Brief Report

Cephalalgia
An International Journal of Headache

International Headache Society

Cephalalgia
31(2) 250–253

DOI: 10.1177/0333102410383588
cep.sagepub.com

SAGE

New daily persistent headache and panic disorder

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Abstract

Background: New daily persistent headache (NDPH) is a primary chronic daily headache that is generally considered to be difficult to treat. Migraine has been linked to comorbid psychiatric conditions, mainly mood and anxiety disorders, but NDPH has never been linked to psychiatric conditions, and never studied extensively for such an association.
Case: We report nine cases (six women and three men) of patients diagnosed with NDPH and panic disorder who were treated for both conditions. Six of them (66%) had good or excellent responses.
Conclusion: The spectrum of anxiety disorders, particularly panic disorder, should be considered in NDPH patients. Simultaneous treatment of both disorders may lead to good outcomes.

Keywords

Chronic daily headache, new daily persistent headache, anxiety, panic

Date received: 18 March 2010; revised: 3 May 2010; 21 June 2010; accepted: 14 July 2010

Introduction

Chronic daily headaches (CDHs) are frequent and disabling headache disorders (1). New daily persistent headache (NDPH) is one of the CDHs, defined as acute headache within three days of onset and persisting for 15 days or more each month for at least three months (2). NDPH is more common in women, typically with some migraine features; its prevalence in headache centers ranges from 11 to 21% (3).

Early in the course of NDPH the diagnosis of secondary causes should be ruled out. NDPH symptoms mimic those attributable to infectious, traumatic, neurovascular and inflammatory causes, as well as cerebrospinal fluid pressure syndromes. NDPH may be a presentation of other primary headaches such as new-onset migraine or tension-type headache. All of these headaches can be difficult to treat.

Migraine has been linked to comorbid psychiatric conditions, mostly mood and anxiety disorders (4–9), but NDPH has never been linked to psychiatric conditions, and never studied extensively for a possible association. We report a case series of nine patients with NDPH and anxiety disorders, particularly panic disorder.

Patients and methods

Patients presented at the São Paulo Headache Center, a tertiary headache center in Brazil, with similar headache histories. All had new daily headaches starting with anxiety symptoms. Table 1 describes patients' gender, anxiety diagnosis, follow-up period, clinical response and treatment strategies used. Patients were followed prospectively; all signed informed consent for their inclusion in this publication. The headache center ethics committee approved the study. Patients were diagnosed by one of the authors (MFP) from January to December 2009.

Diagnosis

Headache diagnosis followed the International Headache Society Classification, second edition (10), modified according to Kung et al. (11). NDPH was defined as: A. Headache that, within three days of onset, fulfills criteria B and; B: Headache is present daily, and is unremitting, for >three months. Criteria C and D were not considered. In other words, Kung criteria accept migraine features as part of the

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Table 1. Patients with new daily headaches and their gender, anxiety diagnosis, follow-up time, clinical response and treatment strategies used

Patient no.	Gender	Headache history (months)	Disability (months lost at work)	Anxiety diagnosis	Follow-up (months)	Clinical response	Treatment strategy (dose in mg)
1	F	12	12	Panic disorder	12	Excellent	TPM 50, ESC 10, CL 2, PSY
2	M	3	3	Panic disorder	11	Excellent	TPM 75, ESC 15, CL 1, PSY
3	M	24	–	GAD + panic subdx	12	Moderate	TPM 100, ESC 10, CL 2,
4	F	3,5	3	Panic disorder	9	Poor	TPM 150, SER 150, DUL 90, ESC 20, AL1, CL4
5	F	6	3	GAD + panic subdx	8	Good	TPM 50, ESC 10, CL 0,5
6	F	14		Panic disorder	8	Good	ESC10, AL 1, PSY
7	M	5	3	Panic disorder	6	Poor	TPM 50, SER 25, ESC 10, AL1, CL4
8	F	30	12	GAD + panic subdx	4	Excellent	TPM 50, ESC 10, CL 1, PSY
9	F	11	6	GAD + Panic subdx	3	Excellent	TPM 100, ESC 10, CL 0,5 PSY

GAD, generalized anxiety disorder; panic subdx, panic disorder subthreshold; TPM, topiramate; ESC: escitalopram; DUL, duloxetine; CL, clonazepan; Al, alprazolam; SER, sertraline; PSY, psychotherapy.

NDPH syndrome. Recently, authors are following this criteria in some studies (11,12).

Psychiatric diagnosis followed the diagnostic criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition (DSM-IV). Subthreshold panic disorder (SPD) was defined according to Batelaan et al. (13). SPD was defined as at least one sudden experience of intense fear in the year prior to the interview, in a situation in which most people would not be afraid. This experience may not be attributable to an organic cause and must have been accompanied by at least four of the 13 panic-related symptoms defined in the DSM-IV.

Clinical response

Clinical response was rated by one of the authors (MFP) as excellent (headache-free within two months of therapy and remaining headache-free until the last follow-up visit), good (headache days decreased >50% within two months of therapy, being headache-free after two months, remaining headache-free until the last follow-up visit), moderate (headache days decreased >50% within two months of therapy, not reaching a headache-free state) and poor (no response or >50% reduction in headache days). The number of headache days was collected through a headache diary filled out by patients.

Treatment strategies

Patients had all their treatments decided either by one of the authors (MFP) alone (patients 1, 2, 5, 6, 8, 9), or in consultation with a psychiatrist (patients 3, 4, 7) when the clinical response was not rated good or excellent. All authors had full access to patients' records.

The treatment of choice for the patients was a combination of topiramate, starting with 25 mg with an expected goal dose of 50 mg daily (however, some patients needed a higher dose), with escitalopram starting at 10 mg daily, and clonazepan 0.5–2.0 mg daily. Doses were increased if needed. According to recent studies, the use of selective serotonin-reuptake inhibitors (SSRIs) (including escitalopram) are the first pharmacologic choice for Panic disorders and have an "A" level of evidence. The use of benzodiazepines (including clonazepam) is controversial, and some guidelines recommend their use for refractory cases in patients without a history of drug dependence and allow their concomitant use during the first weeks of treatment with SSRIs due to their short-term efficacy (level of Evidence "A") (14).

Psychotherapy was strongly recommended to patients. Cognitive behavioral therapy was the first choice, but previous patient experiences, access to health care providers and insurance issues were considered. Some patients had other treatments because of the psychiatrist's opinion or their previous medication history.

Results

Nine patients were studied, of whom six were women and three were men. The mean age was 31.4 years, ranging from 18 to 45. The onset of NDPH ranged from 3 to 30 months prior to evaluation and treatment, with a mean of 12 months. Patients were followed up for three to 12 months, with a mean of 8.1 months.

Psychiatric diagnosis was made for all patients: five patients had panic disorder, four had general anxiety disorder (GAD) and subthreshold panic disorder. The timing of the onset of headache and panic attacks were within the same week for all patients. Patients denied prior headache history. Disability level was significantly high; number of months lost at work was an average of 4.7 months, ranging from 0 to 12.

Four patients had an excellent clinical response, two good, one moderate and two poor outcomes. Six patients (66%) had good or excellent responses. All patients who had good adherence to psychotherapy had an excellent or good clinical response.

Patients with GAD and subthreshold panic had longer duration of illness than those with panic disorder, with an average of 17.7 months of headache history, compared to 8.1 months for those with panic disorder.

Discussion

This is a report on patients who presented with new daily headaches associated with anxiety disorders.

Bigal et al. (15) studied 69 NDPH patients comparing them to 65 chronic post-traumatic headache (CPTH) patients, finding allergies, asthma, hypothyroidism and alcohol consumption more than three times per week to be significant factors associated with the development of NDPH. Diagnosis of mood or anxiety disorders was not assessed properly. In addition, the control group used (CPTH) would not be ideal for the comparison.

Other aspects such as cervical spine joint hypermobility, systemic or central nervous system inflammation, herpes simplex, Epstein-Barr virus infection and stressful life events were investigated as NDPH precursors (16–21).

Migraine has been linked to anxiety (4), panic (22,23) and phobias (5,7). Because NDPH has similarities to migraine it could also be comorbid with anxiety disorders. These cases could signify that an individual can switch abruptly to a brain state that produces not just a daily headache but also panic disorders. The sudden onset of headaches might be associated with the usual sudden onset of the panic disorder syndrome and its spectrum. Panic may also be a trigger for a frequent headache or for a migraine transformation. Further studies are necessary to determine the true influence of psychiatric disorders in NDPH, but anxiety and panic disorders should be extensively investigated and if present, treated in NDPH patients.

SPD has only recently been receiving attention in the medical literature recently (13,24–26). The prevalence of clinical and subthreshold panic in the general population was found to be very high (40%). Subthreshold panic was associated with increased odds of several comorbid disorders, including depression, dysthymia, psychosis, generalized anxiety disorder, bipolar disorder and alcohol and drug use disorders, and was also associated with a greater likelihood of health-care services utilization (24).

SPD is an important issue for the NDPH clinical context. Anxiety diagnosis is more difficult when ''full-blown'' panic disorder is not present; in our sample patients with SPD had double the headache history of those with full-blown panic disorder. This is probably due to the underdiagnosis of this condition. SPD may underlie NDPH in some cases.

Patients in general had a good clinical outcome, with two-thirds having good or excellent clinical response, meaning that they reached a headache-free state and remained headache-free for a significant follow-up period. The treatment strategy chosen for those patients is a combination of one of the best available treatments for panic disorder and for headaches. Although little information about escitalopram in headache disorders is published, its good clinical response and tolerability in panic disorder was considered. Other SSRIs with efficacy for panic, such as fluoxetine and sertraline, are not efficacious for headache disorders. Other drugs, including duloxetine and venlafaxine, would not be as well tolerated as escitalopram, but are, however, good options in this NDPH–PD clinical syndrome. A monotherapy concept could be chosen but the authors' experience and the disorders' severity made us decide on a combination therapy.

Psychotherapy was also included in the treatment program; not many patients adhered to it, but those who did had good or excellent clinical responses. It is possible perhaps that the psychotherapy was helpful independent of anxiety or panic conditions. Other therapeutic strategies should be studied; many regimens could be effective.

These case reports have some limitations that must be highlighted. First, the IHS classification covers only headaches attributable to somatization and delusional disorders, and no criteria exist for headaches secondary to depression or anxiety. Therefore, it is possible that some patients could have headaches secondary to the underlying anxiety/panic disorder and not due to NDPH. Second, it is possible that the relation or co-occurence between NDPH and SPD in these patients could be part of a coincidence or that the NDPH could have triggered psychiatric symptoms rather than the two beginning concurrent—in which case, retrospective bias could have led to the reporting of the simultaneous onset of the two. Third, as mentioned, we did not strictly follow the IHS definition of NDPH, mainly because we were interested in assessing

the proportion of individuals with new-onset CDH that had migraine features.

Conclusion

The onset of NDPH may be associated with the onset of panic disorders. Simultaneous treatment of both disorders may lead to good outcomes.

References

1. Queiroz LP, Peres MFP, Kowacs F, et al. Chronic daily headache in Brazil: a nationwide population based study. *Cephalalgia* 2008; 28(12): 1264–1269.
2. Evans RW. New daily persistent headache. *Curr Pain Headache Rep* 2003; 7(4): 303–307.
3. Bigal ME, Lipton RB, Tepper SJ, Rapoport AM and Sheftell FD. Primary chronic daily headache and its subtypes in adolescents and adults. *Neurology* 2004; 63(5): 843–847.
4. Mercante JP, Bernik MA, Zukerman-Guendler V, Zukerman E, Kuczynski E and Peres MF. [Psychiatric comorbidities decrease quality of life in chronic migraine patients]. [Portuguese.]. *Arq Neuropsiquiatr* 2007; 65(3B): 880–884.
5. Peres MF, Mercante JP, Guendler VZ, et al. Cephalalgiaphobia: a possible specific phobia of illness. *J Headache Pain* 2007; 8(1): 56–59.
6. Tietjen GE, Peterlin BL, Brandes JL, et al. Depression and anxiety: effect on the migraine-obesity relationship. *Headache* 2007; 47(6): 866–875.
7. Corchs F, Mercante JP, Guendler VZ, et al. [Phobias, other psychiatric comorbidities and chronic migraine.] [Portuguese.]. *Arq Neuropsiquiatr* 2006; 64(4): 950–953.
8. Vieira DS, Naffah-Mazacoratti MG, Zukerman E, et al. Cerebrospinal fluid GABA levels in chronic migraine with and without depression. *Brain Res* 2006; 1090(1): 197–201.
9. Mercante JP, Peres MF, Guendler V, Zukerman E and Bernik MA. [Depression in chronic migraine: severity and clinical features.] [Portuguese.]. *Arq Neuropsiquiatr* 2005; 63(2A): 217–220.
10. Headache Classification Committee of the International Headache Society. The international classification of headache disorders. 2nd edn. *Cephalalgia* 2004; 24(Suppl 1): 9–160.
11. Kung E, Tepper S, Rapoport A, Sheftell F and Bigal M. New daily persistent headache in the paediatric population. *Cephalalgia* 2009; 29(1): 17.
12. Robbins MS, Grosberg BM, Napchan U, Crystal SC and Lipton RB. Clinical and prognostic subforms of new daily-persistent headache. *Neurology* 2010; 74(17): 1358–1364.
13. Batelaan N, De Graaf R, Van Balkom A, Vollebergh W and Beekman A. Thresholds for health and thresholds for illness: panic disorder versus subthreshold panic disorder. *Psychol Med* 2007; 37(2): 247–256.
14. Salum GA, Blaya C and Manfro GG. Transtorno do pânico. [Portuguese.]. *Revista de Psiquiatria do Rio Grande do Sul* 2009; 31: 86–94.
15. Bigal ME, Sheftell FD, Rapoport AM, Tepper SJ and Lipton RB. Chronic daily headache: identification of factors associated with induction and transformation. *Headache* 2002; 42(7): 575–581.
16. Rozen T and Swidan SZ. Elevation of CSF tumor necrosis factor alpha levels in new daily persistent headache and treatment refractory chronic migraine. *Headache* 2007; 47(7): 1050–1055.
17. Rozen TD, Roth JM and Denenberg N. Cervical spine joint hypermobility: a possible predisposing factor for new daily persistent headache. *Cephalalgia* 2006; 26(10): 1182–1185.
18. Meineri P, Torre E, Rota E and Grasso E. New daily persistent headache: clinical and serological characteristics in a retrospective study. *Neurol Sci* 2004; 25(Suppl 3): S281–S282.
19. Takase Y, Nakano M and Tatsumi C. [Primary new daily persistent headache (NDPH): clinical characteristics of forty-three cases in Japan]. [Japanese.]. *Rinsho Shinkeigaku* 2003; 43(9): 533–538.
20. Bigal ME, Sheftell FD, Rapoport AM, Tepper SJ, Weeks R and Baskin SM. MMPI personality profiles in patients with primary chronic daily headache: a case-control study. *Neurol Sci* 2003; 24(3): 103–110.
21. Li D and Rozen TD. The clinical characteristics of new daily persistent headache. *Cephalalgia* 2002; 22(1): 66–69.
22. Merikangas KR, Angst J and Isler H. Migraine and psychopathology: Results of the Zurich cohort study of young adults. *Arch Gen Psychiatry* 1990; 47(9): 849–853.
23. Juang KD, Wang SJ, Fuh JL, Lu SR and Su TP. Comorbidity of depressive and anxiety disorders in chronic daily headache and its subtypes. *Headache* 2000; 40(10): 818–823.
24. Bystritsky A, Kerwin L, Niv N, et al. Clinical and subthreshold panic disorder. *Depress Anxiety* 2010; 27(4): 381–389.
25. Batelaan NM, de Graaf R, Spijker J, et al. The course of panic attacks in individuals with panic disorder and subthreshold panic disorder: a population-based study. *J Affect Disord* 2010; 121(1–2): 30–38.
26. Batelaan N, Smit F, de Graaf R, van Balkom A, Vollebergh W and Beekman A. Economic costs of full-blown and subthreshold panic disorder. *J Affect Disord* 2007; 104(1–3): 127–136.