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TUTORIAL

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Headache epidemiology: how and why?

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Abstract The objective is to give an introduction to methods and study designs used in headache epidemiologic studies, to discuss their merits and problems, and to show the potential of such studies. The distinction between descriptive and analytic studies is made, and methodological issues are discussed related to headache case definition, validation of diagnoses, time frame for headache, instruments for data collection, source population and sampling methods, as well as the problems with bias and confounding. Examples of how different designs (case series, ecological, cross-sectional, case-control and cohort studies) have been used in the headache field are then presented. Studies on headache epidemiology are important to document the prevalence and burden of headache disorders. It is as important that studies with an analytical design can prove to be potent tools to disclose causes and risk factors for headache, but a standardisation of methods is needed to increase comparability of studies.

Keywords Migraine headache • Epidemiology • Methodology study design

Introduction

In the literature on headache epidemiology [1], the majority of studies have been descriptive, giving data on the distribution of headache prevalence and the resulting burden and cost among different groups. More recently, analytic epidemiologic studies with the explicit aim of studying causation by considering whether the risk of headache is different for those exposed and not exposed to some factor of interest have been performed. The present paper will focus on some important methodological issues in headache epidemiology, discuss the relative merits of different methodologic designs and the main sources of error, and finally outline the current challenges for headache epidemiology.

Methodology

Case definition, or how to define who has headache (is a case) and who has not, is a problem because headache diagnoses usually are made on the basis of subjective experiences without any objective signs or markers. Even the term "headache" can be ambiguous, and higher headache prevalence will be found in answer to a neutral question ("do you have headache?") than to questions involving some specification of headache degree (e.g., "do you suffer from headache?" or "do you have severe headache?") [2]. This is important when a question about headache is used to screen out non-headache sufferers before the more specific questions about the features of the various headache types are posed. Headache diagnoses are ultimately dependent on self-report, and the quality of recall is of crucial importance. Recall problems may explain why those who answer "no" to the screening question about

headache may nevertheless suffer from headache, even migraine [3]. In addition, cultural differences related to the threshold for reporting pain may contribute to variation in headache prevalence in different regions or over time.

To define the various headache subtypes, most epidemiologic studies have used the criteria of the International Headache Society (IHS) from 1988, or the revision from 2004 (International Classification of Headache Disorders, 2nd edition (ICHD-2)), but often with some modifications. The way these criteria are applied may give rise to large variations in prevalence. Recent studies from the USA [4] and France [5] indicate that the migraine prevalence will almost double if not only strict migraine (ICHD-2, 1.1 and 1.2) but also probable migraine (ICHD-2, 1.6) are counted as migraine.

It is also a problem that multiple headache types often coexist in the same individuals. In the classification it is required that each headache occurring in the same individual gets a separate diagnosis and that secondary causes of headache are excluded. The extent to which multiple headaches can be diagnosed is highly dependent on the method of data collection. To make reliable diagnoses of several coexisting headaches, including the rare primary or secondary headaches, it is necessary that a *personal interview and examination* is performed by a neurologist using the diagnostic criteria (the "gold-standard" method). This approach is expensive and has been used in only a few population studies [6, 7]. However, secondary causes of headache are uncommon in the general population [8], and multiple headache types are of less importance when the study aim is to identify only migraine or tension-type headache (TTH) sufferers. *Screening by other health personnel (nurses, medical students) or instructed lay persons* has been shown to be accurate when the aim is to identify only the most common headache types. *Telephone interviews* may enable diagnosis of more than one of the primary headaches, whereas this has proved to be very difficult with questionnaires. In *questionnaire studies*, the participants are often asked to give an answer based on the overall most distressing headache type. A *recognition-based method*, giving descriptions of migraine and TTH based on the IHS criteria to the participants, has been found to be quite reliable for mass screening of migraine and TTH among adolescents [9].

In many headache epidemiologic studies it is necessary not only to define a case (headache) group but also a *control (reference) group*. As headache is experienced at least occasionally by the great majority of the population, it is hard to find a control group without headache. It may be better to define a reference group with minor headache complaints, e.g., including persons with infrequent TTH (ICHD-2).

As headache usually varies considerably through life, it is important to define the time frame for the headache. *Lifetime prevalence* measures the lifetime occurrence of headache. *One-year prevalence* is often used because it is considered reasonably reliable, and it defines the proportion of the population that has an active disease, therefore being relevant for assessing the burden of headache in society. *The three-month prevalence* gives similar information, and probably also studies not specifying a time frame, only asking a question like "do you suffer from headache?". In general, it is highly advisable to specify a time frame, and most studies to date have been done with the one-year prevalence.

Validation of the diagnostic method to estimate the degree of agreement (sensitivity, specificity, positive and negative predictive values) between the method applied and the gold-standard method in a random sample of participants should be performed in most headache epidemiologic studies [10]. A validation study should be done even if the questionnaire has already been validated, as one method may not be valid in other regions or countries, or at another time.

Defining the source population, i.e. the population from which study participants are drawn, is important for the *representativeness* of the study. Samples from a country, region, city or smaller community may be representative for the whole population, and primary school students for their age group, whereas patients, university students or company employees are probably not representative. To obtain a representative group the sampling method is also important. If the *whole population* cannot be studied, a *random sample* of the population will most probably yield a representative group, or one may use a *stratified sample* to ensure that the studied group is similar to the source population with regard to e.g., age, gender and socioeconomic status.

Even if the source population and sampling methods are adequate, the study population may still not be representative if participation in the study is low and some groups are more likely to participate than others. If headache is the main object of the study, individuals suffering from headache may be more likely to participate than non-headache sufferers, and headache prevalence may be overrated. Likewise, if certain age or socioeconomic groups have a higher non-participation rate than the average, this may distort the results. It is usually desirable that an *evaluation of the non-participants* is performed to assess whether they are different from the participating population with regard to demographic variables, or the participating population can be compared e.g., to census data for the country or town in which the study takes place. If participation is found to vary substantially by demographic characteristics, prevalence rates can be adjusted to compensate for differential participation.

Types of epidemiologic studies

In a *case series*, headache is described and often related to some other factor in a group of patients, e.g., occurrence of migraine attacks have been related to meteorological factors [11] or the menstrual cycle [12]. In addition, several studies have described the prevalence and special features of migraine and headache in patients with other disorders, e.g., Tourette syndrome [13] or idiopathic intracranial hypertension [14]. As there is no control group, only hypotheses about causal factors can be formulated on the basis of such studies.

With *ecological (or correlational) studies*, the headache prevalence in a defined population is related to some other factor, e.g., to employment rate in different districts [15], or migraine prevalence related to altitude [16]. A limitation of this method is that exposure cannot

be linked to particular individuals, and that it is not possible to adjust for possible confounding factors.

In *cross-sectional surveys*, the disease status of individuals in the population is assessed at the same time as exposures of interest, such as demographic factors, comorbid conditions or other suspected risk factors. A *prevalence study* is a cross-sectional study conducted to determine the proportion of the population that has a disease. In virtually all prevalence studies in adults there is a higher proportion of headache sufferers among women than among men. Migraine prevalence typically increases in childhood and youth, and is relatively stable and high in the third to the fifth decade, after which there is a marked decline in both sexes. TTH appears to be less related to age than migraine. Prevalence studies have also given data on attack frequencies, duration and severity. In addition, the impact of headache on public health can be studied by adding questions about influence on work and leisure activities, absenteeism etc.

If a study is repeated on the same individuals, it is possible to calculate headache *incidence*, i.e., the number of new ("incident") cases in a defined population, accumulated over several years, or per time period (e.g. [17]). Cross-sectional studies may also be used to assess associations between headache and suspected risk factors and other disorders.

In *case–control studies*, a group of headache sufferers is compared with a control group (healthy persons or individuals with some other disorders) with regard to either a suspected cause or some other clinical features or factors. An example is the study showing that body mass index was higher and socioeconomic status lower among patients with chronic daily headache than among those with episodic headache [18]. The case–control method has also been used to compare the prevalence of headache among subjects with or without another disorder, e.g., that headache was more prevalent among patients referred for polysomnography for obstructive sleep apnoea than among controls [19].

A limitation of case-control and cross-sectional studies for studying causation is that both disease and suspected cause are measured at the same point in time. Hence, it is not always certain that exposure to the risk factor of interest preceded the onset of illness, particularly when considering exposures that change as a result of medication [20]. This problem is overcome in *cohort studies*, in which groups are selected on the basis of whether they have been exposed to a suspected cause or not, before the onset of illness, and they are subsequently monitored for the occurrence of the outcome of interest. It is important that knowledge about the disease (headache) is not used to define the cohorts, and disease status should be determined in a blinded manner without knowledge of prior exposure status. Selective participation in the follow-up dependent on exposure status may distort results in cohort studies. In cohort studies, it has been demonstrated that depression is a risk factor for migraine but not other headaches after 2 years [21], but whiplash trauma or concussion are not risk factors for headache 1 year or more after the trauma [22, 23]. Similarly, headache and migraine have been found to be risk factors for incident stroke in several cohorts [24, 25].

The true association of a disorder to some exposure may be distorted by bias and confounding. *Selection bias* (related to who participates in the study as a case or control) can result from poor participation or sampling, misdiagnosis of disease status and loss to follow-up. *Information bias* (related to the information about or measurement of exposure) includes measurement problems due to defective instrumentation, non-blinded investigators or differences in recall between groups.

A *confounder* is a third factor that can explain the association between an exposure and a disorder, without itself being on the causal chain between cause and effect. Age, gender and socioeconomic status are important potentially confounding factors in headache epidemiologic studies as well as for many other diseases.

The challenge for headache epidemiology

Epidemiologic studies have demonstrated that headache and migraine are prevalent and entail a high burden on populations in many areas of the world, but we still need documentation from populous areas like China, India, Russia and large parts of Africa. In addition, there are surprisingly few studies on TTH, which is the most prevalent headache type.

Epidemiologic studies have demonstrated large variations in headache prevalence, not only across countries but also over time in the same country. At present, it is hard to determine whether these variations are real or due to methodological differences, and to make meaningful comparisons between different studies it is necessary that the methods in headache epidemiology are standardised. This would have to include how to define the source population, sampling, case ascertainment and phrasing of questions, how to avoid biases and to deal with possible confounders.

It is a cause for concern that some recent studies indicate an increase in headache prevalence over time, and investigations to determine whether the increase is real or whether it is apparent, due to changes in methodology or the threshold for reporting headache in the population, should have high priority. If real, headache epidemiology could be the most important instrument to identify the causes so that the trend can be changed.

References

1. Stovner LJ, Scher AI (2005) Epidemiology of headache. In: Olesen J, Goadsby P, Ramadan N et al (eds) The headaches, Vol 3, 3rd edn. Lippincott Williams & Wilkins, Philadelphia, pp 17–25
2. Stovner LJ, Zwart J-A, Hagen K et al (2005) Epidemiology of headache in Europe. Eur J Neurol 12 (*in press*)
3. Launer LJ, Terwindt GM, Ferrari MD (1999) The prevalence and characteristics of migraine in a population-based cohort: the GEM study. Neurology 53:537–542
4. Patel NV, Bigal ME, Kolodner KB et al (2004) Prevalence and impact of migraine and probable migraine in a health plan. Neurology 63:1432–1438
5. Lanteri-Minet M, Valade D, Geraud G et al (2004) Migraine and probable migraine-results of FRAMIG 3, a French nationwide survey carried out according to the 2004 IHS classification. Cephalalgia 26:1146–1158
6. Rasmussen BK, Jensen R, Schroll M, Olesen J (1991) Epidemiology of headache in a general population – a prevalence study. J Clin Epidemiol 44:1147–1157
7. Sjaastad O, Batnes J, Haugen S (1999) The Vaga Study: an outline of the design. Cephalalgia 19[Suppl 25]:24–30
8. Rasmussen BK, Olesen J (1992) Symptomatic and nonsymptomatic headaches in a general population. Neurology 42:1225–1231
9. Zwart JA, Dyb G, Stovner LJ et al (2003) The validity of 'recognition-based' headache diagnoses in adolescents. Data from the Nord-Trondelag Health Study 1995–97, Head-HUNT-Youth. Cephalalgia 23:223–229
10. Hagen K, Zwart JA, Vatten L et al (2000) Head-HUNT: validity and reliability of a headache questionnaire in a large population-based study in Norway. Cephalalgia 20:244–251
11. Mitsikostas DD, Tsaklakidou D, Athanasiadis N, Thomas A (1996) The prevalence of headache in Greece: correlations to latitude and climatological factors. Headache 36:168–173
12. Stewart WF, Lipton RB, Chee E et al (2000) Menstrual cycle and headache in a population sample of migraineurs. Neurology 55:1517–1523
13. Kwak C, Vuong KD, Jankovic J (2003) Migraine headache in patients with Tourette syndrome. Arch Neurol 60:1595–1598
14. Wall M (1990) The headache profile of idiopathic intracranial hypertension. Cephalalgia 10:331–335
15. Carlsson J (1996) Prevalence of headache in schoolchildren: relation to family and school factors. Acta Paediatr 85:692–696
16. Arregui A, Cabrera J, Leon-Velarde F et al (1991) High prevalence of migraine in a high-altitude population. Neurology 41:1668–1669
17. Lyngberg AC, Rasmussen BK, Jørgensen T, Jensen R (2005) Incidence of primary headache: a Danish epidemiologic follow-up study. Am J Epidemiol 161:1066–1073
18. Scher AI, Stewart WF, Ricci JA, Lipton RB (2003) Factors associated with the onset and remission of chronic daily headache in a population-based study. Pain 106:81–89
19. Sand T, Hagen K, Schrader H (2003) Sleep apnoea and chronic headache. Cephalalgia 23:90–95
20. Zwart JA, Dyb G, Hagen K et al (2004) Analgesic overuse among subjects with headache, neck, and low-back pain. Neurology 61:1540–1544
21. Breslau N, Lipton RB, Stewart WF et al (2003) Comorbidity of migraine and depression: investigating potential etiology and prognosis. Neurology 60:1308–1312
22. Obelieniene D, Schrader H, Bovim G et al (1999) Pain after whiplash: a prospective controlled inception cohort study. J Neurol Neurosurg Psychiatry 66:279–283
23. Mickeviciene D, Schrader H, Obelieniene D et al (2004) A controlled prospective inception cohort study on the post-concussion syndrome outside the medicolegal context. Eur J Neurol 11:411–419
24. Jousilahti P, Tuomilehto J, Rastenyte D, Vartiainen E (2003) Headache and the risk of stroke: a prospective observational cohort study among 35,056 Finnish men and women. Arch Intern Med 163:1058–1062
25. Merikangas KR, Fenton BT, Cheng SH et al (1997) Association between migraine and stroke in a large-scale epidemiological study of the United States. Arch Neurol 54:362–368