Cephalalgia
An International Journal of Headache
International Headache Society

doi:10.1111/j.1468-2982.2008.01836.x

Prevalence of cluster headache in the Republic of Georgia: results of a population-based study and methodological considerations

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Katsarava Z, Dzagnidze A, Kukava M, Mirvelashvili E, Djibuti M, Janelidze M, Jensen R, Stovner LJ, Steiner TJ, on behalf of the Global Campaign to Reduce the Burden of Headache Worldwide and The Russian Linguistic Subcommittee of the International Headache Society. Prevalence of cluster headache in the Republic of Georgia: results of a population-based study and methodological considerations. Cephalalgia 2009; 29:949–952. London. ISSN 0333-1024

We present a study of the general-population prevalence of cluster headache in the Republic of Georgia and discuss the advantages and challenges of different methodological approaches. In a community-based survey, specially trained medical residents visited 500 adjacent households in the capital city, Tbilisi, and 300 households in the eastern rural area of Kakheti. They interviewed all ($n = 1145$) biologically unrelated adult occupants using a previously validated questionnaire. The household responses rates were 92% in Tbilisi and 100% in Kakheti. The survey identified 32 persons with possible cluster headache, who were then personally interviewed by one of two headache-experienced neurologists. Cluster headache was confirmed in one subject. The prevalence of cluster headache was therefore estimated to be 87/100 000 (95% confidence interval < 258/100 000). We used a conservative approach, which has an obvious advantage of high-quality data collection, but is very demanding of manpower and time. □*Cluster headache, prevalence, epidemiology*

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Introduction

Cluster headache (CH) is a strictly unilateral, severe or very severe retro-orbital or temporal headache lasting 15–180 min and accompanied by ipsilateral cranial autonomic symptoms and a sense of restlessness or agitation (1). This set of symptoms makes the condition easily recognizable but, because it is relatively uncommon, it is methodologically challenging to measure its prevalence in general population samples. In fact, few studies exist, and all so far have been done in Western Europe. No data from the eastern European or post-Soviet countries are available yet.

The Republic of Georgia is a Eurasian country in the Caucasus, located on the east coast of the Black Sea and bordered on the north by Russia, on the south by Turkey and Armenia and on the east by Azerbaijan. Its current population is 4.4 million (2). Between 1921 and 1991, Georgia was part of the Soviet Union; it declared independence after the collapse of USSR. Georgia has many socio-economic and cultural similarities with other, mostly European post-Soviet countries (Armenia, Azerbaijan,

the European part of Russia, Byelorus, Ukraine and Moldova). We present a study on the prevalence of CH in Georgia, which is part of an epidemiological survey on the prevalence of primary headaches in that country.

Methods

The study protocol was approved by the Georgian National Council on Bioethics.

The methodology of the study and the validation of the questionnaire have been reported previously (3, 4). The study was performed in the capital city, Tbilisi, and in a rural area of Kakheti in the east part of Georgia. We used the 'cold-calling' method of door-to-door survey (calling unannounced). Prior to the study, medical residents were specifically trained by headache-experienced neurologists (Z.K., A.D., M.K.) to identify migraine, tension-type headache (TTH) and CH. The residents visited adjacent households in pre-defined districts in Tbilisi and villages in Kakheti and asked all biologically unrelated adults (> 18 years old) in the households to undergo a structured, questionnaire-based headache interview, which aimed not to diagnose CH but to screen for possible cases according to these criteria:

A: recurrent headache that was at least two of the following: (i) severe or very severe; (ii) strictly unilateral; (iii) retro-orbital or temporal; and
B: at least one of the following accompanying symptoms or signs: (i) ipsilateral conjunctival injection or tearing; (iii) ipsilateral nasal conjunction or rhinorrhoea; (iii) ipsilateral eyelid oedema; (iv) ipsilateral forehead or facial sweating; (v) ipsilateral miosis or ptosis; and (vi) a sense of restlessness or agitation.

Respondents fulfilling these criteria, either for current or past headache, were later re-interviewed and examined in person by one of two headache experienced neurologists (A.D. and M.K.). CH was diagnosed by International Classification of Headache Disorders, 2nd edn criteria (1). Symptomatic headaches were ruled out by clinical examination and, where necessary, cranial computed tomography or magnetic resonance imaging.

Statistics

Crude prevalence of CH was expressed as the number of cases per 100 000 inhabitants. The 95% confidence interval (CI) was calculated by the method of Bortz (5). The level of significance was set at 0.05.

Results

We interviewed 1701 respondents in 500 households in Tbilisi and 560 in 300 households in Kakheti. The household response rates were 92% in Tbilisi (38 households refused contact with the interviewers) and 100% in Kakheti. The target population consisted of 1145 biologically unrelated adults (e.g. cohabiting couples, but not the blood relatives of either partner). The mean age of the target population was 45.4 ± 12 years, 60% of whom were women.

Suspected CH cases

We identified 32 subjects with or having had possible CH, six of them male, with mean age 39 ± 12 years. All were invited to a neurological consultation to be re-interviewed and examined.

Confirmed CH cases

One respondent with definite CH was identified: a 32-year-old man who had experienced his first cluster attack at the age of 27. Thereafter, he had suffered one or two cluster bouts per year of 14–16 weeks' duration. These were characterized by recurrent attacks, each lasting 45–60 min, of strictly right-sided retro-orbital stabbing headache accompanied by lacrimation, eyelid oedema and rhinorrhoea. He used subcutaneous sumatriptan for acute treatment but had had no preventative medication.

The lifetime prevalence of CH was estimated therefore to be 87 per 100 000 (upper 95% CI limit 258 per 100 000).

Non-confirmed cases

In 31 respondents the suspected diagnosis of CH was rejected. Sixteen had migraine, eight had TTH, five had a combination of migraine and TTH, one had acute frontal sinusitis and one had a brain tumour. All those with migraine had at least one cluster-like autonomic symptom which led to the suspicion of CH. No obvious reason existed for misdiagnosis of CH in the eight respondents who had TTH.

Discussion

To the best of our knowledge, this is the first study to provide data on the prevalence of CH in an eastern European country. In a general population sample of 1145 people in the Republic of Georgia,

we identified one case of CH, past or present. This corresponds to a lifetime prevalence of 87 per 100 000 with a 95% CI upper limit of 258 per 100 000. The power of the study was not enough to estimate both borders of the 95% CI.

Studying the epidemiology of CH is challenging for two key reasons. First, the prevalence of CH is low. Second, its diagnosis can be unreliable in a non-clinical setting. The clinical features of CH may be striking when they occur together, but many of them—stabbing unilateral headache and each of the typical autonomic symptoms—may also feature not only in other trigeminal autonomic cephalalgias (which are rare) but also in migraine. Our questionnaire was sensitive rather than specific for CH, which it needed to be in order not to miss the very few expected cases in a sample of just over 1000. These two factors run counter to each other. On the one hand, ideally the entire sample should be interviewed face-to-face by a headache specialist; on the other, the size of the sample needs to be large. The ideal is therefore heavily demanding of manpower and time.

An alternative is a two-phase approach with a screening procedure and a subsequent validating neurological consultation for all screen-positive cases. The screening can be by self-administered questionnaire, telephone interview or face-to-face interviews by trained lay or medical personnel, which are probably increasingly methodologically sound in that order. We used the last. Even so, this approach is less robust than the ideal: it saves resources but, if a single case is overlooked in a sample of manageable size, the estimated prevalence will be badly erroneous.

A second alternative offers itself in countries where general practitioners' lists cover almost the entire population: data from general practices may be representative. Against this alternative is the low accuracy and limited recorded detail of headache diagnoses made by general practitioners. The final possibility is to investigate a population sample with a higher than average risk (e.g. young men) but, obviously, great caution will be needed in drawing conclusions about the wider population.

Fewer than 10 studies of the prevalence of CH are reported in the world literature, and these have used several approaches. The most exacting methodology was employed in the Vågå study in Norway, in which the lead author, with great commitment, personally interviewed and examined the entire study population in order to determine the prevalence of all rare unilateral headaches (6). This resulted in the highest ever reported prevalence rate of CH of 326 per 100 000 (95% CI 120, 720 per 100 000), a figure not compatible with ours. In Denmark, a sample of 1000 inhabitants of Copenhagen was surveyed for primary headaches by face-to-face interview and neurological examination (7). One case of CH was identified in this study, a finding similar to ours and again not statistically compatible with the prevalence recorded in Vågå. Studies like this are very costly, and therefore hard to replicate in Western Europe and North America, where human resource costs are high. However, in developing countries it may still be possible to perform large-scale epidemiological studies based on face-to-face interviews, at least if they can be performed by lay persons or medical residents, because of the low income rates. Our Georgian study is an example of this. Another is a population-based study in Ethiopia, carried out by trained lay persons, which estimated a prevalence of CH of 30 per 100 000 (8).

In order to make a study feasible, the German Headache Consortium first screened a population of 3336 people by self-administered questionnaire, seeking possible cases of CH. The 182 people suspected to have CH were then examined in person by headache specialists. The diagnosis was confirmed in only four cases, giving a 1-year prevalence of CH of 119/100 000 (95% CI 3, 238/100 000) (9). This finding again is in keeping with ours and not with the Vågå study. Another German study invited a random sample of 1312 inhabitants of the City of Dortmund to a first screening interview, among whom 33 reported attacks of unilateral headache lasting < 6 h with at least one of the typical autonomic symptoms of CH. All of these were then examined by a headache expert. Two cases of CH were identified, a prevalence rate of 150 per 100 000 (upper 95% confidence limit 360 per 100 000) (10). An Italian group screened a sample of 10 071 patients registered in the lists of seven Parma-based general practitioners using a self-administered questionnaire. Of the 111 suspected cases of CH, the diagnosis was confirmed in 21, yielding a prevalence estimate of 279 per 100 000 (95% CI 173, 427) (11). A study in San Marino reviewed the past 15 years' medical records of neurological, ophthalmological and ear, nose and throat practices in the whole republic (12). Suspected cases of CH were examined by neurologists, with the diagnosis confirmed in 15 people. The prevalence rate was estimated at 69 per 100 000, but it was not possible in this study to know precisely what the denominator was. A recent Swedish twin register study has provided an estimate of 151 per 100 000 (13).

These studies to some extent demonstrate the advantages and challenges of different approaches, which were obviously chosen by authors in consideration of prevailing circumstances. There are several important general issues. Studies must be population-based in order to achieve results representative of the population. Whereas it is optimal to conduct expert examinations of the entire sample, this is not possible in most situations and, when attempted, is likely to result in a reduced sample size. We believe that self-administered questionnaires (even if well validated) cannot assure diagnostic accuracy for CH. In the German Headache Consortium study, the diagnosis of CH was found to be correct in only four of 182 putative cases (9), a specificity of 2.2%. In our Georgian study, even trained medical residents misdiagnosed 31 cases, among which, and especially striking, were eight people with pure TTH. We therefore conclude that suspected cases of CH must be confirmed by clinical review by doctors with expertise in headache diagnosis.

Finally, we stress the strengths and challenges of our study. The methodology assured high quality of data collection. We studied a capital city as well as a rural area of the country. We achieved very high response rates of $>92\%$. All subjects with possible CH were reviewed personally by headache-experienced neurologists. The main limitation of the study was that the population sample was too small to allow an accurate estimate of a rare disorder like CH. Ideally, it should have been three to four times as large to have sufficient statistical power.

References

1 Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders, 2nd edition. Cephalalgia 2004; 24 (Suppl. 1):9–160.
2 Statistic yearbook of Georgia. Tbilisi, GA: National Department for Statistics 2005.
3 Katsarava Z, Kukava M, Mirvelashvili E, Tavadze A, Dzagnidze A, Djibuti M, Steiner TJ. A pilot methodological validation study for a population-based survey of the prevalences of migraine, tension-type headache and chronic daily headache in the country of Georgia. J Headache Pain 2007; 8:77–82.
4 Kukava M, Dzagnidze A, Janelidze M, Mirvelashvili E, Djibuti M, Fritsche G et al. Validation of a Georgian language headache questionnaire in a population-based sample. J Headache Pain 2007; 8:321–4.
5 Bortz J. Statistik für Human- und Sozialwissenschaftler, 6. Aufl. ed. Heidelberg: Springer Verlag 2005.
6 Sjaastad O, Bakketeig LS. Cluster headache prevalence. Vaga study of headache epidemiology. Cephalalgia 2003; 23:528–33.
7 Rasmussen BK, Jensen R, Schroll M, Olesen J. Epidemiology of headache in a general population—a prevalence study. J Clin Epidemiol 1991; 44:1147–57.
8 Tekle Haimanot R, Seraw B, Forsgren L, Ekbom K, Ekstedt J. Migraine, chronic tension-type headache, and cluster headache in an Ethiopian rural community. Cephalalgia 1995; 15:482–8.
9 Katsarava Z, Obermann M, Yoon MS, Dommes P, Kuznetsova J, Weimar C, Diener HC. Prevalence of cluster headache in a population-based sample in Germany. Cephalalgia 2007; 27:1014–19.
10 Evers S, Fischera M, May A, Berger K. Prevalence of cluster headache in Germany: results of the epidemiological DMKG study. J Neurol Neurosurg Psychiatry 2007; 78:1289–90.
11 Torelli P, Beghi E, Manzoni GC. Cluster headache prevalence in the Italian general population. Neurology 2005; 64:469–74.
12 D'Alessandro R, Gamberini G, Benassi G, Morganti G, Cortelli P, Lugaresi E. Cluster headache in the Republic of San Marino. Cephalalgia 1986; 6:159–62.
13 Ekbom K, Svensson DA, Pedersen NL, Waldenlind E. Lifetime prevalence and concordance risk of cluster headache in the Swedish twin population. Neurology 2006; 67:798–803.