

Migraine in patients with cluster headache

Poul Gertz Andersson

CEPHALALGIA Andersson PG. Migraine in patients with cluster headache. *Cephalalgia* 1985;5:11-16. Oslo. ISSN 0333-1024

One hundred and twenty seven patients with cluster headache have been compared with 122 patients with migraine. Twenty of the patients with cluster headache have had migraine attacks but only 2 still have migraine attacks after the onset of cluster headache. No migraine patients had cluster headache. Among the 127 patients with cluster headache, one of the parents suffered from cluster headache in 4.7% of the cases. Among the 122 patients with migraine, 0.8% had a parent with cluster headache. Among the 122 patients with migraine 54.9% had parents with migraine, and in the cluster headache group 23.8% of the patients had one parent with migraine. The coexistence of migraine and cluster headache is rare. The two types of headache, as far as the heredity pattern is concerned, are independent entities. *Z* • *Cluster headache, heredity, migraine.*

Poul Gertz Andersson, Neurologic Clinic, Hovedgaden 63, DK-8220 Brabrand, Denmark; Accepted 1984 10 27

"Mild" cluster headache(?)

O Sjaastad, D de Souza Carvalho, Jing-Ming Zhao

CEPHALALGIA Sjaastad O, de Souza Carvalho D, Zhao J-M. "Mild" cluster headache(?). *Cephalalgia* 1988;8:121-126. Oslo. ISSN 0333-1024

Three cases of what *could* be considered "mild" cluster headache have been described. All three patients were generally able to carry out their work during attacks; all three were men and had unilateral headache with the predominant pain in the ocular region. Relatively few symptoms and signs indicated autonomic system involvement, but at least tearing was invariably present on the symptomatic side. The bouts were generally short-lasting in two of the patients (and partly in the third one), fitting the pattern of "mini-bouts". Thus, in one of the cases *four* of the five major criteria (male sex, excruciating severity, cluster phenomenon, autonomic involvement, and unilaterality) were present. In the two other patients the full-blown cluster phenomenon was lacking. Such cases *may* represent the left-side slope of a "Gaussian severity distribution scale" with regard to cluster headache. • *Autonomic function studies, chronic paroxysmal hemicrania, cluster headache, pupils, sweating*

O Sjaastad, D de Souza Carvalho, J-M Zhao, Department of Neurology, Regionsykehuset i Trondheim, Trondheim University Hospital, N-7000 Trondheim, Norway; Correspondence to O Sjaastad; Accepted 2 March 1988

New-onset cluster headache in middle-age and elderly women

A Mosek, R Hering-Hanit* & A Kuritzky†

Department of Neurology, Headache Clinics, Sourasky Medical Center, Td Aviv, *Meir Medical Center, Kfar Saba, †Rabin Medical Center, Petah Tikva, Israel

Cephalalgia

Mosek A, Hering-Hanit R, Kuritzky A. New-onset cluster headache in middle-age and elderly women. *Cephalalgia* 2001; 21:198–200. London. ISSN 0333-1024

Cluster headache is usually considered to affect young men. We hereby report on new-onset cluster headache in middle-aged and elderly women. We performed a retrospective chart review of female patients diagnosed with cluster headache (IHS criteria), and studied the charts of women in whom the headache started after the age of 50 years. Out of 168 patients (26 women, 15%) diagnosed with cluster headache, the headache started after the age of 50 years in seven women, of whom three reported past tension-type or migraine headaches. The mean age at the beginning of the headache was 61 ± 8 years (range 52–72 years). In all cases, the pain was severe, strictly unilateral, and accompanied by at least one autonomic symptom. The average duration of the pain was 70 min (range 20 min–3 h), recurring daily for an average period of 7 weeks (range 1–16 weeks). Five patients had 1–2 pain attacks each day, while the other two experienced up to eight episodes of pain in 1 day. In two patients the periodicity of the pain was currently undetermined. In the remainder, the headache periods recurred every 1–4 years. Cluster headache is commonly considered to be a young-male disorder, but middle-aged and elderly women may also be affected. The characteristics of the pain and its manner of occurrence were similar in our cases to those reported in the young-male population. □ *Cluster headache, women, elderly*

Amnon Mosek, The Department of Neurology, Sourasky Medical Center, 6 Weizmann Street, Aviv 64239, Israel. Tel. +972 3 6974874, fax +972 3 6974872, e-mail mosek@zahav.net

Received 17 May 2000, accepted 19 February 2001

Cluster headache associated with sleep apnoea

ME Nobre, PFM Filho & M Dominici¹

Universidade Federal Fluminense and ¹Sleep Laboratory, Rio de Janeiro, Brasil

Cephalalgia

Nobre ME, Filho PFM & Dominici M. Cluster headache associated with sleep apnoea. *Cephalalgia* 2003; 23:276–279. London. ISSN 0333-1024

This study of sleep changes in patients with cluster headache (CH) was conducted in view of the nocturnal predominance of this condition, the efficacy of oxygen and the fact that the attacks follow oxygen desaturation. Proposed mechanisms include impairment of carotid body activity secondary to hypothalamic vasomotor regulatory dysfunction. Sixteen patients with episodic CH and 29 healthy volunteers underwent nocturnal polysomnography. Five (31.3%) patients with episodic CH were found to have sleep apnoea (SA). Two patients with SA experienced two attacks during the study period. The attacks followed episodes of oxygen desaturation and were associated with REM sleep. In two patients with SA and CH, treatment with continuous positive airway pressure abolished their oxygen desaturation, sleep apnoeas and headaches. Our study confirmed the high percentage of CH associated with SA. We suggest that oxygen desaturation may be a trigger factor in some patients and play a role in the pathogenesis of CH. ▯ *Cluster headache, desaturation, sleep apnoea*

Maria Eduarda Nobre MD, Avenue. das Américas 1155, sala 506, Barra da Tijuca, Rio de Janeiro RJ, Brazil. Tel. (21) 2439 9293, fax (21) 2484 4608, e-mail

eduarda@imagelink.com.br Received 26 February 2001, accepted 6 September 2002

C Sjöstrand, MB Russell¹, K Ekblom, J Hillert & E Waldenlind

Department of Neurology, Karolinska Institute, Karolinska University Hospital, Huddinge, Sweden, and ¹Department of Neurology, Akershus University Hospital, Oslo, Norway

Cephalalgia

Sjöstrand C, Russell MB, Ekblom K, Hillert J & Waldenlind E. Familial cluster headache. Is atypical cluster headache in family members part of the clinical spectrum? *Cephalalgia* 2005; 25:1068–1077. London. ISSN 0333-1024

Familial cluster headache (CH) was analysed in 21 Swedish families. Diagnosis was made according to The International Classification of Headache Disorders 2004. We identified 55 affected, of whom 42 had episodic or chronic CH, one had probable CH and 12 had atypical symptoms. The atypical cases did not fulfil the diagnostic criteria for CH, but had clinical symptoms with more resemblance to CH than to migraine or other trigeminal autonomic cephalgia syndromes. The overall male : female ratio was 1.8 : 1. The overall mean age at onset was significantly lower in the second/third generation than in the first generation (mean age at onset 22 vs. 31 years, SD ± 7 vs. 13 years; $P < 0.01$). This may be anticipation or selection bias, since individuals with late age at onset from the second/third generation may not yet have symptoms. The prevalence of migraine was 24% (13/55), i.e. similar to the prevalence in the general population. The high incidence of atypical CH cases in the Swedish families with other members affected with CH may suggest that the spectrum of CH is broader than previously thought. We suggest that atypical CH in CH families may represent an expanded spectrum of the disease with a common aetiology, i.e. a common genetic background. □ *Atypical cluster headache, cluster headache, genetics and clinical symptoms*

Christina Sjöstrand MD, Department of Neurology, R 52, Karolinska University Hospital, Huddinge, S-141 86 Stockholm, Sweden. Fax: +46 8 585 870 80, e-mail: christina.sjostrand@neurotec.ki.se Received 5 November 2004. accepted 28 January 2005

Cluster Headache Following Head Injury:

A Case Report and Review of the Literature

L. Jay Turkewitz, M.D.^{1,2}, Oliver Wirth, B.A.¹, Gregory A. Dawson, Ph.D.^{1,3}, Joseph S. Casaly, M.D.¹

¹Midwest Center for Head-Pain Management, Troy, Ohio

²Wright State University Department of Neurology, Dayton, Ohio

³Wright State University School of Professional Psychology, Dayton, Ohio

Address all correspondence to: Dr. L. Jay Turkewitz, Midwest Center for Head-Pain Management, 550 Summit Avenue, Suite B, Troy, OH 45373

Accepted for publication: August 31, 1992

SYNOPSIS

A relation between head trauma and cluster headache is frequently described in the literature. The percentage of cluster patients with a history of head injury is approximately 16.5 when several large studies are reviewed. The present paper reports another case where there is close proximity between head injury and the onset of cluster headache. A review of the literature attempts to document the supposition that there is indeed a causal or precipitous role for head injury in cluster cephalgia pathogenesis.

Key Words: cluster headache, head trauma, review

(*Headache* 1992; 32:504-506)

Brief Communications

Treatment of Cluster Headache Attacks With Less Than 6 mg Subcutaneous Sumatriptan

Nora Gregor, MD; Christian Schlesiger, MD; Esra Akova-Öztürk, MD; Christoffer Kraemer, MD; Ingo-Wilhelm Husstedt, MD; Stefan Evers, MD, PhD

Background.—Subcutaneous (SQ) sumatriptan 6 mg is effective in the treatment of acute cluster headache attacks. However, patients sometimes benefit from a dose less than 6 mg.

Objective.—Therefore, we designed a prospective open study to evaluate how many patients benefit from a dose less than 6 mg SQ sumatriptan.

Methods.—We enrolled 81 consecutive patients with cluster headache and recorded their use of SQ sumatriptan and oxygen. Patients regularly using SQ sumatriptan 6 mg were advised to treat attacks with doses less than 6 mg and with oxygen. Efficacy and side effects of the different treatment options (6 mg, 3 mg, 2 mg, and oxygen) were evaluated.

Results.—As a result, 74% of the patients using SQ sumatriptan 3 mg showed efficacy and 89% reported efficacy after 2 mg. Seventy-nine percent reported side effects after the use of SQ sumatriptan 6 mg (29% severe side effects). After the use of 2 mg SQ sumatriptan, only 50% of the patients reported side effects, none of these were classified as severe. Patients' preference was 41% for 6 mg sumatriptan, 28% for doses less than 6 mg, and 31% for oxygen.

Conclusions.—We conclude that sumatriptan in doses less than 6 mg can be effective in the acute treatment of cluster headache attacks. We suggest that patients should have experience in their individual efficacy of sumatriptan doses less than 6 mg.

Key words: cluster headache, sumatriptan, oxygen

(*Headache* 2005;45:1069-1072)

Cluster headache in women: Clinical findings and relationship with reproductive life

Gian Camillo Manzoni, Giuseppe Micieli, Franco Granella, Emilia Martignoni, Stefano Farina, Giuseppe Nappi

CEPHALALGIA Manzoni GC, Micieli G, Granella F, Martignoni E, Farina S, Nappi G. Cluster headache in women: Clinical findings and relationship with reproductive life. *Cephalalgia* 1988;8:37-44. Oslo. ISSN 0333-1024

Cluster headache (CH) occurs rarely among women; for this reason only a limited number of studies have been reported on the characteristics of the disease in the female population. In this study, 82 females (age range, 14-72 years) with episodic (69 cases) or chronic (13 cases) CH were investigated. The clinical features of headache and the physiologic events related to reproductive life were compared with those of various control groups. We did not find any remarkable differences in clinical features between men and women. Unlike other forms of primary headache, the course of CH does not seem to be modified by menstruation, pregnancy, or puerperium. Finally, our data seem to confirm a hypofertility trend, mostly after onset of CH, which had previously been noticed by other authors. • *Cluster headache, headache, migraine, reproductive life*

Studies on nitroglycerin and histamine provoked cluster headache attacks

Andrzej Bogucki

CEPHALALGIA Bogucki A. Studies on nitroglycerin and histamine provoked cluster headache attacks. Cephalalgia 1990;10:71-5, Oslo. ISSN 0333-1024

Attacks of cluster headache provoked by the administration of nitroglycerin (1 mg sublingually) or histamine (0.01 mg/kg subcutaneously) were studied. The constant latency time in individual patients during nitroglycerin and histamine provocation suggested that the same mechanism is involved in both methods of headache induction. Repeated nitroglycerin provocation revealed its tendency to lengthen duration of the refractory period at the end of the bout, when the attacks were less frequent. The "cross studies" on spontaneous and nitroglycerin provoked attacks indicated that the underlying mechanism of both is at least partially the same. • *Cluster headache, histamine, nitroglycerin, provocation*

CACNA1A gene polymorphisms in cluster headache

C Sjöstrand, V Giedratis, K Ekblom, E Waldenlind & J Hillert

Department of Neurology, Karolinska Institute, Huddinge University Hospital, Huddinge, Sweden

Cephalalgia

Sjöstrand C, Giedratis V, Ekblom K, Waldenlind E & Hillert J. CACNA1A gene polymorphisms in cluster headache. Cephalalgia 2001; 21:953-958. London. ISSN 0333-1024

Cluster headache (CH) is a primary headache disorder where the aetiological and pathophysiological mechanisms still are largely unknown. An increased risk of CH in first- and second-degree relatives suggests the importance of genetic factors. Mutations of the P/Q type calcium channel alpha 1 subunit (CACNA1A) gene on chromosome 19p13 have been shown to cause several neurological disorders with a wide clinical spectrum, mainly episodic diseases. Missence mutations of the gene cause familial hemiplegic migraine (FHM) and it is also likely to be involved in the more common forms of migraine. The CACNA1A gene is thus a promising candidate gene for CH. In this study we performed an association analysis of an intragenic polymorphic (CA)_n-repeat with marker D19S1150 and a (CAG)_n-repeat in the 3'UTR region, in 75 patients with CH according to IHS criteria and 108 matched controls. Genotypes and allele frequencies were similarly distributed in patients and controls. Linkage disequilibrium between the two markers was similar in patients and controls. We conclude that an importance of the CACNA1A gene in sporadic CH is unlikely. □ *CACNA1A, cluster headache, genetics*

Cluster headache prevalence. Vågå study of headache epidemiology

O Sjaastad^{1,2} & LS Bakketeig³

¹Vågå Communal Health Centre, Vågåmo and ²Department of Neurology, St Olavs Hospital, Trondheim University Hospital, Trondheim, Norway, and ³University of Southern Denmark, Institute of Public Health, Epidemiology, Odense, Denmark

Cephalalgia

Sjaastad O & Bakketeig LS. Cluster headache prevalence. Vågå study of headache epidemiology. *Cephalalgia* 2003; 23:528–533. London. ISSN 0333-1024

In the Vågå study of headache epidemiology, a search was made also for cluster headache. Of the available 18–65-year-old dalesmen, 1838 (88.6%) could be examined personally (O.S.) – 51.3% females and 48.7% males. Based on current International Headache Society criteria, cluster headache seemed to be present in seven dalesmen, one female and six males (corresponding to a total prevalence of 381 per 100 000; 95% confidence interval (CI) 153–783 per 100 000). Except for the female gender, the female case was fairly typical. In one case, there were short-lasting bouts ('minibouts'). It was felt that this also was a genuine case of cluster headache. If one excluded the latter case, there would be one female and five males [a prevalence of 106 per 100 000 for females, and 558 per 100 000 for males, giving a prevalence in the total population of 326 per 100 000 (95% CI 120–709 per 100 000)]. The confidence interval was considerable. This study therefore does not give a clear indication as to prevalence. □ *Cluster headache, headache, headache epidemiology, headache prevalence*

Ottar Sjaastad, Department of Neurology, St. Olavs Hospital, N-7006 Trondheim, Norway. Tel. +47 73 52 52 76, fax +47 73 86 93 13. Received 12 March 2002, accepted 3 February 2003

Evaluating the IHS criteria for cluster headache – a comparison between patients meeting all criteria and patients failing one criterion

JA van Vliet^{1,4}, PJE Eekers^{2,†}, J Haan^{1,3}, MD Ferrari¹ for the Dutch RUSSH Study Group

¹Department of Neurology, Leiden University Medical Centre, Leiden, ²Department of Neurology, Atrium Hospital, Heerlen and ³Department of Neurology, Rijnland Hospital, Leiderdorp, The Netherlands

Cephalalgia

van Vliet JA, Eekers PJE, Ferrari MD & Haan J for the Dutch RUSSH Study Group. Evaluating the IHS criteria for cluster headache – a comparison between patients meeting all criteria and patients failing one criterion. *Cephalalgia* 2006; 26:241–245. London. ISSN 0333-1024

Cluster headache (CH) is diagnosed according to criteria of the International Headache Society (IHS), but, in clinical practice, these criteria seem too restrictive. As part of a nation-wide study, we identified a group of patients who met all criteria minus one (IHS-CH-1), and assessed in which way they differed from CH patients meeting all criteria (IHS-CH). We performed a nation-wide questionnaire study for CH and CH-like syndromes, including questions based on the IHS criteria, and additional features such as restlessness during attacks, nocturnal onset of attacks, circadian rhythmicity of attacks and response to treatment. IHS-CH and IHS-CH-1 patients were compared. Of 1452 responders to two questionnaires, 1163 were IHS-CH and 289 were IHS-CH-1. The majority of the IHS-CH-1 patients were classified as such because their attacks exceeded 3 h (64%, median attack duration: 5 h), or came in a frequency of less than 1 per 2 days (16%). Age at onset was similar between the groups. The male to female ratio was 3.7 : 1 in the IHS-CH group and around 1.6 : 1 in the IHS-CH-1 groups ($P < 0.005$). Patients with attacks exceeding 3 h less often reported a circadian rhythmicity (IHS-CH-1: 49%, IHS-CH: 64%), episodic periodicity (IHS-CH-1: 65%, IHS-CH: 78%), nocturnal attacks (IHS-CH-1: 67%, IHS-CH: 78%), smoking (IHS-CH-1: 90%, IHS-CH: 80%) and restlessness during attacks (IHS-CH-1: 64%, IHS-CH: 76%) than IHS-CH patients ($P < 0.005$). Photo- or phono-phobia (IHS-CH-1: 67%, IHS-CH: 54%) and nausea (IHS-CH-1: 38%, IHS-CH: 27%) were more frequently reported by patients who reported to have attacks exceeding 3 h ($P < 0.005$). Similar proportions reported effect of verapamil on their attacks (IHS-CH-1: 54%, IHS-CH 61%). We conclude that average attack duration exceeding 3 h was frequently the reason for not fulfilling IHS CH criteria. Symptoms often accompanying CH such as restlessness, nocturnal attacks and an episodic attack pattern were relatively frequently present in IHS-CH-1 patients with longer attacks. These patients may therefore be diagnosed with CH. Attack frequency may not be a useful criterion for the diagnosis of CH. The upper limit of 3 h should be increased in future diagnostic criteria. □ *Cluster headache, IHS criteria, evaluation, criteria*

Prof M.D. Ferrari, Department of Neurology, K5Q Leiden University Medical Centre, PO Box 9600, 2300 RC Leiden, the Netherlands. Tel. +31 71 5262895, fax +31 71 5248253, e-mail m.d.ferrari@lumc.nl Received 9 March 2003, accepted 5 November 2004

The G1246A polymorphism in the hypocretin receptor 2 gene is not associated with treatment response in cluster headache

M Schürks¹, T Kurth², I Geissler³, G Tessmann³, H-C Diener¹ & D Roszkopf³

¹Department of Neurology, University Hospital Essen, University Duisburg-Essen, Essen, Germany, ²Divisions of Preventive Medicine and Aging, Department of Medicine; Brigham and Women's Hospital; Harvard Medical School, and Department of Epidemiology, Harvard School of Public Health, Boston, MA, USA and ³Institute of Pharmacology, Centre for Pharmacology and Experimental Therapeutics, University Hospital, Ernst-Moritz-Arndt University, Greifswald, Germany

Cephalalgia

Schürks M, Kurth T, Geissler I, Tessmann G, Diener H-C & Roszkopf D. The G1246A polymorphism in the hypocretin receptor 2 gene is not associated with treatment response in cluster headache. *Cephalalgia* 2007; 27:363–367. London. ISSN 0333-1024

The risk of cluster headache (CH) is associated with the G-allele of the G1246A polymorphism in the hypocretin receptor 2 (*HCRTR2*) gene. First-line medication is effective in only about 70–80% of CH patients. We hypothesized that the *HCRTR2* G1246A polymorphism is also of pharmacogenetic relevance in CH and may affect treatment response. We performed a prospective cohort study among 184 unrelated White CH patients. While the *HCRTR2* 1246G allele was significantly associated with CH in this group, treatment outcomes with triptans, oxygen, verapamil and corticosteroids remained unaffected. Our results do not support a role of the *HCRTR2* G1246A polymorphism in drug responses in CH. □ *Cluster headache, HCRTR2 polymorphism, hypocretin system, treatment response*

Markus Schürks MD, Department of Neurology, University Hospital Essen, Hufelandstr. 55, D-45122 Essen, Germany. Tel. +49 201 723 2285, fax +49 201 723 5901, e-mail schuerks@hotmail.com Received 11 May 2006, accepted 4 October 2006

Familial Cluster Headache: Report of Three Families

Domenico D'Amico, MD; Massimo Leone, MD; Franca Moschiano, MD; Gennaro Bussone, MD

From the Headache Centre, Neurological Institute "C. Besta," Milan, Italy.

Address all correspondence to Dr. Domenico D'Amico, Centro Cefalee, Istituto Neurologico "C. Besta," Via Celoria, 11, 20133 Milano, Italy.

Accepted for publication July 23, 1995.

We report on three families in which cluster headache is present in more than one member. In one of these families a boy, his father, and paternal grandfather were affected. In the other two families, a father and son and mother and daughter were the affected members. Diagnoses were based on IHS criteria, after examining and taking the history directly from the patient in all but one of the seven cases; the seventh patient was deceased and the diagnosis was based on reports from the affected son. Considered in the light of other recent reports of familial cluster headache, these cases suggest that cluster headache can have a genetic component.

Key words: cluster headache, familial occurrence, genetic factor

Gene Expression Profiling in Cluster Headache: A Pilot Microarray Study

Christina Sjöstrand, MD, PhD; Kristina Duvefelt, BioSci, PhD; Anna Steinberg, MD; Ingela Nilsson Remahl, MD, PhD; Elisabet Waldenlind, MD, PhD; Jan Hillert, MD, PhD

Background.—Cluster headache (CH) is a primary neurovascular headache disorder characterized by attacks of excruciating pain accompanied by ipsilateral autonomic symptoms. CH pathophysiology is presumed to involve an activation of hypothalamic and trigeminovascular systems, but inflammation and immunological mechanisms have also been hypothesized to be of importance.

Objective.—To identify differentially expressed genes during different clinical phases of CH, assuming that changes of pathophysiological importance would also be seen in peripheral venous blood.

Methods.—Blood samples were drawn at 3 consecutive occasions from 3 episodic CH patients: during attacks, between attacks and in remission, and at 1 occasion from 3 matched controls. Global gene expression was analyzed with microarray technology using the Affymetrix Human Genome U133 2.0 Plus GeneChip® Set, covering more than 54,000 gene transcripts, corresponding to almost 22,000 genes. Quantitative RT-PCR on S100P gene expression was analyzed in 6 patients and 14 controls.

Results.—Overall, quite small differences were seen intraindividually and large differences interindividually. However, pairwise comparisons of signal values showed upregulation of several S100 calcium binding proteins; S100A8 (calgranulin A), S100A12 (calgranulin C), and S100P during active phase of the disease compared to remission. Also, annexin A3 (calcium-binding) and ICAM3 showed upregulation. BIRC1 (neuronal apoptosis inhibitory protein), CREB5, HLA-DQA1, and HLA-DQB1 were upregulated in patients compared to controls. The upregulation of S100P during attack versus remission was confirmed by quantitative RT-PCR analysis.

Conclusions.—The S100A8 and S100A12 proteins are considered markers of non-infectious inflammatory disease, while the function of S100P is still largely unknown. Furthermore, upregulation of HLA-DQ genes in CH patients may also indicate an inflammatory response. Upregulation of these pro-inflammatory genes during the active phase of CH has not formerly been reported. Data from this pilot microarray study provide a basis for further studies in CH.

Cluster headache-like headaches: A symptomatic feature?

A report of three patients with intracranial pathologic findings

Esther Greve, Jesper Mai

CEPHALALGIA Greve E, Mai J. Cluster headache-like headaches: A symptomatic feature? A report of three patients with intracranial pathologic findings. *Cephalalgia* 1988;8:7%82. Oslo. ISSN 0333-1024

This report concerns three patients with cluster headache-like headaches associated with intracranial pathologic findings. The question whether the occurrence of cluster headache-like headaches may be a symptomatic feature is still not solved. In two of the three presented cases the cluster headache-like headaches disappeared when the intracranial abnormalities were treated. • *Cluster headache, intracranial aneurysm, pituitary adenoma*

Esther Greve, Jesper Mai, Dept. of Neurology, Vejle Sygehus, DK-7100 Vejle, Denmark; Correspondence to Esther Greve, Spurvej 44, DK-5270 Odense N, Denmark; Accepted 3 February 1988

Primary and secondary chronic cluster headache: two separate entities?

P Torelli, D Cologno, C Cademartiri & GC Manzoni

Headache Centre, Institute of Neurology, University of Parma, Parma, Italy

Cephalalgia

Torelli P, Cologno D, Cademartiri C & Manzoni GC. Primary and secondary chronic cluster headache: two separate entities? *Cephalalgia* 2000; 20:826–829. London. ISSN 0333-1024

The International Headache Society (IHS) classification divides chronic cluster headache (CH) into two subtypes: chronic CH unremitting from onset (CCHU) and chronic CH evolved from episodic (CCHE). The purpose of our study was to point out any similarities and differences between the two chronic CH subtypes and to determine whether or not they can be considered as two separate clinical entities. We reviewed data about 31 CCHE patients and 38 CCHU patients referred to the Parma Headache Centre between 1975 and 1999. Clinically, CCHE patients exhibited statistically significant differences from CCHU patients, i.e. earlier CH onset and duration of attacks varying more frequently between 120 and 180 min. From the point of view of lifestyle, heavy alcohol and coffee drinkers prevailed among CCHU patients, while CCHE patients were more frequently heavy smokers. Based on clinical features, it seems reasonable to suppose that chronic CH may occur as two distinct entities. □ *Headache, cluster headache, chronic cluster headache evolved from episodic, chronic cluster headache unremitting from onset, clinical features*

Paola Torelli, Centro Cefalee, Istituto di Neurologia, Strada del Quartiere 4, 43100 Parma,

Health-related quality of life in patients with cluster headache during active periods

D D'Amico, A Rigamonti, A Solari, M Leone, S Usai, L Grazzi & G Bussone

C. Besta National Neurological Institute, Milan, Italy

Cephalalgia

D'Amico D, Rigamonti A, Solari A, Leone M, Usai S, Grazzi L & Bussone G. Health-related quality of life in patients with cluster headache during active periods. *Cephalalgia* 2002; 22:818–821. London. ISSN 0333-1024

Cluster headache is characterized by excruciatingly painful headaches which occur one or several times during the day. Little is known about the functional consequences of this severe headache form. We assessed health-related quality of life in 56 consecutive patients, 34 of whom were episodic cluster headache patients during an active period, and 22 had chronic cluster headache. All patients completed the Short Form-36 (SF-36). We found lower scores in the studied patients than in those reported in the general population for all SF-36 domains. For most scales the difference was significant ($P < 0.0001$, Student's *t*-test, Bonferroni correction). Our findings suggest that cluster headache has marked functional consequences even when appropriate treatments are used. □ *Cluster headache, health-related quality of life, Short Form 36 (SF-36)*

Gennaro Bussone, Headache Centre, C. Besta National Neurological Institute, Via Celoria 11, 20133 Milan, Italy. Tel. +39 02 2394264, fax +39 02 70638067, e-mail bussone@istituto-besta.it Received 24 April 2002, accepted 29 July 2002

Frovatriptan for the treatment of cluster headaches

HC Siow, P Pozo-Rosich & SD Silberstein

Jefferson Headache Center, Department of Neurology, Thomas Jefferson University, Philadelphia, PA, USA

Cephalalgia

Siow HC, Pozo-Rosich P & Silberstein SD. Frovatriptan for the treatment of cluster headaches. *Cephalalgia* 2004; 24:1045–1048. London. ISSN 0333-1024

Cluster headaches both episodic and chronic are some of the most challenging headaches to treat. Although effective treatments are now available, some patients continue to be unresponsive to standard therapy. We present 17 patients from our practice whom we treated preventively with frovatriptan, a new triptan with a long half-life. The promising results suggest that this medication may be a useful addition to our armamentarium against this painful disorder. □ *Cluster headache, episodic, chronic, frovatriptan*

Hua Chiang Siow, Jefferson Headache Center, Department of Neurology, Thomas Jefferson University Hospital, Gibbon Building, Suite #8130, 111 South Eleventh Street, Philadelphia, PA 19107, USA. Tel. +1 215 955 2243, fax +1 215 955 2060, e-mail siow@juno.com Received 30 September 2003, accepted 12 December 2003

The burden of headache in a patient population from a specialized headache centre

GR Vinding, P Zeeberg, A Lyngberg, RT Nielsen & R Jensen

Danish Headache Centre, Department of Neurology, University of Copenhagen, Glostrup Hospital, Glostrup, Denmark

Cephalalgia

Vinding GR, Zeeberg P, Lyngberg A, Nielsen RT & Jensen R. The burden of headache in a patient population from a specialized headache centre. *Cephalalgia* 2007; 27:263–270. London. ISSN 0333-1024

The aim was to characterize the individual and socio-economic impact of headache in a patient population from The Danish Headache Centre. This was a cross-sectional study using a structured interview, prospective headache diaries and standardized self-administered questionnaires using the ICHD-II criteria. Fifty-five subjects (12 male and 43 female) with a median age of 41 years and a median headache frequency of 15 days/month participated. Very high utilization of the healthcare system and a high absence rate due to headache of 12 days/year were reported. Eighty-one percent experienced a marked decrease in work effectiveness. Overall, 91% felt hampered by their headache on a daily basis and 98% had had expenses for headache medication. Frequent headache disorders are highly costly, especially due to indirect costs. Prevention, early intervention or effective treatment strategies for headache disorders may therefore be highly cost effective, not only for the individual but also for society. □ *Burden of headache, individual and socio-economic impact, specialized headache centre*

Gabrielle R. Vinding, Medical Student, Danish Headache Centre, Department of Neurology, N01, University of Copenhagen, Glostrup Hospital, Nordre Ringvej 57, DK-2600 Glostrup, Denmark. Tel. +45 4323 3068, fax +45 4383 3839, e-mail gabrielle@stud.ku.dk Received 12 June 2006, accepted 8 October 2006

LJ Stovner¹, K Hagen¹, R Jensen², Z Katsarava³, RB Lipton⁴, AI Scher⁵, TJ Steiner⁶ & J-A Zwart¹

¹Norwegian National Headache Centre, Department of Neuroscience, Norwegian University of Science and Technology, and Trondheim University Hospital, Trondheim, Norway, ²Danish Headache Centre, Glostrup University Hospital, Copenhagen, Denmark, ³Department of Neurology, University Hospital Essen, Germany, ⁴Department of Neurology, Albert Einstein College of Medicine, New York, USA, ⁵Preventive Medicine and Biometrics, Uniformed Services University, Maryland, USA, ⁶Division of Neuroscience and Mental Health, Imperial College, London, UK

Cephalalgia

Stovner LJ, Hagen K, Jensen R, Katsarava Z, Lipton R, Scher AI, Steiner TJ & Zwart J-A. The global burden of headache: a documentation of headache prevalence and disability worldwide. *Cephalalgia* 2007; 27:193–210. London. ISSN 0333-1024

This study, which is a part of the initiative 'Lifting The Burden: The Global Campaign to Reduce the Burden of Headache Worldwide', assesses and presents all existing evidence of the world prevalence and burden of headache disorders. Population-based studies applying International Headache Society criteria for migraine and tension-type headache, and also studies on headache in general and 'chronic daily headache', have been included. Globally, the percentages of the adult population with an active headache disorder are 46% for headache in general, 11% for migraine, 42% for tension-type headache and 3% for chronic daily headache. Our calculations indicate that the disability attributable to tension-type headache is larger worldwide than that due to migraine. On the World Health Organization's ranking of causes of disability, this would bring headache disorders into the 10 most disabling conditions for the two genders, and into the five most disabling for women. □ *Burden of disease, epidemiology, headache, 'Lifting The Burden Global Campaign', migraine*

Lars Jacob Stovner, Norwegian National Headache Centre, Department of Neuroscience, Trondheim University Hospital, N-7006 Trondheim, Norway. Tel. +47 7257 5070, fax +47 7359 8795, e-mail lars.stovner@ntnu.no Received 15 May 2006,

Prevalence of *HFE* (Hemochromatosis) Gene Mutations in Patients With Cluster Headache

Innocenzo Rainero, MD, PhD; Chiara Rivoiro, MD; Elisa Rubino, MD; Valentina Milli, PhD; Walter Valfrè, MD; Paola De Martino, MD; Rossana Lo Giudice, MD; Giuseppina Angilella, MD; Lidia Savi, MD; Salvatore Gallone, MD; Lorenzo Pinessi, MD

Objective.—To evaluate whether polymorphisms of the *HFE* gene would modify the occurrence and the clinical features of cluster headache (CH).

Background.—Recent studies suggested that iron metabolism may be involved in the pathophysiology of primary headaches. The *HFE* gene encodes for a protein that modulates iron absorption. Mutations in this gene are responsible for toxic iron overload in several body organs.

Methods.—Genomic DNA was extracted from 109 CH patients and 211 age and sex-matched healthy controls and genotyped for the C282Y and H63D mutations of the *HFE* gene. Allele and genotype frequencies of the *HFE* gene were compared between cases and controls. The clinical characteristics of the disease were compared according to the different *HFE* gene genotypes.

Results.—No C282Y mutation was found in both cases and controls. The prevalence of the H63D mutation was nearly identical in cases and controls. The four patients carrying the *HFE* D63D genotype showed a significantly ($P < .001$) later age at onset of the disease in comparison with both H63H and H63D patients. The remaining clinical characteristics of the disease did not significantly differ in the presence or absence of the H63D mutation.

Conclusion.—Our data do not support the hypothesis that genetic variations within the *HFE* gene are associated with CH. However, the *HFE* gene may influence the disease phenotype and may be regarded as a disease modifier gene.

Diagnostic delays and mis-management in cluster headache

Bahra A, Goadsby PJ. Diagnostic delays and mis-management in cluster headache. *Acta Neurol Scand* 2004; 109: 175–179. © Blackwell Munksgaard 2003.

Objectives – Cluster headache is a stereotyped form of primary headache that while common in terms of neurologic illnesses is much less common as a cause of disabling headache than migraine. **Materials and methods** – We directly interviewed 230 patients with cluster headache. National support groups contributed 76% and 24% came from the National Hospital for Neurology and Neurosurgery Headache Clinic. **Results** – Seventy-two percent were men and 28% women, giving a male to female (M:F) ratio of 2.5:1. Episodic cluster headache (ECH) was recorded in 79% while 21% had chronic cluster headache (CCH). The mean time to diagnosis has dropped from 22 years in the 1960s to 2.6 years in the 1990s, although the mean number of GPs seen before a diagnosis was made remains at three. **Conclusions** – While there has been improvement in the time to diagnosis for cluster headache, a number of physicians will be consulted, and better education is likely to reduce the overall patient suffering.

A. Bahra, P. J. Goadsby

Headache Group, Institute of Neurology, Queen Square, London, UK

Key words: cluster headache; medical treatment; alternative treatment

Professor Peter J Goadsby, Institute of Neurology, The National Hospital for Neurology and Neurosurgery, Queen Square, London WC1N 3BG UK
Tel.: +44 20 7829 8749
Fax: +44 20 7813 0349
e-mail: peterg@ion.ucl.ac.uk

Accepted for publication September 8, 2003