

## **Administración de litio para la prevención de cefaleas en racimos episódicas**

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Stochino ME, Deidda A, Asuni C, Cherchi A, Manchia M, Del Zompo M

El litio permitiría prevenir las cefaleas en racimos episódicas en numerosos pacientes, según un estudio italiano publicado en *Headache*. El litio es un tratamiento de segunda línea al verapamilo en la prevención de la cefalea en racimos por su reducida ventana terapéutica y los efectos adversos potencialmente graves que puede provocar.

El equipo evaluó la respuesta clínica al tratamiento con litio y su tolerancia en la prevención de la cefalea en racimos episódica en un estudio retrospectivo sobre 26 pacientes. Las dosis utilizadas fueron de 450-1.050 mg/día. Veinte pacientes (77%) redujeron al menos en un 50% la frecuencia de los ataques, por lo que se consideró que habían respondido al tratamiento, mientras que 6 pacientes (23%) no alcanzaron dicha mejoría. Quince de los pacientes que respondieron al litio mejoraron significativamente al final de la primera semana de tratamiento y los cinco restantes lo hicieron en la segunda semana. El número medio de ataques al día mejoró significativamente: de 1,8 al inicio del estudio a 1,1 al final de la primera semana y 0,6 al terminar la segunda semana. Cinco pacientes no tuvieron un ataque en la primera semana y 12 en la segunda semana de tratamiento. Tres pacientes mejoraron parcialmente durante el estudio. Cuatro pacientes tuvieron efectos adversos: tres desarrollaron poliuria y dos, polidipsia. Los efectos adversos fueron leves y no hubo que suspender el tratamiento.

Los investigadores están realizando un estudio prospectivo para determinar la efectividad y tolerabilidad a largo plazo del litio y el verapamilo en la prevención de la cefalea en racimos episódica.

## **Cluster headache: conventional pharmacological management**

Becker WJ: *Headache*. 2013 Jul-Aug;53(7):1191-6.

Cluster headache pain is very intense, usually increases in intensity very rapidly from onset, and attacks are often frequent. These clinical features result in significant therapeutic challenges. The most effective pharmacological treatment options for acute

cluster attack include subcutaneous sumatriptan, 100% oxygen, and intranasal zolmitriptan. Subcutaneous or intramuscular dihydroergotamine and intranasal sumatriptan are additional options. Transitional therapy is applicable mainly for patients with high-frequency (>2 attacks per day) episodic cluster headache, and options include short courses of high-dose oral corticosteroids, dihydroergotamine, and occipital nerve blocks with local anesthetic and steroids. Prophylactic therapy is important both for episodic and chronic cluster headache, and the main options are verapamil and lithium. Verapamil is drug of first choice but may cause cardiac arrhythmias, and periodic electrocardiograms (EKGs) during dose escalation are important. Many other drugs are also in current use, but there is an insufficient evidence base to recommend them.

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## **Evaluation of lithium response in episodic cluster headache: a retrospective case series**

*Stochino ME, Deidda A, Asuni C, Cherchi A, Manchia M, Del Zompo M: Headache. 2012 Jul-Aug;52(7):1171-5.*

**OBJECTIVE:** In this study, we attempted to evaluate the response to lithium treatment and its tolerability in the prevention of episodic cluster headache (CH) and to identify clinical predictors of response.

**BACKGROUND:** Verapamil and lithium are the most widely used drugs in the prevention of CH attacks. Lithium is considered a second-line treatment in part because of its potentially severe adverse drug reactions (ADRs). Evidence for the efficacy of lithium in CH prevention is greater in chronic than in episodic patients. In addition, because of its narrow therapeutic window and ADRs (which can be significantly reduced with proper periodical monitoring of blood levels), lithium is recommended only in chronic CH, when other drugs are ineffective or potentially harmful.

**METHODS:** Our primary aim was to determine whether lithium reduced the number of attacks per day (attack frequency). We compared attack frequency in 3 periods: run-in, the first, and the second week of lithium treatment. Responders were defined as patients showing at least a 50% reduction in attack frequency.

**RESULTS:** Lithium response was evaluated in 26 patients. Treatment led to a significant reduction in attack frequency within 2 weeks in a percentage of 77% of responders and

23% of nonresponders. Responders and nonresponders did not differ in terms of demographic and clinical characteristics. Only 15% of patients experienced mild ADRs.

**CONCLUSION:** Our study provides additional evidence on the effectiveness of lithium in the prevention of episodic CH. It also shows the tolerability of lithium, given the short duration of treatment and low dosage.

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## **Management of cluster headache**

*Tfelt-Hansen PC, Jensen RH: CNS Drugs. 2012 Jul 1;26(7):571-80.*

The prevalence of cluster headache is 0.1% and cluster headache is often not diagnosed or misdiagnosed as migraine or sinusitis. In cluster headache there is often a considerable diagnostic delay - an average of 7 years in a population-based survey. Cluster headache is characterized by very severe or severe orbital or periorbital pain with a duration of 15-180 minutes. The cluster headache attacks are accompanied by characteristic associated unilateral symptoms such as tearing, nasal congestion and/or rhinorrhoea, eyelid oedema, miosis and/or ptosis. In addition, there is a sense of restlessness and agitation. Patients may have up to eight attacks per day. Episodic cluster headache (ECH) occurs in clusters of weeks to months duration, whereas chronic cluster headache (CCH) attacks occur for more than 1 year without remissions. Management of cluster headache is divided into acute attack treatment and prophylactic treatment. In ECH and CCH the attacks can be treated with oxygen (12 L/min) or subcutaneous sumatriptan 6 mg. For both oxygen and sumatriptan there are two randomized, placebo-controlled trials demonstrating efficacy. In both ECH and CCH, verapamil is the prophylactic drug of choice. Verapamil 360 mg/day was found to be superior to placebo in one clinical trial. In clinical practice, daily doses of 480-720 mg are mostly used. Thus, the dose of verapamil used in cluster headache treatment may be double the dose used in cardiology, and with the higher doses the PR interval should be checked with an ECG. At the start of a cluster, transitional preventive treatment such as corticosteroids or greater occipital nerve blockade can be given. In CCH and in long-standing clusters of ECH, lithium, methysergide, topiramate, valproic acid and ergotamine tartrate can be used as add-on prophylactic treatment. In drug-resistant CCH, neuromodulation with either occipital nerve stimulation or deep brain stimulation of the hypothalamus is an alternative treatment strategy. For most cluster headache patients there are fairly good treatment options both for acute attacks and for prophylaxis. The big problem is the diagnosis of cluster headache as demonstrated by the diagnostic delay of 7

years. However, the relatively short-lasting attack of pain in one eye with typical associated symptoms should lead the family doctor to suspect cluster headache resulting in a referral to a neurologist or a headache centre with experience in the treatment of cluster headache.