the irregular cadence of neuralgic pain.
- Particular pain patterns including sharp, electric, or shooting made up a substantial component of the erroneous CBZ/OXC/ESL use. Primary stabbing headache can be misdiagnosed as trigeminal neuralgia if the headache phenotype is not well characterised.
- We found facial pain in three-quarters of those inappropriately treated, mostly in migraineurs. Facial pain was reported in 2.3% of migraine mostly in the maxilla, a proportion of TACs.[2]
- In almost two-thirds of our cohort, allodynia was reported as seen in migraineurs[3] whereas 12.5% had a cutaneous trigger. Patients may say they have triggered pain when what they are reporting is allodynic exacerbations of their baseline pain. Dissecting this phenomenon requires very careful history taking.
- Overall, the responses in patients with no clear indication for CBZ/OXZ were poor with only one migraineur reporting a good outcome, and 59% of those exposed having a side effect.

REFERENCES

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