

Stefan Evers

5.1 Introduction

This chapter reviews the guidelines for the pharmacological treatment of headache disorders. It focuses on Europe and on those guidelines available at present for the public community and created according to evidence-based medicine. There are several so-called guidelines published by single persons or scientific societies, which are not part of the International Headache Society; these will not be considered.

Since it would be a major opus to compare all single treatment recommendations for all headache disorders in these dozens of published guidelines, this chapter will mainly discuss the structure of and the systematic differences between these guidelines.

Although the topic of this book includes only pharmacological treatment of headaches, many guidelines also consider non-pharmacological treatment such as different types of psychotherapy, physiotherapy, and interventional treatment.

5.2 Historical Remarks

Guidelines on headache treatment have been published since antiquity. Systematic treatment recommendations for headaches have been given by Aretaios of Cappadocia (80/81 to 130/138) and by Galen (129/131 to 199/215) in particular. For the Islamic world, Avicenna (980 to 1037) published treatment guidelines on headache, which were later introduced in the European medical writings.

S. Evers
Department of Neurology, Krankenhaus Lindenbrunn,
Lindenbrunn 1, Coppenbrügge 31863, Germany
e-mail: everss@uni-muenster.de

In the neurological textbooks (the first by Jason Pratensis (1486–1558), *De cerebri morbis*) until the nineteenth century, the treatment of headache was described but no systematic recommendations were given. Even in the famous textbooks on headache such as “On megrim, sick-headache and some allied disorders” (1873) by Edward Liveing or “Wolff’s headache” (1948) by Harold G. Wolff, no systematic treatment descriptions are mentioned.

The first modern, officially published treatment guideline for headache was probably the guideline by the Italian Headache Society SISC in 1993 based on a wide revision of the existing literature and a consensus conference of Italian headache experts [14]. The method of this guideline was not what we call nowadays evidence-based medicine, but it was already the same principle: reviewing the literature and finding an expert consensus. This first guideline on adults was followed in 1996 by a guideline on children and adolescents published by the same society [18]. After this, several European countries and finally the European Federation of Neurological Societies (EFNS) published different guidelines, which are available until now. All modern guidelines use the International Classification of Headache Disorders (3rd edition) for their recommendations, and only guidelines with this background should be considered in daily practice.

5.3 Systematic Remarks

Guidelines on headache treatment can be classified with respect to several different levels. First, we differentiate between so-called cross-sectional guidelines and diagnosis-related guidelines. Cross-sectional guidelines do not focus on a specific headache diagnosis but on a specific patient group or situation. Among these, we can find guidelines on headache treatment in different age groups (e.g., children and elderly people), guidelines on specific situations (e.g., pregnancy, lactation, headache as emergency; even headache in sports had been addressed), guidelines on specific legal situation (e.g., expert testimony in cases with headache). It is also of particular interest to know who is addressed by the guideline. The details of recommendation might differ with respect to the addressed healthcare workers, there are guidelines addressing general practitioners, addressing emergency physicians, addressing neurologists, addressing headache experts, and addressing nonphysicians such as nurses or chirotherapists.

Another level of differentiation is the source of guideline. Most of the guidelines have been written by a collective of authors appointed by the national scientific headache society. But there are also guidelines created by other scientific societies such as the society for general medicine (General Practitioner guidelines) and others created by legal institutions or health authorities. The latter ones can be in concurrence to scientific society guidelines. As an example, the British Association for the Study of Headache (BASH) published a guideline on the treatment of migraine; in parallel, there is a guideline by the National Institute for Health and Care Excellence (NICE) on headache in adults, including migraine. This refers also to the applicability and relevance of the guidelines. In some countries, such as in Germany and Switzerland, the national guidelines are only recommendations for

the physicians (and related professions) but are not regular documents of the authorities. Therefore, physicians do not have to stick to these guidelines, and reimbursement of treatment does not necessarily depend on these guidelines. In other countries such as Belgium or the United Kingdom, physicians are not independent in their decision to treat headache but have to stick to the guidelines developed by the authorities. In particular, reimbursement of treatment costs by the national health system is restricted to those procedures listed in such guidelines.

Further, the regional level can be different for guidelines. Normally, guidelines are published by a national scientific society dealing with headache. Most countries have their own national headache society; in some countries, this is part of the national neurological society. The only exception in Europe is the United Kingdom where we have the BASH guideline and the NICE guideline for England (see above) and separately the guideline on headache by the Scottish Intercollegiate Guidelines Network (SIGN). There are some examples for supranational, but not European guidelines; the German-speaking countries have created common guidelines in the same language for all three countries (Austria, Germany, and Switzerland), with some final specific remarks only valid for the health system of one of these countries.

On the European level, the EFNS started its guideline program with the European Handbook of Neurological Management in 2006. This also included guidelines on the treatment of migraine and of cluster headache. Since then, more new and revisions of older guidelines in the field of headache have been published by the EFNS. The International Headache Society (IHS) as the global scientific society for headache has explicitly waived the idea to publish treatment guidelines for headache disorders, although this was a controversial debate. This decision was based on the fact that, particularly in headache treatment, the national health systems have a major impact on the medical pathways and that these systems are very different all over the world. So, international treatment guidelines might cause more problems than solving problems in countries with no national guidelines. A specific role is played by the Cochrane library, which does not publish treatment guidelines as such but which publishes recommendations for different treatment procedures in the field of headache, which can be used for treatment guidelines. These Cochrane recommendations are purely evidence-based and do not consider national health system restrictions.

Furthermore, the grade of evidence is also different between some guidelines. We have different systems of evaluating the evidence in the scientific literature, and according to these different methods, we have different grading systems for the level of evidence. The system introduced by the EFNS is the most often used one, but it is not applicable to all systems.

5.4 Comparison of Guidelines

In Table 5.1, all available treatment guidelines for headache disorders published by the responsible national scientific societies are presented; the EFNS guidelines are also included.

Table 5.1 Guidelines on headache treatment published by the national scientific headache societies and the EFNS in the Internet or in scientific journals

Austria	See also Germany
Belgium	Guideline for migraine treatment in primary care (Internet)
	Guideline for the management of chronic migraine [22]
Croatia	Evidence-based guidelines for treatment of primary headaches [27]
Denmark	Guideline for diagnosis and treatment of headache disorders and facial pain [3]
Finland	Guideline on migraine treatment – Migreenin käypä hoito (internet)
France	Revised French guidelines for the diagnosis and management of migraine in adults and children [16]
	Chronic migraine and chronic daily headache [17]
Germany	Treatment of headache in pregnancy and lactation [4]
	Treatment of migraine [7]
	Treatment of headaches in children and adolescents [8]
	Self-medication in migraine and tension-type headache [12]
	Treatment of chronic headache including tension-type headache [26]
	Treatment of rare idiopathic headache disorders [6]
	Treatment of cluster headache [19]
Treatment of trigeminal neuralgia [23]	
Italy	Italian guidelines for primary headaches: 2012 revised version [24]
Hungary	Guideline on headache treatment (Internet)
Netherlands	Diagnostic and therapeutic guideline on chronic headache without neurological abnormalities (internet)
Portugal	Therapeutic recommendations for headache [21]
Spain	Manual book on diagnosis and treatment of headache [13]
Switzerland	Therapeutic recommendations for primary headaches 2014 (Internet)
	See also Germany
UK	Guidelines for All Healthcare Professionals in the Diagnosis and Management of Headache Disorders (Internet)
	Headache in sports [15]
EFNS	Treatment of migraine [9]
	Treatment of cluster headache [20]
	Treatment of tension-type headache [2]
	Treatment of trigeminal neuralgia [5]
	Treatment of rare idiopathic headache disorders [10]
Treatment of medication-overuse headache [11]	

In general, the recommendations in all guidelines are very similar both for acute and for prophylactic drug treatment. All guidelines recommend the use of NSAIDs and of triptans in acute migraine treatment. Ergotamine derivatives are not drugs of first choice any more in the guidelines after the year 2010. For the prophylactic drug treatment, beta-blockers and anticonvulsant drugs (valproic acid and topiramate) are first choice in all guidelines. There is a considerable difference in some countries with respect to antidepressants in migraine prophylactic treatment. This has

also been noticed in previous comparisons of migraine guidelines [1], and this is also a major difference to the US American guideline on migraine prevention [25].

Systematic comparisons for the treatment of other headache disorders cannot be made since in many countries only migraine guidelines exist. For tension-type headache and for cluster headache, the available evidence on drug treatment is poor and only very few trials exist. Therefore, evidence-based treatment guidelines are difficult to create. For other primary headache disorders, only one guideline could be identified [6]; the available evidence for drug treatment in this group is even poorer. There are no guidelines on the treatment of secondary headaches and only a few on the treatment of trigeminal neuralgia and facial pain.

With respect to cross-sectional guidelines, only children and adolescents have been addressed in more than one guideline. Often, all age groups were included in one guideline but discussed separately in different chapters. Since specific trials on different patient groups in headache treatment are rare, good evidence is hard to obtain for cross-sectional guidelines.

According to a previous analysis of guidelines [1], guidelines are developed to assist the physician in making appropriate choices in the treatment of headache patients. To ensure their optimal use, guidelines need to be kept up to date; they should encompass the most recent published evidence and therapeutic strategies. Because guidelines are needed to set recognizable and acceptable standards of good practice, their adoption in primary care should be encouraged. This has, however, not been the case in most guidelines published in Europe.

5.5 Critical Remarks

After a boom in the years between 2000 and 2010, many guidelines have not been updated and almost no new guidelines have been published. It might be that there was a period with enthusiasm on evidence-based medicine, which has now gone down. However, it is important to update guidelines regularly. The quality of guidelines even depends on a regular update, which should be dated in the prior guideline. Another problem might be that human and financial resources are more limited nowadays to create a guideline. This is even more a problem since the requirements to write an accepted guideline have increased.

Another problem is that in most countries, only guidelines on the treatment of migraine exist. Guidelines on other primary headaches can be found only infrequently and guidelines on secondary headaches do not exist (with the exception of medication-overuse headache). The basic principles of migraine treatment are well known and presented in several neurological textbooks. However, the treatment of rare idiopathic headache disorders is a major problem even for neurologists and some guidance would be of benefit. In tension-type headache, several recommendations which are not evidence-based exist in the literature and it would be important for GP and even neurologists to be informed about which recommendation is evidence-based and which is not. With respect to secondary headaches, treatment recommendations are often restricted to the treatment of the underlying disorder.

This is, however, not always appropriate. It should be considered that some secondary headaches are primarily seen by headache specialists such as headaches associated with changes in intracranial pressure. For these headache disorders, evidence-based treatment guidelines are warranted.

The question arises whether it would be sufficient to have only one European headache guideline for the different headache disorders rather than several national guidelines that are nearly identical. There is of course a major benefit for the headache community if only one guideline exists, which is updated regularly and supervised by the most accepted headache experts. On the other hand, such a guideline could not consider the impacts of the national health systems on treatment decisions. The availability of drugs, the reimbursement of pharmacological treatment, the procedures of outpatient and inpatient vary considerably between the different European countries. In addition, there are also cultural aspects that should be integrated in treatment guidelines (e.g., willingness of a population to take drugs for pain or to give children drugs for pain). A solution could be that a guideline manual is created, which encompasses several drug profiles and the evidence of these drugs for specific headache disorders, and which is complemented by specific national recommendations.

Finally, a problem is that only a few European guidelines are published internationally. Internet publications of guidelines are mainly written in the native language and can therefore not be discussed in the scientific community and cannot be understood by others who are in the process of writing guidelines. Guidelines published in scientific journals should be written both in the native language to attract as many physicians as possible and in English to allow a scientific debate on these guidelines.

References

1. Antonaci F, Dumitrache C, De Cillis I, Allena M (2010) A review of current European treatment guidelines for migraine. *J Headache Pain* 11:13–19
2. Bendtsen L, Evers S, Linde M, Mitsikostas DD, Sandrini G, Schoenen J, EFNS (2010) EFNS guideline on the treatment of tension-type headache – report of an EFNS task force. *Eur J Neurol* 17:1318–1325
3. Bendtsen L, Birk S, Kasch H, Aegidius K, Sørensen PS, Thomsen LL, Poulsen L, Rasmussen MJ, Kruuse C, Jensen R, Danish Headache Society (2012) Reference programme: diagnosis and treatment of headache disorders and facial pain. Danish Headache Society, 2nd Edition, 2012. *J Headache Pain* 13(Suppl 1):S1–S29
4. Bingel U, Evers S, Reister FA, Ebinger F, Paulus W (2009) Behandlung der Migräne und idiopathischer Kopfschmerzsyndrome in Schwangerschaft und Stillzeit. *Nervenheilkunde* 28:896–906
5. Cruccu G, Gronseth G, Alksne J, Argoff C, Brainin M, Burchiel K, Nurmikko T, Zakrzewska JM, American Academy of Neurology Society, European Federation of Neurological Society (2008) AAN-EFNS guidelines on trigeminal neuralgia management. *Eur J Neurol* 15:1013–1028
6. Evers S, Frese A, May A, Sixt G, Straube A (2005) Therapie seltener idiopathischer Kopfschmerzkrankungen. *Nervenheilkunde* 24:217–226

7. Evers S, May A, Fritsche G, Kropp P, Lampl C, Limmroth V, Malzacher V, Sandor P, Straube A, Diener HC (2008) Akuttherapie und Prophylaxe der Migräne. *Nervenheilkunde* 27:933–949
8. Evers S, Kropp P, Pothmann R, Heinen F, Ebinger F (2008) Therapie idiopathischer Kopfschmerzen im Kindes- und Jugendalter. *Nervenheilkunde* 27:1127–1137
9. Evers S, Afra J, Frese A, Goadsby PJ, Linde M, May A, Sándor PS, European Federation of Neurological Societies (2009) EFNS guideline on the drug treatment of migraine – revised report of an EFNS task force. *Eur J Neurol* 16:968–981
10. Evers S, Goadsby P, Jensen R, May A, Pascual J, Sixt G, EFNS task force (2011) Treatment of miscellaneous idiopathic headache disorders (Group 4 of the IHS classification) – report of an EFNS task force. *Eur J Neurol* 18:803–812
11. Evers S, Jensen R, European Federation of Neurological Societies (2011) Treatment of medication overuse headache – guideline of the EFNS headache panel. *Eur J Neurol* 18:1115–1121
12. Haag G, Diener HC, May A, Meyer C, Morck H, Straube A, Wessely P, Evers S, DMKG, DGN, OKSG, SKG (2011) Self-medication of migraine and tension-type headache: summary of the evidence-based recommendations of the Deutsche Migräne und Kopfschmerzgesellschaft (DMKG), the Deutsche Gesellschaft für Neurologie (DGN), the Österreichische Kopfschmerzgesellschaft (ÖKSG) and the Schweizerische Kopfwehgesellschaft (SKG). *J Headache Pain* 12:201–217
13. Insa SD (ed) (2011) *Guía oficial de la sociedad Española de neurología para el diagnóstico y tratamiento de las cefaleas*. Thomson Reuters, New York
14. Italian Society for the Study of Headache (SISC) (1993) Guidelines and recommendations for the treatment of migraine. *Funct Neurol* 8:441–446
15. Kernick DP, Goadsby PJ, Royal College of General Practitioners, British Association for the Study of Headache (2011) Guidance for the management of headache in sport on behalf of The Royal College of General Practitioners and The British Association for the Study of Headache. *Cephalalgia* 31:106–111
16. Lanteri-Minet M, Valade D, Geraud G, Lucas C, Donnet A (2014) Revised French guidelines for the diagnosis and management of migraine in adults and children. *J Headache Pain* 15:2
17. Lanteri-Minet M, Demarquay G, Alchaar H, Bonnin J, Cornet P, Douay X, Dousset V, Géraud G, Guillouf V, Navez M, Radat F, Radenne S, Revol A, Valade D, Donnet A (2014) Démarche diagnostique générale devant une céphalée chronique quotidienne (CCQ) – Prise en charge d'une CCQ chez le migraineux : céphalée par abus médicamenteux et migraine chronique/Recommandations de la SFEMC, ANLLF et SFETD. *Rev Neurol* 170:162–176
18. Lanzi G, Balottin U, Zambrino CA, Cernibori A, Del Bene E, Gallai V, Guidetti V, Sorge F (1996) Guidelines and recommendations for the treatment of migraine in paediatric and adolescent patients. Italian Society for the Study of Headache. *Funct Neurol* 11:269–275
19. May A, Evers S, Straube A, Pfaffenrath V, Diener HC (2004) Therapie und Prophylaxe von Clusterkopfschmerzen und anderen trigemino-autonomen Kopfschmerzen. *Nervenheilkunde* 23:478–490
20. May A, Leone M, Afra J, Linde M, Sándor PS, Evers S, Goadsby PJ, EFNS Task Force (2006) EFNS guidelines on the treatment of cluster headache and other trigeminal-autonomic cephalalgias. *Eur J Neurol* 13:1066–1077
21. Monteiro JM, Fontes Ribeiro CA, dos Santos Luzeiro IM, de Araujo Sousa Fernandes Machado MG, Ferreira Lopes Esperansa PM (2009) Recomendacoes terapeuticas para cefaleias. *Sinapse* 9(Suppl 1):1–36
22. Paemeleire K, Louis P, Magis D, Vandenhede M, Versijpt J, Vandersmissen B, Schoenen J (2014) Diagnosis, pathophysiology and management of chronic migraine: a proposal of the Belgian Headache Society. *Acta Neurol Belg*. doi:10.1007/s13760-014-0313-z
23. Paulus W, Evers S, May A, Steude U, Wolowski A, Pfaffenrath V (2002) Therapie und Prophylaxe von Gesichtsschmerzformen und andere Formen der Gesichtsschmerzen. *Nervenheilkunde* 21:255–268
24. Sarchielli P, Granella F, Prudenzano MP, Pini LA, Guidetti V, Bono G, Pinessi L, Alessandri M, Antonaci F, Fanciullacci M, Ferrari A, Guazzelli M, Nappi G, Sances G, Sandrini G, Savi

- L, Tassorelli C, Zanchin G (2012) Italian guidelines for primary headaches: 2012 revised version. *J Headache Pain* 13(Suppl 2):S31–S70
25. Silberstein SD, Holland S, Freitag F, Dodick DW, Argoff C, Ashman E, Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society (2012) Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology* 78:1337–1345
 26. Straube A, May A, Kropp P, Katsarava Z, Haag G, Lampl C, Sándor PS, Diener HC, Evers S (2007) Therapie primärer chronischer Kopfschmerzen: Chronische Migräne, chronischer Kopfschmerz vom Spannungstyp und andere chronische tägliche Kopfschmerzen. *Nervenheilkunde* 26:186–199
 27. Vuković Cvetković V, Kes VB, Serić V, Solter VV, Demarin V, Janculjak D, Petravić D, Lakusić DM, Hajsek S, Lusić I, Bielen I, Basić S, Sporis D, Soldo SB, Antončić I, Croatian Society for Neurovascular Disorders, Croatian Medical Association (2012) Evidence based guidelines for treatment of primary headaches – 2012 update. *Acta Clin Croat* 51:323–378