Prevalence and Clinical Hallmarks of Primary Exercise Headache in Middle-aged Japanese on Health Check-up

Sayori Hanashiro, Takanori Takazawa, Yuji Kawase and Ken Ikeda

Abstract

Objective We examined the prevalence and clinical features of primary exercise headache (PEH) in middle-aged Japanese population.

Methods A headache specialist interviewed middle-aged subjects serially on health check-up. The primary headaches were diagnosed according to the International Classification of Headache Disorders (ICHD-III beta). Cardiovascular disease (CVD) risk and radiological findings were analyzed. Prevalence of PEH and clinical features were assessed.

Results Among 2,546 subjects (1,588 men and 958 women), thirty subjects (13 men and 17 women) were diagnosed with PEH. The prevalence of PEH was 1.19%, 0.82% in men and 1.77% in women. The mean age [standard deviation (SD)] of the subjects was 44.3 (8.8) years and their mean duration (SD) of PEH was 4.5 (7.0) months. Headache occurred bilaterally (23 patients) or unilaterally (7 patients), and in the occipital (16 patients), frontal (10 patients) or diffuse region (4 patients). The persistent headache time ranged from 5 minutes to 12 hours. The degree of headache severity was classified as mild (13 patients), moderate (5 patients) or severe degree (12 patients). PEH was triggered by gym training (16 patients), swimming (6 patients), running (6 patient) and skiing (2 patients). All patients were exercise beginners or played a sport occasionally. No patients visited physicians for headache consultation. Other primary headaches coexisted in 20 patients (67%). Twenty patients had migraine without aura (MO). Seven patients had headache associated with sexual activity. Five patients had cough headache. Two patients had CVD risk factors.

Conclusion The present study of PEH indicated the prevalence of 1.2% and the female/male ratio of 2.1 in middle-aged Japanese. The comorbidity rate of MO was high. PEH may not be an uncommon headache in middle-aged MO sufferers and sport beginners.

Key words: primary exercise headache, prevalence, middle age, health check-up, clinical hallmark, migraine

(Intern Med 54: 2577-2581, 2015)
(DOI: 10.2169/internalmedicine.54.4926)

Introduction

Primary exercise headache (PEH) is an uncommon primary headache disorder that is currently defined by the 3rd edition (beta version) of the International Classification of Headache Disorders (ICHD-III beta). PEH occurs particularly in hot weather or at high altitude, lasting within 48 hours, brought on exclusively during or after strenuous physical exertion. This headache is not accounted better by any other diagnosis with ICHD-III beta (1).

Previous epidemiological surveys described various prevalence of PEH in European countries, New Zealand and Taiwan (2-7). Those results supported the close linkage between environmental factors, age and PEH development. However, little is known about the epidemiology of PEH among the Japanese population. The present study was aimed to examine the prevalence and the clinical profile of PEH among middle-aged Japanese on health check-up.
Study population

All subjects were recruited between July 2005 and June 2007 in PL Tokyo Health Care Center through agreements with many Japanese companies or visitors. Most subjects were middle-aged individuals, employed or worked at home because the Japanese national program of health checks is aimed at workers between the age of 40 and 60 years. These participants lived in the Kanto Plain region, mainly in the greater Tokyo metropolis, and also in a small number of neighboring prefectures of Eastern Japan. Subjects came from families all over Japan, and were not from any specific region (8, 9). The subject demographics had no selection criteria that would bias the diagnosis of PEH. The present study was approved by the institutional review board of PL Tokyo Health Care Center. The informed consent for this study was obtained from all participants.

Diagnosis of PEH and other primary headaches

The primary headaches, including migraine, PEH and other primary headache disorders, were diagnosed according to the criteria of ICHD-III beta (1). A board-certified and experienced neurologist with headache professional qualification (K.I.) interviewed the headache history on physical and neurological examination. One or more of exercise-induced headache episodes in the previous year was confirmed.

Prevalence and clinical assessment of PEH subjects

We evaluated the lifetime prevalence and the clinical profile of PEH sufferers. The clinical assessment included headache portion, headache duration, persistent time of an attack, headache severity, comorbidity of other primary headaches and the previous history of physician visit. Cardiovascular disease (CVD) risk was also analyzed using the following 9 factors: obesity (body mass index ≥25.0 kg/m²); current smoker; heavy drinkers (ethanol intake ≥34 g/day); hypertension (systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg) or currently under treatment; diabetes mellitus (fasting blood sugar ≥126 mg/dL or hemoglobin A1c ≥6.5%) or currently under treatment; dyslipidemia (serum low-density lipoprotein cholesterol ≥140 mg/dL or high-density lipoprotein cholesterol <40 mg/dL) or currently under treatment; atrial fibrillation; prior history of CVD or stroke; and contraceptives use. Fasting blood samples were obtained from the antecubital vein in all subjects. For the final diagnosis of PEH and differentiating secondary causes of exercise headache, brain magnetic resonance imaging and angiography were performed in all subjects with exertional headache.

Study participants

A total of 2,546 subjects (1,588 men and 958 women) participated in the present study. The mean age [standard deviation (SD)] of subjects was 52.0 (5.3) years, 52.3 (5.1) in men and 51.3 (5.8) in women. This group did not include any professional athletes or occupational players.

Lifetime prevalence of PEH and migraine

The headache specialist (K.I.) interviewed all participants serially. Thirty subjects (13 men and 17 women) were diagnosed with PEH. The overall prevalence of PEH was 1.19%, 0.82% in men and 1.77% in women. Migraine was diagnosed in 349 subjects (116 men and 233 women). The subject number of migraine with aura (MA) and migraine without aura (MO) were 26 subjects (10 men and 16 women) and 323 subjects (106 men and 217 women), respectively. The prevalence of migraine was 13.7%, 7.3% in men and 24.3% in women. Those subjects with MA was 1.0%, 0.6% in men and 1.7% in women and those with MO was 12.7%, 6.7% in men and 22.7% in women.

Clinical profile of PEH subjects

Clinical hallmarks of PEH sufferers are summarized in Table 1. The mean age (SD) was 44.3 (8.8) years, 43.0 (8.0) in men and 47.4 (10.5) in women. The mean duration (SD) of PEH was 4.5 (7.0) months, 1.8 (0.8) in men and 6.3 (8.8) in women. Twenty-nine patients (97%) complained of pulsating pain. The remaining one patient (3%) reported non-pulsating pain. Headache occurred on bilateral sides (23 patients) or on unilateral side (7 patients). Additionally, headache was localized in the occipital region (16 patients), the frontal portion (10 patients) or diffuse region (4 patients). The persistent time of an attack was varied from 5 minutes to 12 hours. The severity of headache was classified as mild degree (self-control) in 13 patients, moderate degree (painkillers need) in 5 patients and severe degree (bed rest requirement) in 12 patients. PEH-triggered exercises were gym training in 16 patients, swimming in 6 patients, running in 6 patients and skiing in 2 patients. PEH patients had no constant training habits. All patients were exercise beginners or played a sport occasionally. No patients visited physicians for headache consultation. In addition to PEH, one or more of other primary headaches coexisted in 20 patients (67%). Twenty patients (67%) had MO. The coexistent percentage of PEH and MO was 6.2%, 9.7% in men and 4.6% in women. Seven patients (24%) had headache associated with sexual activity (HASA). Five patients (18%) had cough headache (CH). The estimated prevalence of primary HASA was 0.27%, 0.25% in men and 0.31% in women. That of primary CH was 0.20%, 0.19% in men and 0.20% in women. With respect to the prognosis of PEH, 28 patients were followed up for 1 to 12 months after the diagnosis of
All of these patients recovered naturally from PEH. The remaining two patients had provided no more information.

**Laboratory analyses of CVD risk in PEH subjects**

Laboratory CVD risk studies revealed smoking, diabetes mellitus, dyslipidemia and prior history of angina pectoris in one man. This patient had both CH and PEH. Contraceptives were used in a patient with PEH and HASA (Table 1). Other patients had no CVD risk factors.

|                       | Total (n = 30) | Men (n = 13) | Women (n = 17) |
|-----------------------|---------------|--------------|---------------|
| **Prevalence**        | 1.19%         | 0.82%        | 1.77%         |
| Mean age (SD) years   | 44.3 (8.8)    | 43.0 (8.0)   | 47.4 (10.5)   |
| Mean duration (SD) months | 4.5 (7.0)   | 1.8 (0.8)    | 6.3 (8.8)     |
| Persistent time of an attack | 5 min-12 h | 5 min-2 h    | 30 min-12 h   |
| Pulsating pain n (%)  | 29 patients (97) | 12 patients (92) | 17 patients (100) |
| **Headache side**     |               |              |               |
| Bilateral n (%)       | 23 patients (77) | 11 patients (85) | 12 patients (71) |
| Unilateral n (%)      | 7 patients (23)  | 2 patients (15)  | 5 patients (19)  |
| **Headache portion**  |               |              |               |
| Diffuse n (%)         | 4 patients (13) | 2 patients (15) | 2 patients (12) |
| Frontal n (%)         | 10 patients (34) | 5 patients (38) | 5 patients (29) |
| Occipital n (%)       | 16 patients (53) | 6 patients (47) | 10 patients (59) |
| **Severity of headache** |            |              |               |
| Mild degree n (%)     | 13 patients (43) | 8 patients (62) | 5 patients (29) |
| Moderate degree n (%) | 5 patients (17)  | 1 patient (8)   | 4 patients (24)  |
| Severe degree n (%)   | 12 patients (40) | 4 patients (30) | 8 patients (47) |
| **Triggered exercises** |         |              |               |
| Gym training n (%)    | 16 patients (53) | 9 patients (69) | 7 patients (41) |
| Swimming n (%)        | 6 patients (21)  | 2 patients (15)  | 4 patients (24)  |
| Running n (%)         | 6 patients (21)  | 1 patient (8)   | 5 patients (29)  |
| Skiing n (%)          | 2 patients (5)   | 1 patient (8)   | 1 patient (6)    |
| **Physician visit n (%)** | None (0) | None (0) | None (0) |
| **Comorbidity of OPH** |             |              |               |
| MO n (%)              | 20 patients (67) | 10 patients (77) | 10 patients (59) |
| HASA n (%)            | 7 patients (23) | 4 patients (30) | 3 patients (18) |
| CH n (%)              | 5 patients (17) | 3 patients (23) | 2 patients (12) |
| **Prognosis**         |              |              |               |
| Good                  | 28 patients (95) | 12 patients (92) | 16 patients (94) |
| Unknown               | 2 patients (5)  | 1 patient (8)  | 1 patient (6)    |
| CVD risk profile n (%) | 2 patients (5) | 1 patient (8) | 1 patient (6) |

CH: cough headache, CVD: cardiovascular disease, HASA: headache associated with sexual activity, MO: migraine without aura, OPH: other primary headaches

**Discussion**

The present PEH study showed the lifetime prevalence was 1.19% and the female/male ratio of 2.1 in middle-aged Japanese on health check-up. Upon clinical analyses of PEH patients, the comorbidity rate of other primary headaches was high (67%). MO, HASA or CH coexisted. Particularly, the prevalence of PEH was 6.2% in migraineurs without aura, 9.7% in men and 4.6% in women. PEH patients had no prior history of exercise habits. Physical exercise was started for recent 2-3 months or experienced occasionally. Major CVD risk factors were found in 2 patients. All patient had no physician visit for headache consultation. The prognosis of PEH was good in all patients except for 2 patients without information.

The concept of PEH was mentioned first in 1968 by Rooke (10) who published 103 patients with exertional headache. Finally, 93 patients seemed to have benign underlying causes. He addressed that exertional headache may be a primary headache disorder (10). The International Headache Society identified “benign exertional headache” as a distinct entity belonging to other primary headache disorders by the first edition of ICHD in 1988 (11). Recently, the diagnostic name has been changed from primary exertional headache by 2nd edition of ICHD (ICHD-II) (12) to PEH by ICHD-III beta (1).

Main previous epidemiological studies of PEH are listed chronologically in Table 2. The prevalence of PEH was varied from 0.1% to 26% (2-7). The first survey suggested the prevalence of 1% among 2,008 residents in Copenhagen, Norway (2). The second survey in New Zealand reported that 77 of 295 medical or college students (26%) experienced exercise-induced nontraumatic headache (3). The Norwegian Vågå study showed the prevalence of 12.3 % in among 1,646 respondents (4). The prevalence of 10.2% was described in among 1,963 Taiwanese middle-school students (6). The largest series of patients were surveyed by Pascual et al. (5). They examined 6,412 patients in a Spanish headache clinic, and first clarified the clinical features of PEH patients. This study contained radiological evaluation by brain computed tomography or MRI in all PEH patients. A total of 9 patients (8 men and 1 woman) were diagnosed as PEH. The prevalence was 0.14%. Patient ages ranged from 17 to 53 years with the mean age of 40. PEH duration was 1 day to 4 years. A pulsating pain lasted from 1 hour to
4 days. Three patients (33%) had MO and three (33%) had primary HASA. Frequent comorbidity between PEH and other primary headaches was exposed (5). In 2012, Van der Ende-Kastelijn et al. (7) conducted an online survey of PEH in the Dutch athletic population. Among 14,131 participants of a cycling competition, 4,000 cyclists were chosen. The questionnaire responses were matched to the diagnostic criteria of ICHD-II (12). A total of 1,045 individuals were consistent with the diagnosis of PEH and the prevalence was estimated as 26%. Possible risk factors for developing PEH included intense exercise, dehydration and warm weather whereas the frequency of PEH tended to decline with age (7). The present study based on health check-up indicated the PEH prevalence of 1.19% and female predominance among middle-aged Japanese. These epidemiological data were in the similar result to the Copenhagen population-based study (age of 25-64 years) reported by Rasmussen and Olesen in 1992 (2). The same prevalence and female predominance could contribute to the similar age group between both surveys.

With respect to the comorbidity of PEH and other primary headaches, the present study highlighted high coexistent rate of MO (69%), in addition to HASA and CH. A previous study reported by Pascual et al. (5) also suggested that MO or HASA is frequently comorbid (33%). A Japanese article described 13 patients (7 men and 6 women) with primary CH. The mean age (SD) was 43.1 (13.8) years. The age of those patients was in the similar age to our PEH patients. Of interest, 6 patients (46%) had complication of PEH (13). In three studies by Pascual et al. (5), Teramoto (13) and ours, all participants were directly interviewed by headache specialists compared to other surveys (2-4, 6, 7). Valsalva-like breath-holding was found in patients with PEH, HASA and CH. In our 5 patients with both PEH and CH, the common profile revealed throbbing pain in the bilateral occipital region. However, the persistent time of a headache attack differed between PEH and CH. That of CH was much shorter compared to PEH. Besides CH and HASA, the identical constitutional and environmental condition might exist between patients combined with PEH and MO. The prevalence of PEH was reported at high rates of 10% or 26% among adolescents or athletes (3, 6, 7), whereas our patients without exercise habits started physical exercise or sometimes played a sport. Otherwise, the prevalence of PEH was 6.2% in MO sufferers. Thus, the present study supported that PEH development might not be uncommon in middle-aged migraineurs and sport beginners.

It is noted that our patients with PEH had not visited physicians, neurologists or headache specialists for headache examination. The recognition and the prophylactic pharmacotherapy of PEH are not well known in Japan (5, 14-16). Most of our patients had a good prognosis and recovered naturally. These social and medical backgrounds seemed to cause no previous history of headache consultation in our patients.

The selection bias was a major limitation in the present study. Most of our participants were middle-aged individuals, and differed from general population, including young and elderly people. Future prospective studies of younger population interviewed by headache specialists are needed to elucidate the precise age prevalence, and the endogenous and exogenous pathogenesis of PEH.

The authors state that they have no Conflict of Interest (COI).

Acknowledgement

We would like to thank Professor Yasuo Iwasaki, Department of Neurology, Toho University Omori Medical Center for the critical suggestion and support in this study.

References

1. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia 33: 629-808, 2013.
2. Rasmussen BK, Olesen J. Symptomatic and nonsymptomatic headaches in a general population. Neurology 42: 1225-1231, 1992.
3. Williams SJ, Nukada H. Sport and exercise headache: part 2. Diagnosis and classification. Br J Sports Med 28: 96-100, 1994.
4. Sjaastad O, Bakketeig LS. Exertional headache. I. Vågå study of headache epidemiology. Cephalalgia 22: 784-790, 2002.
5. Pascual J, González-Mandly A, Martín R, Oterino A. Headaches precipitated by cough, prolonged exercise or sexual activity: a prospective etiological and clinical study. J Headache Pain 9: 259-266, 2008.
6. Chen SP, Fuh JL, Lu SR, Wang SJ. Exertional headache - a survey of 1963 adolescents. Cephalalgia 29: 401-407, 2009.
7. Van der Ende-Kastelijn K, Oerlemans W, Goedegebure S. An online survey of exercise-related headaches among cyclists. Headache 52: 1566-1573, 2012.
8. Ikeda K, Kashihara H, Hosozawa K, et al. Brain check-up-based study of migraine in Japan. Headache Care 2: 259-266, 2008.
9. Ikeda K, Hirayama T, Iwamoto K, et al. Pulse wave velocity study in middle-aged migraineurs at low risk cardiovascular disease risk. Headache 51: 1239-1244, 2011.
10. Rook ED. Benign exertional headache. Med Clin North Am 52: 801-808, 1968.

Table 2. Main Epidemiological Reports of PEH.

| Reference number | Population (n) | Age years | Country | Prevalence | Sex predominance |
|------------------|----------------|-----------|---------|------------|-----------------|
| 2                | Community residents (n = 2,008) | 25-64 | Norway | 1% | Female |
| 3                | Medical or college students (n = 295) | Adolescents | New Zealand | 26% | Female |
| 4                | Community residents (n = 1,646) | 18-65 | Norway | 12% | Female |
| 5                | Headache clinic patients (n = 6,412) | ND | Spain | 0.1% | Male |
| 6                | School students (n = 1,963) | 13-15 | Taiwan | 10% | Female |
| 7                | Cyclists (n = 4,000) | Mainly 16-75 | Netherlands | 26% | Female |
| Present study    | Health check-up (n = 2,546) | Middle age | Japan | 1.2% | Female |
11. Headache Classification Committee. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. Cephalalgia 8: 1-96, 1988.

12. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders. 2nd edition. Cephalalgia 24 (Suppl 1): 1-160, 2004.

13. Teramoto J. Primary Cough Headache. In: Nerve Syndrome VI. 2nd ed. Nippon Rinsho, Osaka, 2014: 737-739 (in Japanese).

14. Diamond S. Prolonged benign exertional headache: its clinical characteristics and response to indomethacin. Headache 22: 96-98, 1982.

15. Pascual J, Iglesias F, Oterino A, Vázquez-Barquero A, Berciano J. Cough, exertional, and sexual headaches: an analysis of 72 benign and symptomatic cases. Neurology 46: 1520-1524, 1996.

16. Ikeda K, Kawase Y, Takazawa T, Yoshii Y, Kawabe K, Iwasaki Y. Prophylactic effects of propranolol hydrochloride on primary exertional headache: comparative trial of indometacin. Shinkei Chiryo-gaku (Neurological Therapeutics) 25: 605-608, 2008 (in Japanese, Abstract in English).