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Interictal Burden of Cluster Headache: Results of the EUROLIGHT Cluster Headache Project, an Internet-Based, Cross-Sectional Study of People With Cluster Headache

Pohl, Heiko ; Gantenbein, Andreas R ; Sandor, Peter S ; Schoenen, Jean ; Andrée, Colette

Abstract: **OBJECTIVE** The aim of this study was to measure the interictal burden (IIB) associated with cluster headache (CH). **BACKGROUND** CH is characterized by an alternation of excruciatingly painful attacks and pain-free periods. Absence of pain does not necessarily imply absence of symptoms, though. Some may persist or improve more slowly than pain; others may arise in between attacks. **METHODS** Participants filled out an online survey based on the EUROLIGHT questionnaire. Inclusion criteria were a reported diagnosis of CH and residency in a European country; exclusion criteria were refusal to give informed consent and to complete the questionnaire. **RESULTS** Most of the burden was related to higher headache frequencies: ongoing symptoms despite pain freedom, impaired autonomy due to avoidance of triggers, reluctance to tell others about the disease, and the feeling of not being understood by family and friends, employers and colleagues. Irreversible, potentially accumulating burden may occur if headache frequency is high; examples are impairment of career options, relationships, and family planning issues. Worrying about future attacks and avoiding potential triggers occur independently from attack frequency and disease duration. There were no differences between the in-bout and the out-bout period among participants with episodic CH. Participants with chronic CH reported greater IIB. **CONCLUSIONS** Even between attacks CH can have a huge and potentially irreversible impact on life. Different types of IIB were identified, all of which may contribute to the total burden of disease. As cumulative burden might be irreversible, prevention strategies need to be developed.

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Interictal Burden of Cluster Headache

Results of the EUROLIGHT Cluster Headache Project, an internet-based, cross-sectional study of people with cluster headache

Authors

Heiko Pohl MD¹, Andreas R. Gantenbein MD², Peter S. Sandor MD², Jean Schoenen MD³, and Colette Andrée PhD⁴

Affiliations

¹ Department of Neurology, University Hospital Zurich, Switzerland

² RehaClinic group and University of Zurich, Switzerland

³ Headache Research Unit, Department of Neurology-Citadelle Hospital, University of Liège, Belgium

⁴ Migraine Action Switzerland and Department of Pharmaceutical Sciences, University Basel, Switzerland

Corresponding Author

Heiko Pohl, MD, Department of Neurology, University Hospital Zurich, Switzerland,
Frauenklinikstrasse 26, 8091 Zurich, Switzerland, heiko.pohl@usz.ch, ORCID identifier: 0000-0002-2778-6790

Abstract

Objective. – The aim of this study was to measure the interictal burden associated with cluster headache.

Background. – Cluster headache is characterised by an alternation of excruciatingly painful attacks and pain-free periods. Absence of pain does not necessarily imply absence of symptoms, though. Some may persist or improve more slowly than pain; others may arise in between attacks.

Methods. – Participants filled out an online survey based on the EUROLIGHT questionnaire. Inclusion criteria were a reported diagnosis of cluster headache and residency in a European country; exclusion criteria were refusal to give informed consent and to complete the questionnaire.

Results. – Most of the burden was related to higher headache frequencies: ongoing symptoms despite pain freedom, impaired autonomy due to avoidance of triggers, reluctance to tell others about the disease and the feeling of not being understood by family and friends, employers and colleagues. Irreversible, potentially accumulating burden may occur if headache frequency is high; examples are impairment of career options, relationships, and family planning issues. Worrying about future attacks and avoiding potential triggers occur independently from attack frequency and disease duration. There were no differences between the in-bout and the out-bout period among participants with episodic cluster headache. Participants with chronic cluster headache reported greater interictal burden.

Conclusions. – Even between attacks, cluster headache can have a huge and potentially irreversible impact on life. Different types of interictal burden were identified, all of which

may contribute to the total burden of disease. As cumulative burden might be irreversible, prevention strategies need to be developed.

Keywords

Cluster headache; interictal burden; cumulative burden; self-concealment; fear-avoidance model

Abbreviations

CH	cluster headache
CI	confidence interval
IIB	interictal burden
n.r.	not reported
OR	odds ratio
SD	standard deviation

Introduction

Cluster headache is characterised by episodes of excruciatingly painful headache attacks and pain-free periods.(1) Absence of pain, however, does not necessarily imply absence of symptoms. Some, like allodynia,(2) may persist longer than the pain itself; others like fearful apprehension of further attacks may arise independently.

The investigation of burden is important as only known problems may be targeted selectively. Different studies have done so in the past, usually focussing on migraine and tension type headache.(3, 4) So far, cluster headache has received less attention. Snoer et al. concentrated on postictal symptoms which were reported to last up to 120 minutes after attacks.(5) In addition, during the bout, neuropsychological deficits were described.(6-10)

The aim of this study was to evaluate the interictal burden (IIB) in cluster headache (CH) using the data collected as part of the EUROLIGHT Cluster Headache Project.(11)

We define interictal burden as stresses and strains associated with the disease and present in the absence of a headache attack. In patients with episodic CH, IIB can be subdivided into burden in and outside the active period. Only the individual burden of patients will be considered here – consequences for family, friends and colleagues are beyond the scope of this article.

Methods

Design and sampling methods have already been described elsewhere.(11) In short, the study was designed as cross-sectional and internet-based; data were collected anonymously.

Inclusion criteria were a self-reported diagnosis of CH and a residency in a European country; exclusion criteria were refusal to give informed consent and to complete the questionnaire.

Patient associations as well as national headache societies were made aware about the study and were asked to share study information with eligible patients.

Participants filled out a survey online that consisted of the EUROLIGHT questionnaire from which questions designed to diagnose migraine and tension type headache in population-based surveys had been removed. New questions allowing assessing symptoms and treatment approaches typical for CH had been added.(11, 12) The diagnosis of episodic and chronic CH was validated according to the ICHD-3 beta criteria and only participants with a validated diagnosis were included into further analyses.

Questions regarding interictal burden addressed interictal freedom from symptoms, as well as anxiety, avoidance, self-concealment and cumulative burden. Ictal burden was assessed using the number of headache days in the last 30 days.(11, 12)

The relationship between interictal symptoms and the course of disease will be evaluated. Three types of associations between a disease and interictal symptoms may be postulated (see Table 1): random occurrence throughout the course of disease (type 1), correlations with disease duration or headache frequency (type 2a and type 2b, respectively), or dependence on changes in headache frequency (type 3). In addition, in CH, the differences between the in-bout and the out-bout period (interictal vs. “interbout”) as well as between episodic and chronic CH need to be taken into account. We considered a patient suffering from episodic CH as out-bout if he had not had an attack in the last 30 days prior to the survey. Other participants with episodic CH were considered in-bout.

When filling out the questionnaire, participants could decide freely whether they wanted to answer a question. Therefore, missing data had to be expected. In this paper, we will refer to missing data as “not reported” (n.r.).

The study was approved by the National Research Ethics Committee (CNER) Luxembourg.

Analyses were performed at the University Hospital Zurich using SPSS version 25 (IBM, USA) and Microsoft Excel 2016 (Microsoft, USA). Categorical variables are described as proportions ([%]) and continuous variables as means and standard deviations (SDs). Chi-square and Fisher's exact tests of significance as well as Mann-Whitney-U-Test were used. The effect size r of the latter was calculated as published,(13) and interpreted as large effect when $r=0.5$, as medium when $r=0.3$, and small when $r=0.1$. Correlation between ordinate variables was measured using Spearman's rho. Significance level was set at 0.05. P-values were corrected for multiple testing according to Bonferroni, i.e. observed p-values were multiplied with the total number of comparisons. If the calculated value exceeded 1.0, $P=1.0$ is reported. The extent of association in contingency tables is measured calculating Odds Ratios (OR) and their 95% confidence interval (CI).

Results

A total of 1514 individuals completed the questionnaire; 1165 participants whose diagnosis of definite cluster headache had been validated according to the criteria published in the ICHD-3 beta(11) were included in the analysis. Among these, 813 were male (69.9%; 2 n.r.). A majority of 79.3% (19 n.r.) was either employed or studying, 74.3% were married or living with a partner (26 n.r.). The estimated participation rate is low and ranges between 0.01 and 0.62% per country. Mean age was 42.2 ± 10.7 years (6 n.r.). See Table 2 for further demographic data. Most commonly, a disease onset in the third life decade was reported (33.2%, 8 n.r.), followed by the second and fourth decade (25.7% and 21.7%, respectively). A majority of the participants (69.9%, 2 n.r.) had had at least one headache day in the 30 days

prior to the survey. Among the participants suffering from episodic CH, 521 (60.8%) were considered in-bout (2 n.r.).

Of those included in the analysis, 306 participants (26.8%) reported suffering from chronic CH (23 n.r.) with confirmed validity of the diagnosis in 253 (82.7%). When analysing the burden of chronic CH, we only included datasets, which fulfilled diagnostic criteria.

Interictal symptoms

When asked to think about the last headache-free day, more than half reported having not felt symptom-free (58.1%; 88 n.r.). Those who reported presence of symptoms recounted a higher number of headache days during the last 30 days ($P < 0.001$, $r = 0.15$). Participants with chronic CH reported interictal symptoms more frequently ($P = 0.007$, $OR = 1.81$ [95%-CI 1.33-2.47]). However, we found no association between disease duration and persisting symptoms ($P = 1.0$, $r = 0.06$). There was no difference between the in-bout and out-bout period ($P = 1.00$, $OR = 0.765$ [95%-CI: 0.57-1.02]) in patients with episodic CH.

Interictal worrying and avoidance

To assess emotional aspects of the interictal period, participants were asked to think about the last headache-free day and answer questions with regard to that day.

Two thirds (69.2%, 67 n.r.) responded having been worried or anxious about their next attack, and about half of them (47.8%, 67 n.r.) reported having avoided “something” to prevent further headache attacks. Neither the number of headache days in the last month ($P = 1.00$), nor suffering from chronic CH ($P = 1.00$, $OR = 1.14$ [95%-CI 0.84-1.57]), nor being out-bout ($P = 1.00$); $OR = 0.955$ [95%-CI 0.733-1.352]), nor disease duration ($P = 1.00$, $r = 0.06$) had an influence on worrying.

Having had more headache days during the past month was not associated with avoidance of potential triggers on headache-free days ($P=0.077$; $r=0.10$). Avoidance was not more frequent among those suffering from chronic CH ($P=0.145$, $OR=1.563$ [95%-CI 1.167-2.095]) and not associated with longer disease duration ($P=1.00$). It was, however, more common in those worrying about further attacks ($P<0.001$, $OR=8.903$ [95%-CI 6.503-12.188]). The feeling of being “always”, “often” or “sometimes” in control of the disease was not associated with the attempt to avoid triggers ($P=1.00$, $OR=1.306$ [95%-CI 1.022-1.669]). Avoiding did not differ between patients in-bout and out-bout ($P=1.00$, $OR=0.825$ [95%-CI 0.619-1.100]).

Feeling understood and self-concealment

Half of the participants (50.5%; 35 n.r.) reported avoiding telling others about their disease. This behaviour was not influenced by the feeling of being “rarely” or “never” in control of the disease ($P=0.200$, $OR=1.429$ [95%-CI 1.123-1.819]). It was more common among those who worried about future attacks ($P=0.002$, $OR=1.743$ [95%-CI 1.339-2.267]), and those with more headache days during the last month ($P<0.001$, $r=0.14$). Conversely, a longer disease duration ($P=0.244$, $r=0.09$) and living in partnership ($P=0.056$, $OR=0.632$ [95%-CI 0.481-0.832]) had no influence on avoidance to talk with others about the disease. Participants with chronic CH avoided telling others about their disease more frequently ($P<0.001$, $OR=2.278$ [95%-CI 1.693-3.065]). Among those with episodic CH, being in- or out-bout had no significant influence ($P=1.00$, $OR=0.819$ [95%-CI 0.619-1.083]).

Three out of four (77.5%; 46 n.r.) felt that their family and friends understood and accepted their disease. This was less common among those who thought having the disease “rarely”, or “never” under control ($P<0.001$, $OR=0.473$, [95%-CI 0.356-0.629]) and those suffering from chronic CH ($P=0.007$, $OR=0.537$ [95%-CI 0.390-0.740]). Disease duration had no influence on the feeling of being understood by the family ($P=0.075$; $r=0.10$). Having had a smaller number

of headache days during the last month was associated with the feeling of being understood more frequently ($P=0.022$; $r=0.11$). Those who avoided telling others about their disease reported less frequently that their family accepted and understood their disease ($P<0.001$, $OR=0.312$, [95%-CI 0.229-0.424]). There was no difference between participants who were in-bout and out-bout ($P=1.00$, $OR=0.998$, [95%-CI 0.703-1.417])

About half of the participants (45.6%) experienced their colleagues at work as not understanding and accepting (98 n.r., in addition, 166 considered that question not applicable). This feeling was less common among those who felt being in control of their headaches “always”, “often” or “sometime” ($P=0.010$, $OR=0.595$ [95%-CI 0.453-0.781]) but not among those with chronic CH ($P=1.00$, $OR=0.72$ [95%-CI 0.52-0.99]). There was no difference between patients with episodic CH who were either in-bout or out-bout ($P=1.00$, $OR=1.186$ [95%-CI 0.871-1.617]). The feeling of colleagues understanding and accepting their disease was associated with less avoidance to tell others about their headaches ($P<0.001$, $OR=0.305$ [95%-CI 0.231-0.402]). There was no significant association between disease duration and being understood by colleagues and employers ($P=1.00$). The number of days absent from work during the last month did not influence the feeling of not being understood by employers and colleagues ($P=0.054$, $r=0.15$); 541 participants (46.4%) did not disclose the number of days they had been absent from work. The number of headache days during the last month, had no impact on the feeling of being understood and accepted by employers and colleagues ($P=0.100$; $r=0.10$).

Cumulative burden

A majority (74.7%) of the participants did not consider their education having been impaired by CH (68 n.r.; four datasets could not be included because multiple mutually exclusive answers had been chosen, i.e. “yes” and “no”). Among those who thought their disease had

interfered with their education, a minority of about one fifth (19.9%, 55 participants) had interrupted education. Those with a disease onset before the age of 20 reported a negative impact on their education more frequently ($P<0.001$, $OR=3.933$ [95%-CI 2.930-5.278]). Among those 77 participants with ongoing education, a majority (58.1%, 3 n.r.), found their disease having impaired their education.

While the year of age in which education was completed had been assessed, only the decade of disease onset was asked. We identified 55 participants (25.8%) who reported their disease having influenced their education even though they later recounted that their first attacks had occurred after the end of their education (239 participants did not provide enough information to make that calculation).

A majority (57.6%) of participants estimated that their headache disorder did have a negative influence on their career (20 n.r., six had answered both “yes” and “no”). Significantly more participants with chronic CH than with the episodic form found that their career had been impaired ($P<0.001$; $OR=3.263$ [95%-CI 2.344-4.543]). Disease duration did not influence that judgement ($P=1.00$), a higher attack frequency in the last month did ($P<0.001$, $r=0.21$).

Whether participants with episodic CH were in-bout or out-bout had no influence on that evaluation ($P=1.00$, $OR=0.718$ [95%-CI 0.54-0.95]).

Less than half of the participants (42.3%; 103 n.r.) reported their disease having reduced earnings. Considering only those who had completed education, the proportion remained similar (41.2%). Sex ($P=1.00$, $OR=1.237$ [95%-CI 0.949-1.613]) did not have an influence on that judgement. Chronic CH ($P<0.001$, $OR=3.318$ [95%-CI 2.442-4.508]) as well as a higher number of headache days during the last month ($P<0.001$, $r=0.25$) were significantly more frequently associated with reduced income. However, longer disease duration was not associated with reduced earnings ($P=1.00$). Whether participants with episodic CH were in-

bout or out-bout had no influence on that judgement ($P=1.00$, $OR=0.699$ [95%-CI 0.47-1.25]).

A small number of participants (57 participants, 4.9%) reported being on a disability rent.

About one sixth of the participants (13.6%, 68 n.r., two chose both “yes” and “no”) reported having less or no children because of their disease. Women and those suffering from chronic CH did so significantly more frequently ($P=0.014$, $OR=1.930$ [95%-CI 1.350-2.758], $P<0.001$, $OR=2.859$ [95%-CI 1.953-4.184], respectively). More than half of the participants (57.3%) who reported family planning having been influenced had chosen to have no children at all. Those who had more headache days during the last month, reported an impairment of family planning more frequently ($P<0.001$, $r=0.17$). Disease duration and age at disease onset had no influence on the decision of having children ($P=1.00$, and $P=0.126$). There was no difference between participants who were in-bout or out-bout ($P=1.00$, $OR=0.770$ [95%-CI 0.47-1.25])

A clear majority of the participants (87.2%; 85 n.r.) had never had a relationship breakdown because of the headaches. Men did not report a separation or divorce more frequently than women did ($P=1.00$, $OR=0.864$ [95%-CI 0.578-1.290]). In addition, a diagnosis of chronic CH was not more common among those who reported a failed relationship ($P=0.139$, $OR=1.857$ [95%-CI 1.237-2.788]). Conversely, more headache days in the last month ($P=0.001$, $r=0.13$) were associated with relationship breakdowns in the past. Disease duration had no significant influence ($P=1.00$).

Discussion

The EUROLIGHT Cluster Headache Project represents a large data set of CH patients from 17 European countries. This study provides data on self-reported interictal burden of patients suffering from CH. The sampling technique as well as sampling biases have been discussed previously.⁽¹¹⁾ The study’s strengths are the very large sample size and the large number of

countries of origin. It is likely that women and patients with chronic CH were overrepresented in this sample, due to a selection bias.⁽¹¹⁾ A further limitation is the self-reported diagnosis, which might lead to a sampling error. In order to reduce that bias, we only included participants whose diagnosis could be validated based upon their responses in the questionnaire. In addition, most of the participants reported having had at least one headache day within the 30 days prior to the survey, implying that the data presented here might largely reflect the in-bout burden. However, patients have only been asked about headache days in general, not cluster headache days in particular, leading to some uncertainty on that regard. Owing to the study design, the sample is not population-based. Statistical correction of the sampling bias was not possible as information on non-participants were unavailable. Because of that, we did not draw conclusions about incidence and prevalence. Instead, we narrowed the analysis to the investigation of relationships between subgroups and influencing factors, as these conclusions are less likely to be affected by the sampling error. Finally, because of the cross-sectional design, causality cannot be assessed.

Table 3 gives an overview of the identified interictal burden as well as their type; the definitions used for the burden subtypes are summarised in Table 1. The allocation of burden types must be interpreted with caution: the questionnaire used in this study does not assess whether changes in headache frequency occurred at the onset of symptoms. Therefore, type 3-burden cannot be identified at all and would probably be considered as type 2b-burden. In addition, it may be impossible to distinguish between very long-lasting type 1-burden and type 2a-burden using a cross-sectional design, as we would expect both types to be found more frequently with longer disease duration. Burden that does not correlate with disease duration, attack frequency or changes in attack frequency (type 1 burden), has not necessarily been caused by CH. It might have occurred randomly or be the consequence of a comorbidity.

Interictal symptoms

Symptoms between attacks were common and were associated with a higher attack frequency. We did not inquire which symptoms persisted in particular, though. If investigated further, this finding might prove helpful when deciding about working capacity after a seemingly aborted cluster headache attack.

Interictal symptoms in active period but the absence of pain have previously been described. In one case report, neuropsychological deficits in attention and executive functions linked to the in-bout period were described and considered unlikely to be the consequence of sleep deprivation as the patient only had diurnal attacks.(6) The finding of impaired executive functions was confirmed by one controlled study,(7) while other studies reported “diffuse cerebral neuronal dysfunction”(8), impaired verbal memory(9) or impaired working memory.(10) Another common symptom between CH attacks is allodynia.(2) In addition, fatigue and a feeling of “decreased energy” are often reported to persist for up to two hours after attacks.(5)

Interestingly, in-bout participants did not report persisting symptoms in the absence of pain more frequently than out-bout patients did. This finding is difficult to interpret because the nature of these symptoms is unknown. In future research, the time passed since the last attack should be assessed to investigate how long it takes persisting symptoms to pass.

Interictal worrying and avoidance

Many participants worried about further attacks and tried to do “something” in order to prevent them. Interestingly, neither attack frequency nor disease duration had an influence on worrying and avoiding trigger factors. Therefore, this burden should always be sought, even at low attack frequencies.

While avoidance is always prone to interfere with autonomy (and thereby becomes a burden), it does even more so when avoidance does not result in a reduced attack frequency. Unsurprisingly, worrying about further attacks was associated with trying to prevent these attacks. In other diseases, this has led to the development of the fear-avoidance model according to which fear of pain leads to the attempt of avoiding painful experiences and possibly phobic behaviour.(14)

In this survey, we did not investigate whether the patients' strategies were helpful or just prevented them from living normally. More research is needed to differentiate between cause and effect.

Feeling understood and self-concealment

Many participants avoid telling others about their cluster headache – in particular, patients with chronic CH and a high attack frequency as well as those who worry about future attacks. Overall, the data suggest that not wanting to talk about the disease is associated with a higher ictal burden. Results from studies in other chronic pain disorders might help understanding that phenomenon.

The term “self-concealment” has been coined to describe “the active concealment from others of personal information that one perceives as negative or distressing.”(15) One study showed that in patients suffering from chronic pain, self-concealment was “positively associated with pain intensity [...], self-reported symptoms [...], and perceived stress [...]; and negatively associated with basic need satisfaction [...] and life satisfaction [...].”(16) The authors explained these findings by the self-determination theory according to which autonomy, competence, and relatedness are needs that must be satisfied in order to reach well-being.(17) Being determined to conceal personal details hampers autonomy and not

receiving empathy from others prevents relatedness. Thus, based upon these findings, one would expect self-concealing patients to benefit from being encouraged to talk to others – in contrast to those who never felt any need for conversation. Further research on that topic might prove helpful to many patients.

Most participants felt understood by their families but understanding seemed to decline with an increasing number of attacks and the feeling of not being in control of the attacks.

Employers' understanding was influenced neither by disease duration nor headache frequency. Those who avoided talking about their disease felt understood by their families and colleagues less frequently, confirming the above-discussed negative role of self-concealment.

Cumulative burden

Very long-lasting or irreversible burden may sum up over the years or lead to subsequent discomfort and contribute towards cumulative burden. However, assessment is challenging as patients are asked to report retrospectively about the influence of one variable on their life and objective markers are not available. Thus, recall bias must be expected. This is exemplified by the fact that some participants estimated their headaches having influenced education even though their answers to later questions led us to the assumption that their disease must have started after the end of their education.

Most commonly, a disease onset in the third life decade was reported. Consequently, a minority and mostly those with an early disease onset reported an influence of the disease on education. If the disease was present during education, there was a high likelihood of interference, interruptions occurring rarely.

Unsurprisingly, patients reported a greater influence of their disease on their careers and earnings than on their education. A higher headache frequency in the last 30 days was associated with an impaired career and reduced earnings. This finding suggests that a negative impact on job and earnings might largely be a consequence of the ictal burden. Interestingly, the proportion of participants reporting an impact of the disease on their career did not increase with the number of years suffering from the disease, possibly implying that this type of burden may occur early or be reversible. The fact that lost earnings were reported primarily by those having a high attack frequency may indicate that a higher ictal burden may lead to lost money. In future research, this aspect of IIB should receive further attention, evaluating whether early aggressive treatment preventing high attack frequencies suffices to reduce the impact on career and earnings.

About one sixth of the participants reported family planning and partnership being affected by the disease – primarily those whose disease onset had been in younger years. While relationship breakdowns affected both sexes equally, women found family planning more often challenging, possibly owing to the traditional role allocation between women and men. In any case, chronic CH, headache frequency and the impact of headache attacks had a negative impact on both family planning and the persistence on relationships.

The surprisingly low number of divorces and broken-up relationships in CH patients seems to contrast with the high divorce rates in the general population. In 2011, in the European Union 46.1 divorces per 100 marriages were reported.⁽¹⁸⁾ It needs to be borne in mind, however, that in the questionnaire we only asked for disease-related divorces and separations, and that this sample cannot be regarded as representative. Joshi et al. found no significant difference in divorce rates between patients suffering from CH and controls.⁽¹⁹⁾

Differences between episodic and chronic CH

The differences between participants with chronic and episodic CH are depicted in Figure 1. In general, participants with chronic CH had a higher IIB and experienced less understanding and acceptance by family and friends.

Worrying about future attacks, avoidance of potential triggers, feeling understood and accepted by colleagues and employers as well as having had a failed relationship were not more or less common among participants with chronic CH. Given that the former three were categorised as “type 1 burden”, these burdens were not to be expected more often among participants with chronic CH (which is characterised by a higher attack frequency).

Conversely, a failed relationships occurring more frequently at higher attack frequencies, we would have expected that type of burden to be more common in participants with chronic CH. However, this was not confirmed by the calculations. Even though the confidence interval of the odds ratio did not contain “1”, the P-value was above 0.05 after correction for multiple testing. Perhaps the number of failed relationships among the participants is too small to detect any differences.

These data suggest that there is no qualitative difference between participants with chronic and episodic CH. Yet, we find that distinction justified and important as it emphasises semantically the greatly increased ictal and interictal burden in that patient group.

Differences between the interictal burden of participants with episodic CH in and outside the active period

The differences between the interictal burden in and outside the active period are summarised in Figure 2. We did not identify any difference between these groups. While some of the different types of burden are likely to remain stable over the course of time (e.g.

having had relationship break-down, having lost money, etc.), others are not (e.g. persisting symptoms on the last pain-free day, worrying about future attacks etc.). While it seems likely that the importance of certain types of burden fades with time passing since the last attack, we were unable to test that hypothesis, because that information was not available.

Conclusion

The data of this survey show that CH attacks have a long-lasting and potentially accruing impact on life. We identified different aspects of IIB (see Table 3) all of which may contribute substantially to the total burden of disease. Importantly, the results emphasise that the suffering of people with CH often does not end when pain subsides. This headache disorder influences and dominates the thoughts and the lives of many persons enduring it.

In future trials investigating the success of a treatment of CH, IIB should be assessed, too.

Study endpoints should not focus on pain alone. In addition, further strategies are needed to prevent irreversible burden.

Clinical implications

- Symptoms in the interictal phase are commonly associated with a higher attack frequency.
- Worrying about future attacks and avoidance of potential triggers do not depend on CH alone, but also on factors unrelated to the disease.
- Many participants avoid telling others about their cluster headache, in particular those who did not feel having their disease under control.
- If the disease is present during education, there is a high likelihood of interference, but interruptions occur only rarely.

- The proportion of participants reporting an impact of the disease on their career did not increase with the number of years suffered from the disease. This finding might implying that this type of burden may occur early or be reversible.

Conflicts of interest

HP has no conflicts of interest to disclose. ARG has received honoraria for lectures and consulting from Allergan, Almirall, Curatis, Eli Lilly, Mepha/TEVA, Novartis, and Roche. PSS has worked as advisor for Novartis, Lilly, Teva and Roche. He has received lecture honoraria from Biomed and Novartis and research funding from the Swiss National Foundation, and the RehaClinic Research Fund; no research or travel grants from industry. JS has worked as consultant for Cefaly Technology, as advisor for Novartis Benelux, Teva and Allergan Benelux. He has received lecturer honoraria from Novartis Benelux and Teva and has received a research grant from Electrocore. CA has worked as advisor for Cefaly, Novartis, Teva Grünenthal, and Eli Lilly, Switzerland.

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