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## CHAPTER 11

# Cluster headache and other trigemino-autonomic cephalgias

S. Evers,<sup>1</sup> J. Áfra,<sup>2</sup> A. Frese,<sup>1,3</sup> P. J. Goadsby,<sup>4</sup> M. Linde,<sup>5</sup> A. May,<sup>6</sup> P. S. Sándor<sup>7</sup>

<sup>1</sup>University of Münster, Germany; <sup>2</sup>National Institute of Neurosurgery, Budapest, Hungary; <sup>3</sup>Academy of Manual Medicine, Münster, Germany; <sup>4</sup>University of California, San Francisco, CA, USA, and UCL, Institute of Neurology, Queen Square, London, UK; <sup>5</sup>Cephalea Headache Centre, Läkarhuset Södra vägen, Gothenburg, Sweden; <sup>6</sup>University of Hamburg, Germany; <sup>7</sup>University of Zurich, Switzerland

### Objectives

These guidelines aim to give evidence-based recommendations for the treatment of cluster headache attacks, for the prophylaxis of cluster headache, for the treatment of paroxysmal hemicranias, and for the treatment of SUNCT syndrome. A brief clinical description of the headache disorders is included. The definition of the headache disorders follows the diagnostic criteria of the International Headache Society (IHS).

### Background

The second edition of the classification of the IHS provided a new primary headache grouping named the trigemino-autonomic cephalgias (TAC) [1]. All these headache syndromes have two features in common: relatively short-lasting, unilateral, severe headache attacks and typical accompanying cranial autonomic symptoms (although the latter are not obligatory). These autonomic symptoms occur on the side of headache and comprise lacrimation, conjunctival injection, rhinorrhoea, miosis, and ptosis. The following syndromes belong to the TAC:

- episodic and chronic cluster headache
- episodic and chronic paroxysmal hemicrania

- SUNCT syndrome (short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing).

These syndromes differ in duration, frequency, and rhythmicity of the attacks, and in the intensity of pain and autonomic symptoms. The pathophysiology of TAC has been in the focus of intensive research for several years [2–4].

The purpose of this paper is to give evidence-based treatment recommendations for the different TAC. The recommendations are based on the scientific evidence from clinical trials and on the expert consensus by this EFNS task force. The legal aspects of drug prescription and drug availability in the different European countries will not be considered. The definitions of the recommendation levels follow the EFNS criteria [5].

### Search strategy

A literature search was performed using the reference databases MEDLINE, Science Citation Index, and the Cochrane Library; the key words used were ‘cluster headache’, ‘paroxysmal hemicrania’, ‘SUNCT’, ‘treatment’, and ‘trial’ (last search in March 2009). All papers published in English, German, or French were considered when they described a controlled trial or a case series on the treatment of at least five patients (or fewer in paroxysmal hemicrania or SUNCT syndrome). In addition, a review book [6] and the German treatment recommendations for cluster headache [7] were considered.

## Method for reaching consensus

All authors performed an independent literature search. The first draft of the manuscript was written by the chairman of the task force. All other members of the task force read the first draft and discussed changes by email. A second draft was then written by the chairman and was again discussed by email. All recommendations had to be agreed to by all members of the task force unanimously. The background of the research strategy and of reaching consensus and the definitions of the recommendation levels used in this paper have been described in the EFNS recommendations [5]

## Clinical syndromes

The diagnosis of a headache belonging to the TAC is based on the patient's history and on a neurological examination. Electrophysiological and laboratory examinations, including examination of the cerebrospinal fluid (CSF), are not helpful. For the first diagnosis and in the case of an abnormal neurological examination, a cranial magnetic resonance imaging (MRI) or a computed tomography (CT) scan should be performed to exclude abnormalities of the brain. Particularly in older patients, mass lesions or malformations in the midline have been described to be associated with symptomatic cluster headache.

### Episodic and chronic cluster headache (IHS 3.1)

The diagnostic criteria of cluster headache are presented in table 11.1. Cluster headache is defined as a paroxysmal, strongly unilateral, very severe headache, typically with a retro-orbital maximum of pain. The occurrence of cranial autonomic symptoms such as Horner's syndrome, lacrimation, and rhinorrhoea ipsilateral and simultaneous to the pain is obligatory (but can be replaced by restlessness/agitation). The attacks occur up to eight times a day, sometimes with a nocturnal preponderance, and last between 15 and 180 min, rarely several hours. The episodic form of cluster headache occurs in 80% of patients with bouts lasting between 7 and 365 days separated by pain-free remission periods longer than one month. Sometimes, asymptomatic periods lasting even years can be observed. If the cluster attacks occur for longer than

**Table 11.1** Diagnostic criteria of cluster headache.

<b>A</b>	At least five attacks fulfilling criteria B–D
<b>B</b>	Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15–180 min if untreated
<b>C</b>	Headache is accompanied by at least one of the following: <ol style="list-style-type: none"> <li>1. ipsilateral conjunctival injection and/or lacrimation</li> <li>2. ipsilateral nasal congestion and/or rhinorrhoea</li> <li>3. ipsilateral eyelid oedema</li> <li>4. ipsilateral forehead and facial sweating</li> <li>5. ipsilateral miosis and/or ptosis</li> <li>6. sense of restlessness or agitation</li> </ol>
<b>D</b>	Attacks have a frequency from one every other day to eight per day
<b>E</b>	Not attributed to another disorder

1 year without remission periods or with remission periods lasting less than 1 month, the diagnosis is chronic cluster headache. This is the case in 15–20% of patients. The two forms do not necessarily evolve from one another. Often, the attacks start at the same time of day or night, frequently about 1–2 h after falling asleep (mostly during the first REM period in the sleep) or in the early morning. Cluster headache is regarded as a bio-rhythmic disorder because the attacks often occur with a strong periodicity and because the cluster bouts regularly occur during spring and autumn. Furthermore, changes of the diurnal release of hormones involved in biorhythmicity have been detected. The lifetime prevalence of cluster headache is between 0.06 [8] and 0.4% [9], with a male to female ratio between 2.5:1 and 7.1:1 [10]. In recent years, the number of female patients who report cluster headache has increased [11, 12]. It is not clear if this is a genuine change or simply increased recognition. A genetic background for cluster headache has not been described but is likely [13]. Cluster headache can be seen in children and is just as devastating in that age group. There is a familial occurrence in 2–7%. On average, the headache starts at the age of 28–30 years (but can start in every age). After 15 years, 80% of the cluster headache patients still have attacks [10].

### Episodic and chronic paroxysmal hemicrania (IHS 3.2)

Paroxysmal hemicrania was first described in 1974 in its chronic form ([14]; for recent review see [15]). The paroxysmal headache attacks, the character and localization

**Table 11.2** Diagnostic criteria of paroxysmal hemicrania.

- A** At least 20 attacks fulfilling criteria B–D
- B** Attacks of severe unilateral orbital, supraorbital, or temporal pain lasting 2–30 min
- C** Headache is accompanied by at least one of the following:
  1. ipsilateral conjunctival injection and/or lacrimation
  2. ipsilateral nasal congestion and/or rhinorrhoea
  3. ipsilateral eyelid oedema
  4. ipsilateral forehead and facial sweating
  5. ipsilateral miosis and/or ptosis
- D** Attacks have a frequency above five per day for more than half the time, although periods with lower frequency may occur
- E** Attacks are prevented completely by therapeutic doses of indomethacin
- F** Not attributed to another disorder

of pain, and the autonomic symptoms are very similar to those observed in cluster headache. In contrast to cluster headache, the attacks are shorter (2–30 min) and more frequent (more than five attacks per day). The autonomic symptoms are often less severe than in cluster headache. The diagnostic criteria of paroxysmal hemicrania are given in table 11.2. Some patients report that their attacks can be triggered by irritation of the neck, in particular in the cervical segments C2 and C3. As for cluster headache, there is an episodic and a chronic form of paroxysmal hemicrania. The criteria for this differentiation are the same as in cluster headache (see above). The most important criterion for the diagnosis of paroxysmal hemicrania is the complete response to indomethacin. Within 1 week (often within 3 days) after the initiation of indomethacin at an adequate dose the attacks disappear, and this effect is maintained long term. The prevalence is very low, exact figures are not known. It is estimated that the paroxysmal hemicranias comprise about 3–6% of all TAC. The headaches usually start between the age of 20 and 40 years, although children as young as 3 years old with clear indomethacin responses have been described [16]. In contrast to cluster headache, the male to female ratio is 1:3.

### SUNCT syndrome (IHS 3.3)

The name of this syndrome (short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing) describes its typical clinical features. It was first described in 1989 [17]; for review see [18]. The

**Table 11.3** Diagnostic criteria of SUNCT syndrome.

- A** At least five attacks fulfilling criteria B–D
- B** Attacks of unilateral orbital, supraorbital or temporal stabbing or pulsating pain lasting 5–240 s
- C** Pain is accompanied by ipsilateral conjunctival injection and lacrimation
- D** Attacks occur with a frequency from 3–200 per day
- E** Not attributed to another disorder

diagnostic criteria are given in table 11.3. SUNCT syndrome is characterized by very short (5–240 s) attacks with neuralgiform pain quality and severe intensity. The attacks occur in a frequency of in average 60 per day (3–200 per day), are strictly unilateral (peri-orbital), and are often triggered by touching, speaking, or chewing. When triggerable, there is no refractory period of triggering attacks. The autonomic symptoms are mostly restricted to lacrimation and conjunctival injection. Distinct episodic and chronic forms of SUNCT syndrome are yet to be recognized in formal classifications, but both types occur. The most important differential diagnosis is classical trigeminal neuralgia. In trigeminal neuralgia, unlike in SUNCT syndrome, autonomic symptoms are not prominent and triggered attacks have a clear refractory period. SUNCT syndrome is uncommon and its true frequency is completely unclear. The male to female ratio is 1:4. The diagnosis of SUNCT syndrome follows the same algorithm as described for cluster headache.

### Treatment of cluster headache

The treatment of cluster headache is based on empirical data rather than on a pathophysiological concept of this disorder [4, 19]. Drug treatment can be divided into acute attack abortion and prophylaxis [7, 20]. Non-drug treatment is ineffective in nearly all patients. It has, however, to be considered that drug treatment in cluster headache shows a placebo rate similar to that observed in migraine treatment [21](table 11.4).

### Attack treatment

Inhalation of pure (100%) oxygen with a flow of at least 7 l/min (sometimes more than 10 l/min) is effective

**Table 11.4** Treatment recommendations for cluster headache, paroxysmal hemicrania, and SUNCT syndrome. For exact doses see text. (A denotes effective, B denotes probably effective, C denotes possibly effective)

	Cluster headache	paroxysmal hemicrania	SUNCT syndrome
Attack treatment	oxygen inhalation (A) sumatriptan 6 mg s.c. (A) zolmitriptan 5 mg nasal (A) sumatriptan 20 mg nasal (A) zolmitriptan 10 mg oral (B) lidocaine nasal (B) octreotide (B)	none	none
Prophylactic treatment	verapamil (A) steroids (A) lithium (B) methysergide (B) topiramate (B) ergotamine tartrate (B) valproic acid (C) melatonin (C) baclofen (C)	indomethacin (A) verapamil (C) NSAIDs (C) topiramate (C)	lamotrigine (C)

in abortion of cluster headache attacks [22–24]. The inhalation should be for 20 min in a sitting, upright position with a face mask. There are no contraindications known for the use of oxygen. It is safe and without side effects. About 60% of all cluster headache patients respond to this treatment with a significant pain reduction within 30 min [25, 26].

In double-blind, placebo-controlled trials, the 5-HT<sub>1B/D</sub> agonist sumatriptan injected subcutaneously is effective in about 75% of all cluster headache patients (i.e. pain-free within 20 min) [27, 28, 29]. It is safe and without side effects in most of the patients even after frequent use [30, 31]. Contraindications are cardio- and cerebrovascular disorders and untreated arterial hypertension. The most unpleasant side effects are chest pain and distal paresthesia. In open prospective observational studies [32, 33], even 3 mg subcutaneous sumatriptan is effective in the majority of patients. Zolmitriptan 5 mg nasal spray has also been shown to be effective in two placebo-controlled trials and has recently been approved by the EMEA for the acute treatment of cluster headache [34, 35]. In single open and double-blind, placebo-controlled trials, sumatriptan nasal spray 20 mg [36, 37] and oral zolmitriptan 10 mg [38] were also effective within 30 min. In the latter

study, only patients with episodic cluster headache responded.

Oral ergotamine has been used in the treatment of cluster headache attacks for more than 50 years [39–41] and is effective when given very early in the attack. It was then recommended for the acute cluster headache attack treatment as an aerosol spray [42–45]. However, more recent trials are missing. The intranasal application of dihydroergotamine in cluster headache attacks was not superior to placebo in a single trial [46]. Very recently, the intravenous application of 1 mg dihydroergotamine over 3 days has been shown to be effective in the abortion of severe cluster attacks in an open retrospective trial [47].

For short-term prophylaxis, ergotamine has also been studied. Ergotamine suppositories need a long time until the onset of efficacy. They have been proposed in a dose of 2 mg for short-term prophylaxis, given in the evening to prevent cluster headache attacks in the night [48]. Also, regular intramuscular or subcutaneous injections of ergotamine tartrate 0.25–0.5 mg have been studied successfully in the prevention of nightly attacks [49, 50].

The nasal installation of lidocaine (1 ml with a concentration of 4–10%; the head should be reclined by 45° and

rotated to the affected side by 30 to 40°) is effective in at least one-third of patients [51–55]. The use of lidocaine evolved from early observations that cocaine is effective in aborting cluster headache attacks. This has been supported in an open and not controlled trial with 10% intranasal cocaine [55].

Recently, 100 µg subcutaneous octreotide has been shown to be effective in the treatment of acute cluster headache attacks in a double-blind, placebo-controlled trial [56].

Meanwhile, also in cluster headache patients, a risk for the development of medication overuse headache has been shown, in particular if there is a comorbidity or a family history of migraine [57].

### Prophylactic drug treatment

Verapamil in a daily dose of 240–960 mg has been established as drug of first choice in the prophylaxis of episodic and chronic cluster headache [7, 20], although only a few double-blind, placebo-controlled trials which are properly designed and useful for high-grade level of evidence are available. Controlled trials compared verapamil and lithium with placebo, showing an efficacy of both substances with a more rapid action of verapamil [58], or compared verapamil 360 mg with placebo showing superiority of verapamil [59]. In some cases, a daily dose of more than 720 mg can be necessary [60]. Regular ECG controls are required to control for increase in cardiac conduction time. Sometimes, echocardiography can be necessary due to the negative inotropic effects of verapamil. Side effects of verapamil are bradycardia, oedema, constipation, gastrointestinal discomfort, gingival hyperplasia, and dull headache. There is no evidence for the optimal way of dosing verapamil. An increase of 80 mg every 3 days is recommended. The full efficacy of verapamil can be expected within 2 to 3 weeks. Since verapamil is usually well tolerated, it is also drug of first choice for continuous treatment in chronic cluster headache. In the first 2 weeks of verapamil administration, corticosteroids are also administered by some clinicians. In two small open studies, nimodipine was also effective [61, 62].

There are insufficient randomized, placebo-controlled trials for the use of corticosteroids in cluster headache. Several open studies and case series have been published and reviewed by Ekbom [63]. All reported efficacy of corticosteroids given in different regimes (30 mg predni-

sone and higher; 2 × 4 mg dexamethasone per day). By expert consensus, steroids are recommended for short-term use over 2–3 weeks when rapid control of attacks is desired. However, some patients are attack-free only under steroids and rarely continuous administration of steroids is necessary. There is no evidence on which to use corticosteroids, although their high morbidity suggests caution, short courses, and avoidance in chronic cluster headache. For the beginning of corticosteroid treatment, prednisone 60–100 mg given once a day for at least 5 days is recommended, to be decreased by 10 mg every day. At high dose, about 70–80% of all cluster headache patients respond to steroids. Intravenous and oral application of steroids can successfully be combined [64]. In the experience of the task force, 500 mg methylprednisone intravenously for up to 5 days can be even more effective.

Lithium (given as lithium carbonate) has been studied in cluster headache prophylaxis in a daily dose between 600 and 1500 mg in more than 20 open trials reviewed by Ekbom [65]. An improvement in chronic cluster headache was reported to be as high as 78% (63% in episodic cluster headache). A recent placebo-controlled trial, however, did not show any efficacy of lithium in episodic cluster headache [66]. In a comparative, double-blind crossover study, lithium and verapamil showed similar efficacy with a more rapid improvement and better tolerability for verapamil [58]. Lithium should be monitored by the plasma level which should be between 0.3 and 1.2 mmol/l [67]. Regular control of liver, renal, and thyroid function and of electrolytes is required. Major side effects are hypothyroidosis, tremor, and renal dysfunction. Lithium is commonly used in cluster headache. This is, however, based on very small and open studies with the evidence being somewhat more convincing in chronic cluster headache. Therefore, lithium is recommended in particular for chronic cluster headache and only when other drugs are ineffective or contraindicated.

The antiserotonergic drug pizotifen (3 mg per day) has been shown to be effective in cluster headache prophylaxis in a single-blind, placebo-controlled older trial [68]. However, its use is limited by side effects such as tiredness and weight gain.

Methysergide has been recommended as prophylactic drug in episodic cluster headache [7, 63]. However, no placebo-controlled, double-blind studies are available.

The efficacy rates reported in open studies were reviewed by Ekblom [63]. The number of patients with a benefit of methysergide ranged between 20 and 73%; it was more effective in episodic cluster headache. The doses applied in the open studies varied from 4 mg to 16 mg. In the experience of the task force, methysergide can be given in a daily dose of up to 12 mg (starting with 1 mg per day). Since there is small but important incidence of pulmonary and retroperitoneal fibrosis, the continuous use of methysergide is limited to a maximum of 6 months.

Valproic acid has been studied in two open trials with acceptable results [69, 70] and in one controlled study in which it did not differentiate from placebo [71]. The objective evidence, and our experience, is that valproic acid is generally ineffective in cluster headache but can be tried as drug of third choice in a daily dose between 5 and 20 mg per kg body weight.

Open studies suggest that topiramate [72–74] and gabapentin [75] are effective in the prophylaxis of cluster headache. The recommended dose is at least 100 mg per day, the starting dose should be 25 mg. Main side effects are cognitive disturbances, paraesthesias, and weight loss. It is contraindicated in nephrolithiasis.

The pre-emptive use of 5-HT<sub>1B/D</sub> agonists (triptans) in cluster headache remains controversial. Oral sumatriptan (100 mg) given three times a day were not effective in preventing cluster headache attacks in a placebo-controlled trial [76]. In open trials, 40 mg eletriptan per day [77] or 2.5–5 mg naratriptan per day [78] reduced the number of cluster headache attacks.

For the ipsilateral intranasal application of capsaicin, two open [79, 80] and one double-blind, placebo-controlled [81] trials have been published showing an efficacy in about two-thirds of patients after repeated application. Intranasal application of civamide showed a modest efficacy in a recent double-blind, placebo-controlled study [82]. Although such studies are claimed to be blinded, this is a major design issue given the irritating nature of the nasally applied treatment.

Oral melatonin 10 mg was effective in a single double-blind, placebo-controlled study [83]. In cluster headache refractory to other medication, however, melatonin used open-label did not produce any additional efficacy [84].

There is very weak evidence from a small open study for the efficacy of baclofen 15–30 mg [85], and insufficient evidence for the efficacy of botulinum toxin [86] or transdermal clonidine [87] in the prophylactic treatment

of cluster headache. These approaches in our experience offer nothing useful to patients with cluster headache.

Hyperbaric oxygen inhalation was suggested to be effective as prophylaxis in an open trial [88]. However, a more recent placebo-controlled, double-blind trial could not confirm that hyperbaric oxygen is effective in preventing cluster headache attacks [89].

There is no evidence for a superiority of combined prophylactic drug treatment in cluster headache, although this question has not been systematically studied.

### **Interventional and surgical treatment**

It has been observed that greater occipital nerve blockade resulted in a significant reduction of cluster headache attacks in up to two-thirds of patients [90, 91] or less [92]. This finding confirmed previous observations but needs to be replicated in controlled trials. Also, suboccipital injection of short- and long-acting steroids was shown to be effective in the prophylaxis of cluster headache in a double-blind, placebo-controlled trial [93, 94].

If all drugs are ineffective, contraindicated, or not tolerated, and a secondary cluster headache has been excluded, surgical treatment can be discussed. Surgical procedures should be approached with great caution because no reliable long-term observational data are available and because some procedures can induce trigeminal neuralgia or anaesthesia dolorosa [63]. Unlike in trigeminal neuralgia, surgical treatment of cluster headache is not a causal therapy and continuation of cluster headache after the procedure is observed regularly. Different methods have been suggested to prevent cluster headache: application of glycerol or local anaesthetics into the cisterna trigeminalis of the Gasserian ganglion [95]; radiofrequency rhizotomy or gamma knife treatment of the Gasserian ganglion [96] or of the trigeminal nerve [97]; microvascular decompression [98]; resection or blockade of the N. petrosus superficialis [99] or of the ganglion sphenopalatinum [100, 101]. However, there are also case reports on different surgical procedures [102–104] and one prospective study on gamma knife treatment [105, 106] showing long-term inefficacy of surgical treatment in TACs.

Given that trigeminal destructive procedures have certain morbidity and that nerve root section has a well-described morbidity, the task force sees these procedures as supplanted by neuromodulatory procedures. Deep brain stimulation of the posterior inferior hypothalamus

has been shown to be effective in about half or more of patients with intractable cluster headache [107–111]. This method is only useful for prevention, not for acute attack abortion [112]. Also, electrical stimulation of the greater occipital nerve has been described as efficacious in intractable chronic cluster headache in open-label studies [113–115]. These two methods appear to be the most promising as prospective therapeutic option in patients with otherwise intractable chronic cluster headache.

### Recommendations

*Level A* As first choice, acute attacks of cluster headache should be treated with the inhalation of 100% oxygen with at least 7 l/min over 15 min (Class II trials) or with the subcutaneous injection of 6 mg sumatriptan or the intranasal application of zolmitriptan 5 mg (Class I trials). As second choice, sumatriptan 20 mg nasal spray can be used (Class I trial with minor efficacy or more side effects).

Prophylaxis of cluster headache should be first tried with verapamil in a daily dose of at least 240 mg (maximum dose depends on efficacy or tolerability; ECG controls are obligatory with increasing doses). Although no Class I or II trials are available, steroids are clearly effective in cluster headache. Therefore, the use of at least 100 mg oral up to 500 mg i.v. per day methylprednisone (or equivalent corticosteroid) over 5 days (then tapering down) is recommended.

*Level B* Intranasal lidocaine (4%) can be tried in acute cluster headache attacks if Level A medication is ineffective or contraindicated. Oral zolmitriptan 10 mg is effective in some patients (Class I trial but high dose produces many side effects and limits practical use).

Methysergide and lithium are drugs of second choice if verapamil is ineffective or contraindicated. Corticosteroids can be used for short courses where bouts are short or to help establish another medicine. Topiramate is promising but only open trials exist at this point. Melatonin is useful in some patients. Except for lithium, the maximum dose depends on efficacy and tolerability. Ergotamine tartrate is recommended in short-term prophylaxis (Class III studies). In spite of positive Class II studies, pizotifen and intranasal capsaicin should not be used because of side effects.

*Level C* Baclofen 15–30 mg and valproic acid showed possible efficacy and can be tried as drugs of third choice. Surgical procedures are not indicated in most patients with cluster headache. Patients with intractable chronic cluster headache should be referred to centres with expertise in both destructive and neuromodulatory procedures to be offered all reasonable alternatives before a definitive procedure is conducted.

## Treatment of paroxysmal hemicrania

By definition, indomethacin in a daily dose of up to 200 mg is completely effective [116–118]. For the same reason, no placebo-controlled trials exist. Indomethacin should be administered in three or more doses per day because of its short half-life time of 4 h. Many patients need a high dose of indomethacin only in the first weeks of treatment, then a lower dose can be tried. Very rarely, doses higher than 200 mg per day are required. The major contraindication is a gastrointestinal disorder. Gastrointestinal discomfort and bleedings are the major side effects. Therefore, a proton pump inhibitor should be given in addition. For diagnostic and rapid therapeutic purposes, the so-called indo-test has been suggested [119]. Intramuscular indomethacin 50 mg should result in freedom of attacks within 30 min.

There is no drug of similar efficacy to indomethacin for the treatment of paroxysmal hemicrania. However, open studies (Class IV) suggest a moderate efficacy of alternative drugs if indomethacin is not tolerated. The best evidence in these open studies has been observed for verapamil [118, 120]. Fewer positive reports have been published for acetazolamide [121], topiramate [122, 123], and the NSAIDs piroxicam [124] and acetylsalicylic acid [14, 118]. Subcutaneous sumatriptan is ineffective [125]. Anaesthetic blockades of pericranial nerves [126] are said to be ineffective, although one of us has seen excellent response to greater occipital nerve blockade.

In summary, paroxysmal hemicrania is to be treated with indomethacin up to 200 mg (Level A recommendation). Alternatively, verapamil, topiramate, and different NSAIDs can be tried (Level C recommendation).

## Treatment of SUNCT syndrome

There is no consistently effective treatment known for SUNCT syndrome, including high doses of indomethacin and anaesthetic blockades [127]. No controlled trials have been published, and the rareness of the syndrome makes this a difficult task. However, some case reports have been published with individual efficacy of some drugs. Because of the extreme burden caused by this disorder, all reasonable treatment options should be tried.

Among all drugs tried in SUNCT syndrome, lamotrigine was most efficacious in the published case reports

(however, the majority of patients did not respond to this drug) [128–130]. Other treatment options include gabapentin [131–133], topiramate [28, 134], oxcarbazepine [135], verapamil [136], intravenous lidocaine [137], steroids [138], and intravenous phenytoin [139]. In part, these drugs were applied in combination.

Recently, also in SUNCT syndrome, stimulation of the hypothalamus has been described as efficacious in some cases [140, 141].

In summary, no recommendation can be given for the treatment of SUNCT syndrome. Treatment with lamotrigine (at least 100 mg) is considered the first-line option.

### Conflicts of interest

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