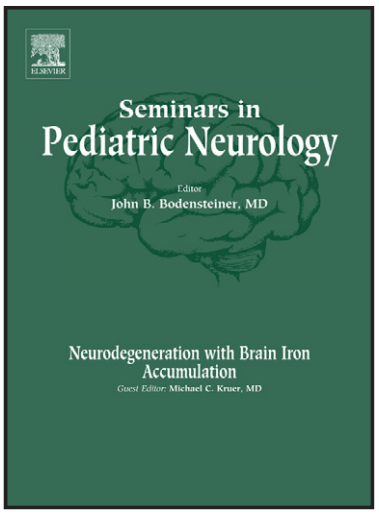

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Trigeminal Autonomic Cephalalgias in Children and Adolescents

Cluster Headache and Related Conditions

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Abstract

Cluster headache is a primary headache disorder that can occur in children and adolescents, and is a member of the broader diagnostic group of Trigeminal Autonomic Cephalalgias (TACs). It is characterized by repeated attacks typically lasting between 15-180 minutes of severe unilateral side-locked headache with cranial autonomic features. Acute treatment of the cluster attack can include the use of triptans or high flow oxygen. Preventive measures typically start with the use of verapamil. The other TACS, paroxysmal hemicrania and SUNCT/SUNA, have also been reported in children, and should be considered when the clinical presentation is at all unusual.

Headache is a common childhood complaint. Headache disorders can be divided into primary, of which the most disabling in childhood years is typically migraine, and secondary, which are due to an underlying disease. Trigeminal autonomic cephalalgias (TACs) are a group of primary headache disorders that are about one hundred times less common than migraine. TACs are characterized by repetitive, relatively brief episodes of severe unilateral pain associated with ipsilateral cranial autonomic features including rhinorrhea, nasal congestion, lacrimation and conjunctival injection. They include cluster headache, paroxysmal hemicrania and SUNCT/SUNA syndrome (short-lasting unilateral neuralgiform headache with conjunctival injection and tearing/cranial autonomic features). Hemicrania continua is considered a TAC although the pain itself is continuous. They each differ in the duration, frequency and rhythmicity of attacks. All are reported more commonly in adults, but do occur in children, although as with much in pediatric neurology, the syndromes can be less well developed such that clinical vigilance is required to make the diagnoses[1].

Cluster Headache

Cluster headache is the most common TAC. The prevalence in adults is less than 1 percent and has a male predominance[2]. The prevalence in childhood and adolescence has been estimated to be 0.1 %, based on a study of 18 year old Swedish men[3]. Studies have noted childhood onset at ages between 5 and 19 years. The current concept of cluster headache is as a central nervous system disorder involving an interaction between diencephalic pain modulatory centers in the hypothalamic region and the cranial autonomic outflow[4]. Symptoms include several headache

episodes per day, generally with circadian rhythmicity and often waking the patient from sleep[5], although without any predilection for sleep stage[6]. The attacks come in bouts lasting weeks in duration, the pattern giving rise to the term "cluster". The headache is a severe, unilateral orbital, supraorbital or temporal head pain lasting 15 minutes to 3 hours with associated unilateral autonomic features and associated restlessness[1]. An important differential diagnosis in childhood that is not so clearly seen in adults is of primary stabbing headache, severe, spontaneous jabs of pain lasting seconds to a few minutes that are without cranial autonomic symptoms[1]. It is our experience that this syndrome can be very much more disabling with very frequent attacks in children; it is responsive to indomethacin.

Just as with adults, children may experience thrashing about or emotional outbursts during the attack, which may well be driven by the brain area involved in the disorder[7]. When the bout are separated by a month, the disorder is labelled episodic cluster headache, while without a break the term applied is chronic cluster headache. There is a familial predisposition at a population level[8]. The diagnosis is made clinically. Neuroimaging should be considered in side-locked headaches to exclude an underlying brain lesion, with particular emphasis on the pituitary and cavernous sinus region[9]. Cluster headache can be difficult to differentiate from migraine since migraine attacks may have cranial autonomic symptoms[10] and cluster headache patients may have photophobia and phonophobia[11]. Lateralization of symptoms in TACs generally, and certainly in cluster headache, is a god pointer to the diagnosis. In TACs photophobia and phonophobia when present tends to lateralize to the side of pain[12], as do the cranial autonomic symptoms[13]. Typically, the childhood migraineur will have a bilateral or alternating unilateral

headache with nausea, bilateral photophobia, sometimes evidenced by the child seeking relief by sleep in a dark room, and when present bilateral, les prominent, cranial autonomic features. .

Trigger factors for cluster headache in adults can include alcohol, volatile chemicals or a warm environment.[14] In children, a warm environment and second hand smoke exposure are .

In adults, acute therapy can include the use of oxygen at a rate of 12-15 liters per minute for at least 15 minutes using a nonrebreather mask[15]. Triptans are a mainstay of acute therapy. Controlled trials in adults have investigated the efficacy of subcutaneous sumatriptan[16,17], nasal sumatriptan[18] and nasal zolmitriptan[19,20] in acute cluster headache. Regular use of oral sumatriptan is ineffective[21], and medication overuse headache is a recognized issue with oral triptans in cluster headache[22]. Our experience is that these triptans are also useful in pediatric and adolescent cluster headache.

In patients with episodic cluster headache where the bout length is limited, transitional preventive medications may be useful. Greater occipital nerve injection with lidocaine (2%) and depo-methylprednisolone can foreshorten the bout without any other treatment and is very well tolerated even in the young[23]. Some would use an oral corticosteroid taper, as is done in adults,[14] we find this less attractive in children. When a preventive medication is required for longer bouts of episodic cluster headache or for chronic cluster headache, verapamil is the preferred choice[14]. Cluster headache patients often require substantial doses ranging between 3-10 mg/kg/day, most likely due to the fact that the action is within the brain and verapamil is a P-glycoprotein pump

substrate[24]. For most patients with cluster headache ECG monitoring for PR interval prolongation will be required[25]. In childhood melatonin or topiramate are reasonable alternatives.

Paroxysmal Hemicrania and SUNCT/SUNA Syndrome

Paroxysmal hemicrania is said to be rare in children, although there are no data available and in specialist clinics their frequency seems similar to what can be seen in comparable adult clincis.. Attacks of unilateral, often stabbing, headaches are shorter (2-30 minutes), and more frequent (typically more than five per day) than in cluster headaches[26]. These headaches are exceptionally responsive to treatment with indomethacin[27]. In adult patients, a typical indomethacin trial begins with 25 mg daily for each of three days, then if needed the dose is increased to 50 mg three times a day for three days, and if the patient still has not responded, then going to 75 mg three times a day for two weeks. Within this trial, one can typically determine indomethacin responsiveness. Indomethacin is continued at the lowest effective dose for the shortest time possible.

SUNCT/SUNA syndrome is also said to be rare in children, although there are no epidemiological data available. Attacks are very short in duration (seconds to minutes), triggered by touching the face or chewing, have limited associated autonomic features and occur up to hundreds of times per day[28]SUNCT/SUNA most often responds to lamotrigine[29]. There is some limited controlled trial evidence for the use of topiramate in SUNCT[30].

Table 1 International Classification of Headache Disorders-3: Diagnostic Criteria for Cluster Headache[1]

A. At least five attacks fulfilling criteria B–D

B. Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15–180 minutes (when untreated)

C. Either or both of the following:
   1. at least one of the following symptoms or signs, ipsilateral to the headache:
      a) conjunctival injection and/or lacrimation
      b) nasal congestion and/or rhinorrhoea
      c) eyelid edema
      d) forehead and facial sweating
      e) forehead and facial flushing
      f) sensation of fullness in the ear
      g) miosis and/or ptosis
   2. a sense of restlessness or agitation

D. Attacks have a frequency between one every other day and eight per day for more than half of the time when the disorder is active

E. Not better accounted for by another ICHD-3 diagnosis.

Table 2: Acute Treatment Options for Pediatric Cluster Headache		
Medication	**Typical dose**	**Side effects**
Sumatriptan or Zolmitriptan	Children over the age of 10 years and 50 kg typically tolerate 20 mg nasal Sumatriptan: Children 6-10 years should first start with the 5 mg nasal spray form of Sumatriptan	Paresthesias, chest tightness, worsening headache
Oxygen 100%	High flow at 12 liters/minute with a rebreathing mask	Headache may return if oxygen is discontinued. Consider concurrent use of triptan.

Table 3: Cluster Headache: Suggested Preventive Agents		
Medication	**Typical Target Dose**	**Side Effects/Monitoring**
Verapamil	3 to 10 mg/kg/day; Typical adult dose is 240 to 960mg/day	Constipation; dizziness; need to follow EKG (AV block) at higher doses
Melatonin	0.1-0.2 mg/kg/day Typical adult dose is 8-15 mg/day	Sleepiness
Topiramate	1-2 mg/kg/day. Typical adult dose is at least 100 mg daily	Cognitive concerns, weight loss, renal stones, decreased sweating

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