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Chapter 4

Impact of the Headache on the Individual and Family

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Headache is a heterogeneous condition that varies widely with respect to global severity and severity of individual attacks. Recent efforts have focused on improving the diagnostic criteria for classifying headache (4,22), but less effort has been directed toward developing reliable, valid, and clinically useful methods for assessing the impact or severity of headache on patients. Most work has primarily been focused on migraine and chronic headaches.

Migraine is a highly prevalent episodic chronic headache disease, which typically affects the sufferers during their most productive years (12,29,30,36,45). During an attack, people with severe migraine are almost completely incapacitated by a throbbing headache; nausea, vomiting, or both; and increased sensitivity to light and sound. They try to alleviate these symptoms by taking various drugs early in the attack. Very rarely, the migraineur allows the attack to take its course without treatment. Migraine is debilitating because it obstructs family obligations and social plans, results in absenteeism from work, impairs the ability to perform normal tasks at home, school, or in the workplace, produces suffering and emotional stress, and impairs health-related quality of life (HRQOL) (13,26,31,36,42,47). For that reason, migraine places a heavy economic burden on both the individual and society.

In a report issued by the World Health Organization (WHO), migraine is ranked number 12 among women and 19 in the population for degree of handicap (63). In attempts to rank the severity of different diseases, migraine has been ranked among those causing the greatest degree of handicap, together with conditions like quadriplegia, dementia, and active psychosis (34,39,40). This again clearly shows how serious migraine is and how much it affects sufferers' everyday life, particularly bearing in mind that migraine affects the individual intermittently without apparent permanent injury and because mortality, as far as is known, among migraineurs is not higher than in the general population (41).

MEASURING IMPACT OF HEADACHE

Measurement of migraineurs' HRQOL and disability should be taken as a multidimensional concept (Fig. 4-1). A generally applicable definition of HRQOL includes both subjective perception of one's life situation and objectively quantifiable health factors (8,14). Accordingly, physical and social functioning as well as emotional and mental health status are very important issues to the individual (Fig. 4-1).

A population-based sample of migraine sufferers in Sweden ($N = 423$) was asked to rank what they value most in life by choosing from 3 of 10 alternatives. At the top of the ranking list were family life, work performance, good economy, and leisure activities/meaningful time off, which were reported by 65%, 40%, 33%, and 29%, respectively (26). The level impact of migraine on their favorite activities is demonstrated in Figure 4-2.

Assessment of Disability

The impact of migraine disability is usually measured through self-administered questionnaires. An ideal questionnaire has to be reliable, valid, and short (completed within 5 minutes). The questionnaire has to measure individual patients at all levels of severity (from mild to severe impact), enable comparisons of scores across questionnaires, and have the sensitivity to track changes over time. There are a number of validated instruments that have been developed to quantify disability: the Migraine-Specific Quality of Life Questionnaire (25), the Subjective Symptom Assessment Profile (SSAP) (15), the Minor Symptoms Evaluation Profile (MSEP) (7), the Short-Form 36 (SF-36) (37,38,42,61), the Headache Disability Inventory (23,24), the Headache Impact Questionnaire (HImQ) (54,55), Migraine Disability Assessment Questionnaire (MIDAS) (51–53), the Headache Impact Test (HIT) (2,60),

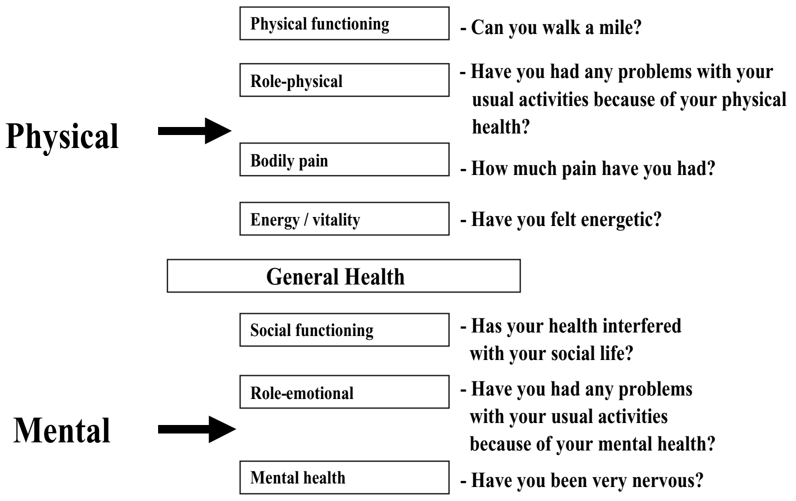

FIGURE 4-1. Chart of multidimensional concept approach to quality of life and migraine patients' disability.

and the Migraine Attack Severity Scale (17,18), which use different distinctive approaches to measurement. Principal differences among questionnaires are reflected in their methods of administration, which can be anything from Internet/computerized, to paper-based self-administered evaluations. With respect to recall periods, they can differ from the first 24 hours of the migraine attack to consider the last 1- to 3-month period with migraine attacks.

Because of the definition of HRQOL used or the aspects of disability we are interested in, these instruments can be focused to patient's emotional well-being, headache severity, and ability to cope with headaches or work productivity. Some of these assessment tools have the restriction of disability meaning minutes, hours, or days during which work, school, home activities were missed or affected by 50% or more (MIDAS and HImQ). Although restriction of activities from a time perspective has high face validity, research in other therapeutic areas has suggested that it may be a challenge for patients to accurately recall time missed after 2 to 4 weeks. In addition, some of the currently available assessment tools are not likely to demonstrate changes over time because of different migraine interventions. Indeed, the full impact of migraine is not easy to measure, although some instruments have been developed to quantify migraine disability and improve communication between patients and healthcare professionals.

Almost all, if not all, migraineurs take medications, whether nonprescription or prescription, in an attempt to rapidly relieve the most debilitating symptoms of the migraine attack—pain, nausea, phono- and photophobia (9,26,30,35). The success of medications and other treatments dictates the extent of the sufferer's immediate disability, which may range from beginning to resume activities within hours to being immobilized in bed for days, arising only with the urge to vomit. Despite of treatment used, total recovery still seems to follow the natural duration of the attack. We developed a questionnaire for measuring disability and patients' quality of life during the migraine attack, namely, the Minor Symptoms Evaluation Profile-Acute (MSEP-Acute) (Fig. 4-2) (11). Figure 4-2 (left) clearly shows the difference between patients' answers in the MSEP-Acute questionnaire done between and during migraine attack, when the answers were left shifted

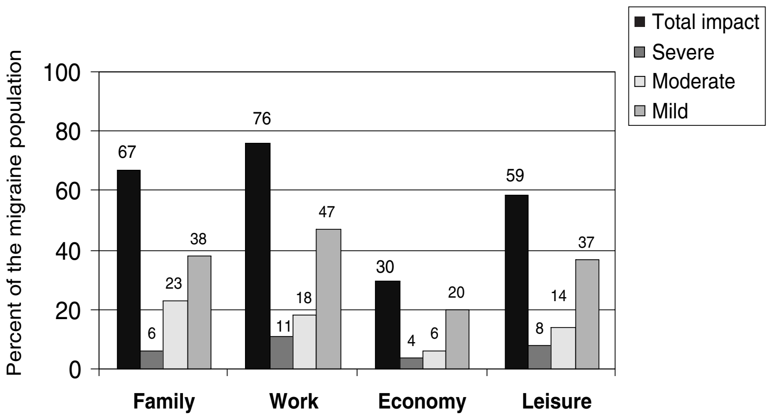

FIGURE 4-2. The impact of migraine on the favorite activities family life, work performance, good economy, and leisure in a population-based sample of migraine sufferers in Sweden ($N = 422$) (26).

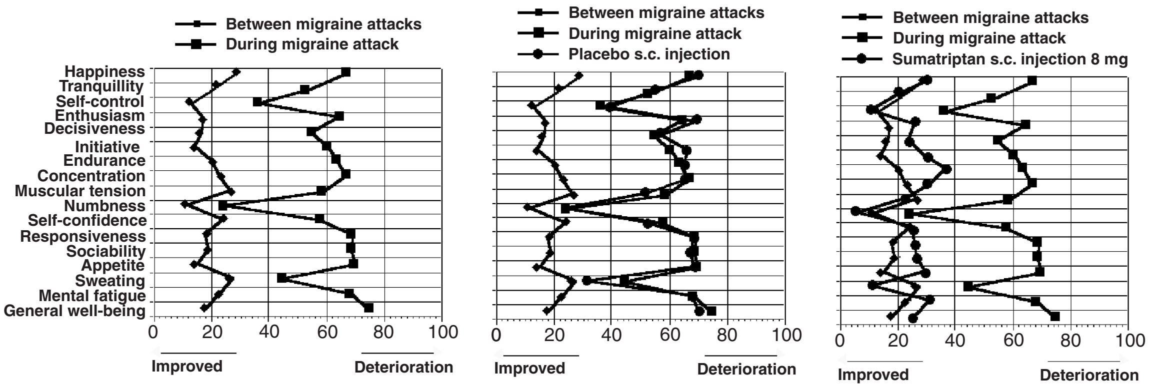

FIGURE 4-3. The MSEP-acute assessments before and after acute migraine treatment with sumatriptan 8-mg subcutaneous injection and placebo (11).

at baseline and right shifted toward "deterioration" during the attack. Although placebo did not change these results (middle), sumatriptan 8-mg subcutaneous injection caused an improvement and shifted the answers toward baseline values obtained outside the migraine attacks (see Fig. 4-2).

Another illustrative example for using the self-administered standardized questionnaires is the SSAP test, developed for general well-being evaluation of migraine patients and other patient categories (Fig. 4-3). In Figure 4-3, through the SSAP diagram, it can be demonstrated that the area of symptoms between migraineurs without migraine attack is larger than that of age and gender-matched controls. From this evaluation it appears that migraine affects the symptom profile of the migraineurs also during days when they are not suffering attacks. Thus, in addition to the disability perceived during the migraine attack, it seems that some impairment is also experienced between the attacks (6,10,27). The unpredictability of migraine and anxiety about future attacks often thus has an interictal influence. When population-based sample of migraineurs were asked about recovery, 43%, 43%, and 9%, respectively (4% no response), stated that they recovered "completely," "more or less" and "not at all" between the attacks (26). In other words, less than half recovered fully between the attacks.

Moreover, there are other questionnaires, like the SF-36, which by evaluating eight different dimensions, enable us to compare quality of life in migraineurs with that of patients with other diseases. Subjects ($n = 845$) were surveyed 2 to 6 months after participation in a placebo-controlled clinical trial and asked to complete a questionnaire including the SF-36 Health Survey, a migraine severity measurement scale and demographics. Results were adjusted for severity of illness and comorbidities. Scores were compared with responses to the same survey by the U.S. sample and by patients with other chronic conditions, like depression and osteoarthritis (42).

In a recent similar study, a subsample of migraine sufferers were evaluated with a new, even shorter generic health survey, the SF-8 Health Survey (SF-8), an alternate form that uses one question to measure each of the eight SF-36 domains (59). Data from 7557 participants surveyed via the Internet and mail were used to document the burden of migraine on HRQOL and to compare the relative burden of migraine with other chronic conditions using the SF-8. The HRQOL of migraineurs was similar to those with congestive heart failure, hypertension, and diabetes, and is better than those with depression (59). In addition, migraine sufferers experienced better physical health but worse mental health than those with osteoarthritis. These results support prior research indicating that the burden of migraine on functional health and well-being is considerable and comparable to other chronic conditions known to have substantial impact on HRQOL.

Socioeconomic Factors

An evaluation of the full impact of migraine on patients and society is necessary to account for socioeconomic aspects of direct healthcare cost that may include hospitalization, office and emergency room visits, and drug administration. Apart from the direct costs, hidden indirect costs such as loss of productivity at work also exist. If we compare direct and indirect costs, normally we can observe that the indirect cost is about 70 to 80% of the total costs. From a patient's perspective, the loss of time attributable to headache disability in social, leisure, and family activities also contributes to impair their quality of life. It is, however, difficult to translate migraineurs' HRQOL and disability caused by their migraine per se into money. Accordingly, it is not always easy to demonstrate substantial benefits of migraine therapy on headache disability (6). This could possibly be caused by the fact that most disability is suffered at home, whereas the majority of tests are addressing the impact of disability on work performance, school performance, and so on. In addition, absenteeism from work or school is very limited (about 6 days per year out of 98.4 days with migraine per year) (9). These data suggest that although migraineurs are present at work, school, and so on during many of their attacks they do so with reduced functional status, a scenario often described as *presenteeism*. A recent telephone survey that was conducted of a random sample ($N = 4007$) of the population aged 16 to 65 years of mainland England demonstrated that an estimated 5.7 working days were lost per year for every working or student migraineur, although the most disabled 10% accounted for 85% of the total (50). All together, these factors make it difficult to evaluate the real burden of migraine and to extrapolate the total costs of their migraine attacks.

A retrospective study using linked medical and pharmacy claims data that allowed identification of families and individuals with migraine indicates that the total healthcare costs of a family with a migraineur were 70% higher than those of the nonmigraine family, with most of the difference concentrated in outpatient costs (48). Migraine families incur far higher direct and indirect healthcare costs than nonmigraine families, with variation depending on which family member is the clinically detected migraineur and possible comorbid conditions (43,48).

Assessing Disability in Clinical Practice

Presently, the magnitude of impact of headache and migraine is generally measured by two of the most useful and reliable patient disability and life-of-quality questionnaires, namely, the MIDAS and the Internet-based HIT.

Migraine Disability Assessment

The MIDAS questionnaire is a brief, self-administered questionnaire designed to quantify headache-related disability (51,53,55,56). Headache sufferers answer five questions, noting the number of days in the past 3 months of activity limitations because of migraine. The MIDAS score is the sum of missed work or school days, missed household chores days, and missed nonwork activity days, and days at work or school plus days of household chores where productivity was reduced by half or more in the last 3 months. The MIDAS scores are then categorized by disability level—Little or no disability (0 to 5), Mild disability (6 to 10), Moderate disability (11 to 20), and Severe disability (20+) (53).

The reliability and internal consistency of the MIDAS score is high, as tested in a population-based sample of headache sufferers when MIDAS scores are substantially higher in migraine cases than in nonmigraine cases, supporting the validity of the measurement (52). In addition, Stewart et al. (56) conducted another trial to examine the test–retest reliability and internal consistency of the overall MIDAS score using population-based samples of migraine sufferers across the U.S. and U.K. A total of 97 migraine-headache sufferers from the United States and 100 from the United Kingdom completed the MIDAS questionnaire twice at an average of 3 weeks apart from one another. The result of this first international population-based study to assess the reliability of disability-related scores for migraine shows that the reliability and internal consistency of the MIDAS is similar to those of other migraine questionnaires. However, the MIDAS requires fewer questions, is easier to score, and provides intuitively meaningful information on lost days of activity (56).

Headache Impact Test

The HIT is a tool to measure the impact that headaches have on a person's ability. It is a new, Internet-based test that has been implemented to assess the wide effects of migraine by quantifying the impact of headache frequency and severity on migraineurs' lives (available at: www.headachetest.com). HIT is a dynamic, computer-adaptive questionnaire that has been shown to be reliable, sensitive, and valid for clinical settings. The HIT scores show the effect that headaches have on patients' normal life and the ability to function with respect to their treatment (60). A paper-based, shorter version of the HIT questionnaire has been developed for people without access to the Internet or without computer knowledge (60).

HIT was developed by a team of international headache experts from neurology and primary care medicine in collaboration with the psychometricians who developed the SF-36 health assessment tool. In fact, HIT was adapted from widely used headache impact measures that were validated independently for the purpose of creating HIT. Thus, this test was developed from a number of established measurement tools that have been used successfully for years. The HIT includes 54 questions that assess pain, disability, and affective distress presented through a standardized scoring range of 36 to 78 (60). From the final score on a 1- to 2-minute questionnaire, HIT yields a very accurate description of the impact that headaches have on patients' life and ability to function. HIT is a widely used headache impact questionnaire able to consider at the same time frequency and severity of pain, role and social functioning, energy, fatigue, cognition, and emotional distress, producing a more accurate estimate of individual patient scores (Table 4-1). HIT assessments also meet standards based on clinical criteria by estimating the severity of headache impacts and sensitive to changes in severity over time.

There is also a standardized short paper version of HIT, called HIT-6, based on six questions, that functions as well as the standard HIT version. Figure 4-4 displays the results of the Landmark study presented at the 6th Congress of the European Headache Federation, with the objective of

TABLE 4-1 Content of Widely Used Headache Impact Questionnaires

	HDI	*HImQ*	*MIDAS*	*MSQ*	*HIT-6*
Pain (frequency/severity)		X	X		X
Role functioning	X	X	X	X	X
Social functioning	X	X	X	X	X
Energy/fatigue				X	X
Cognition	X			X	X
Emotional distress	X			X	X

Abbreviations: HDI, Headache Disability Inventory; HImQ, Headache Impact Questionnaire; MIDAS, Migraine Disability Assessment Questionnaire; MSQ, Migraine Specific Quality of Life Questionnaires; HIT-6.

determining the sensitivity of HIT-6 in measuring headache impact. Data on headache characteristics and treatment regimen is available from 4287 subjects who completed HIT-6 (see Fig. 4-4) (58). The results of the Landmark study clearly shows that the burden of headache may be translated into frequency or severity.

Both MIDAS and HIT are scientifically valid measures of migraine severity and have the potential to improve communication between patients and physicians, assess migraine severity, and act as outcome measures to monitor treatment efficacy. However, HIT is considered to be the most reliable method for evaluating an individual patient's progress over time with greater accessibility and coverage of the spectrum of headache than MIDAS.

Impact of Headache Therapy on Disability

A prospective, observational study without a control group assessed the outcomes of migraineurs in a mixed model staff/independent practice association managed care organization for patients previously diagnosed as having migraine who received their first prescription for sumatriptan (33). Data collected included medical as well as pharmacy claims and patient surveys to measure changes in satisfaction, HRQOL, workplace productivity, and nonworkplace activity after sumatriptan therapy was initiated. A total of 178 patients completed the study. Results obtained showed significant decreases in the mean number of migraine-related physician office visits, emergency department visits, and medical procedures in the 6 months after sumatriptan therapy compared with the 6 months before sumatriptan was used ($P < .05$) (33). There were also improvements in patient satisfaction and significant reductions in time lost from workplace productivity and nonworkplace activity.

Unfortunately, there are very limited double-blind and controlled prospective data on the effects of headache therapy on disability in this respect. A prospective sequential multinational (five countries) study concurrently evaluated the effects of subcutaneous sumatriptan on clinical parameters, HRQOL measures, workplace productivity, and patient satisfaction (6). Patients ($N = 58$, aged 18 to 65 years) diagnosed with moderate to severe migraine treated their symptoms for 24 weeks with subcutaneous sumatriptan after a 12-week period of treating symptoms with their customary (nonsumatriptan) therapy. Patients used diary cards to record information concerning the

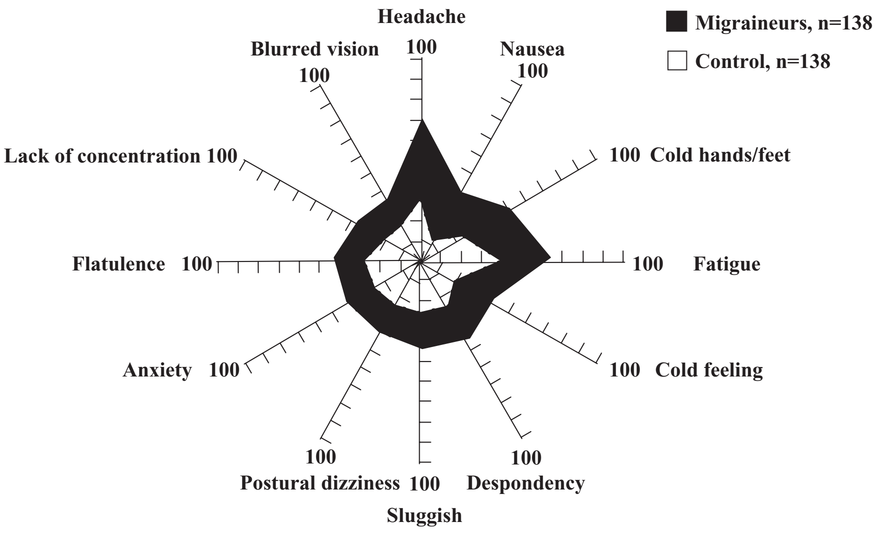

FIGURE 4-4. Results of the SSAP questionnaires test, widely used to compare well-being of migraine patients between attacks with that of an age- and gender-matched control group (10).

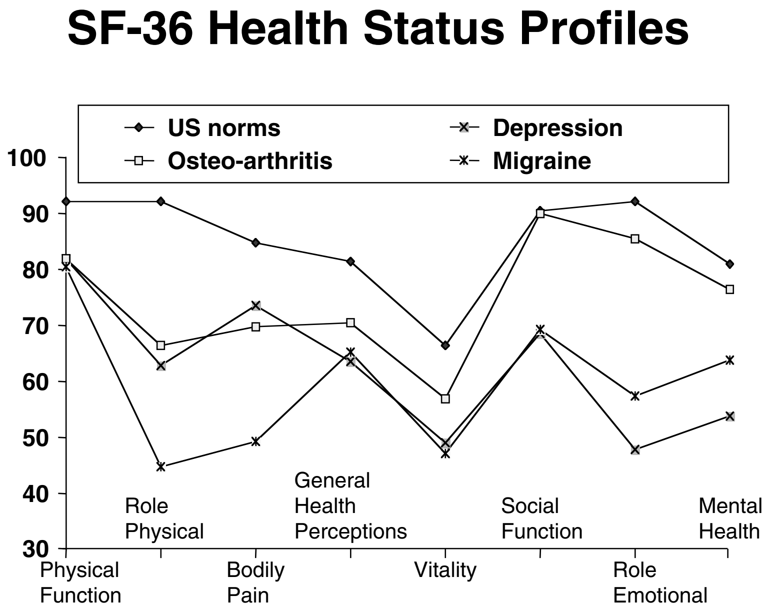

FIGURE 4-5. Results of the Short-Form 36 (SF-36), questionnaires test, widely used for comparing and evaluating eight different dimensions in migraineurs with those of patients with other diseases (42). SF-36 measures quality of life in eight different aspects: physical functioning, role-physical function, bodily pain, general health, vitality, social function, role-emotional, and mental health. The -◆- line in the SF-36 scores is the norm for the U.S. general population. The -✕- line reflects the scores in patients with migraine, whereas -✕- and -□- lines reflect the scores in patients with depression and osteoarthritis, respectively. Migraine patients have the lowest physical functioning and bodily pain scores but the general health perception is also low. However, patients with depression have the lowest score in social functioning, role-emotional well-being and mental health.

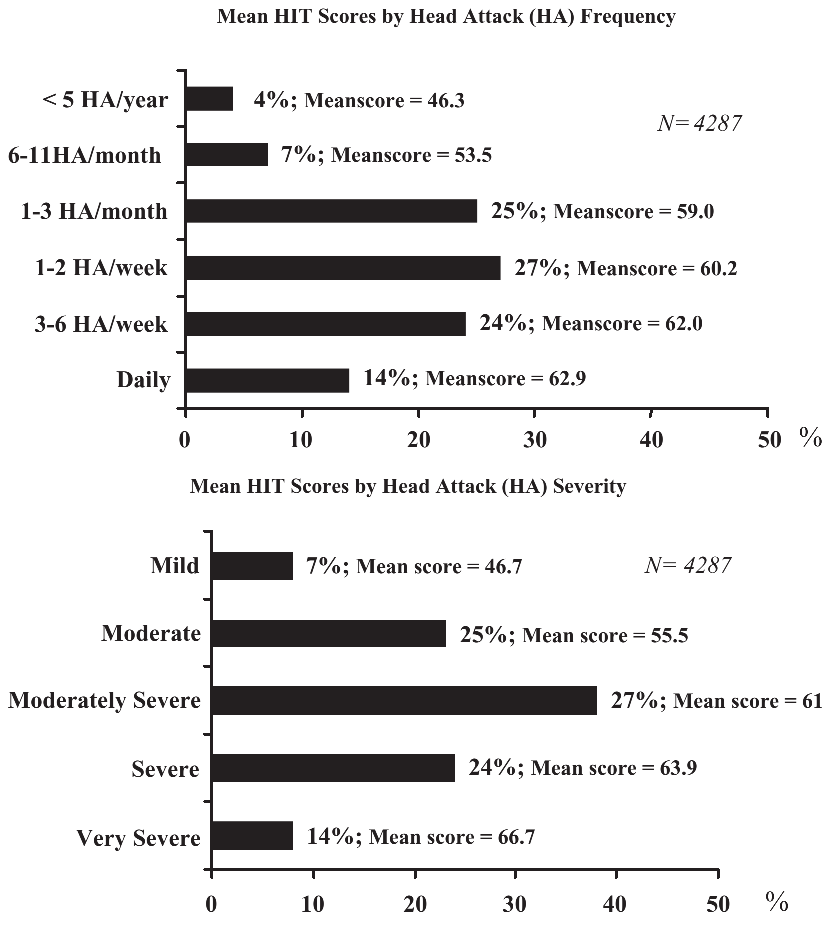

FIGURE 4-6. Results of the landmark study in determining the sensitivity in measuring headache impact of a standardized version of Headache Impact Test (HIT)—HIT-6 (58).

effects of migraine on workplace productivity and nonworkplace activity time. The average workplace productivity time lost was 23.4 hours per patient during 12 weeks of customary therapy, compared with 7.2 and 5.8 hours per patient during the first and second 12-week periods of sumatriptan therapy, respectively. An average of 9.3 hours of nonworkplace activity time was lost per patient during the customary therapy phase, compared with 3.2 and 2.8 hours during the first and second 12-week periods of sumatriptan therapy, respectively. Treatment of migraine with subcutaneous sumatriptan compared with customary therapy was associated with an average gain per patient of approximately 16 hours of workplace productivity time and 6 hours of nonworkplace activity time, over a 3-month period (6).

In a phase III, multinational, randomized clinical trial, 692 patients treated a migraine attack with eletriptan 40 mg or 80 mg, or placebo (21,62). Patients responded to questionnaire seeking information concerning the amount of time lost from usual activities during the attack. Time loss assessments were made 24 hours after the last dose taken and recorded in a diary. Patients receiving either dose of the active compound were unable to perform their usual activities for a median period of 4 hours compared with 9 hours experienced by those taking placebo. This difference was highly statistically significant ($P < .001$) (62). The time saving associated with eletriptan use reflected the differences in efficacy findings in the clinical component of the study.

CONCLUSIONS

Although 8 out of 10 people suffer from different types of headaches, the severity of their pain is often not communicated properly to their doctors. Research shows that when doctors understand exactly how headaches are affecting their patients, they are able to provide a better and fully successful treatment program. In particular, migraine can be difficult to manage in primary care, where it is underrecognized, underdiagnosed, and undertreated. Migraine care could only be improved by incorporating assessments of migraine impact into management strategies. Research has shown that measuring headache-related disability, together with assessments of pain intensity, headache frequency, tiredness, mood alterations, and cognition, can be used to assess the impact of migraine on sufferers' lives and society.

Convincing findings indicate that migraine on an individual level causes a lot of suffering and emotional stress; prevents people working, doing housework, and engaging in leisure pursuits; influences social life and the family situation; reduces quality of life; and influences sufferers' financial situation (1,3,5,13,16,19,20,28,30,32,42,44–46, 49,50,54). Apart from the disability and immediate suffering the patient experiences during the attacks, there also seem to be adverse effects between the attacks (10,57). It has, however, been difficult to demonstrate substantial benefits of migraine therapy on headache disability. One reason may be that only a fraction of the whole migraine attack has been assessed in most studies. Another possibility is that the effect of one class of drugs always has been compared with active controls. Further, currently available assessment tools may not be enough sensitive in demonstrating change over time. More prospective information on the natural history of migraine attacks would be extremely useful to all within the migraine research field, not least the migraineurs. This type of information would significantly help us to communicate the migraine issue to those who still may be in doubt with respect to the consequences migraine may have.

REFERENCES

1. Bigal ME, Lipton RB, Stewart WF. The epidemiology and impact of migraine. *Curr Neurol Neurosci Rep*. 2004;4(2):98–104.
2. Bjorner JB, Kosinski M, Ware JE, Jr. Using item response theory to calibrate the Headache Impact Test (HIT) to the metric of traditional headache scales. *Qual Life Res*. 2003;12(8):981–1002.
3. Burton WN, Conti DJ, Chen CY, et al. The economic burden of lost productivity due to migraine headache: a specific worksite analysis. *J Occup Environ Med*. 2002;44(6):523–529.
4. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. Headache Classification Committee of the International Headache Society. *Cephalalgia*. 1988;7:1–96.
5. Clouse JC, Osterhaus JT. Healthcare resource use and costs associated with migraine in a managed healthcare setting. *Ann Pharmacother*. 1994;28(5):659–664.
6. Cortelli P, Dahlöf C, Bouchard J, et al. A multinational investigation of the impact of subcutaneous sumatriptan. III: Workplace productivity and non-workplace activity. *Pharmacoeconomics*. 1997;1:35–42.
7. Dahlöf C. Minor Symptoms Evaluation (MSE) Profile—a questionnaire for assessment of subjective CNS-related symptoms. *Scand J Prim Health Care Suppl*. 1990;1:19–25.
8. Dahlöf C. Assessment of health-related quality of life in migraine. *Cephalalgia*. 1993;13(4):233–237.
9. Dahlöf CGH. Benefits of treatment on headache disability—a personal view on selected data. In: Olesen J, Steiner TJ, Lipton RB, eds. *Frontiers in headache research: reducing the burden of headache*. Oxford University Press; 2003:27–41.
10. Dahlöf CG, Dimenäs E. Migraine patients experience poorer subjective well-being/quality of life even between attacks. *Cephalalgia*. 1995;15(1):31–6.
11. Dahlöf C, Edwards C, Toth A. Sumatriptan injection is superior to placebo in the acute treatment of migraine—with regard to both efficacy and general well-being. *Cephalalgia*. 1992;12(4):214–220.
12. Dahlöf C, Linde M. One-year prevalence of migraine in Sweden: a population-based study in adults. *Cephalalgia*. 2001;21(6):664–671.
13. Dahlöf CG, Solomon GD. The burden of migraine to the individual sufferer: a review. *Eur J Neurol*. 1998;5(6):525–533.
14. Dimenäs ES, Dahlöf CG, Jern SC, et al. Defining quality of life in medicine. *Scand J Prim Health Care Suppl*. 1990;1:7–10.
15. Dimenäs ES, Wiklund IK, Dahlöf CG, et al. Differences in the subjective well-being and symptoms of normotensives, borderline hypertensives and hypertensives. *J Hypertens*. 1989;7(11):885–890.
16. Edmeads J, Mackell JA. The economic impact of migraine: an analysis of direct and indirect costs. *Headache*. 2002;42(6):501–509.
17. El Hasnaoui A, Vray M, Blin P, et al. Assessment of migraine severity using the MIGSEV scale: relationship to migraine features and quality of life. *Cephalalgia*. 2004;24(4):262–270.

18. El Hasnaoui A, Vray M, Richard A, et al. Assessing the severity of migraine: development of the MIGSEV scale. *Headache*. 2003; 43(6):628–635.
19. Ferrari MD. The economic burden of migraine to society. *Pharmacoeconomics*. 1998;13(6):667–676.
20. Holmes WF, MacGregor EA, Dodick D. Migraine-related disability: impact and implications for sufferers' lives and clinical issues. *Neurology*. 2001;56(6 Suppl 1):S13–S19.
21. Inder TE, Wells SJ, Mogridge NB, et al. Defining the nature of the cerebral abnormalities in the premature infant: a qualitative magnetic resonance imaging study. *J Pediatr*. 2003;143(2):171–179.
22. The International Classification of Headache Disorders: 2nd edition. *Cephalalgia*. 2004;1:9–160.
23. Jacobson GP, Ramadan NM, Aggarwal SK, et al. The Henry Ford Hospital Headache Disability Inventory (HDI). *Neurology*. 1994;44(5):837–842.
24. Jacobson GP, Ramadan NM, Norris L, et al. Headache disability inventory (HDI): short-term test-retest reliability and spouse perceptions. *Headache*. 1995;35(9):534–539.
25. Jhingran P, Osterhaus JT, Miller DW, et al. Development and validation of the Migraine-Specific Quality of Life Questionnaire. *Headache*. 1998;38(4):295–302.
26. Linde M, Dahlöf C. Attitudes and burden of disease among self-considered migraineurs—a nation-wide population-based survey in Sweden. *Cephalalgia*. 2004;24(6):455–465.
27. Lipton RB, Hamelsky SW, Kolodner KB, et al. Migraine, quality of life, and depression: a population-based case-control study. *Neurology*. 2000;55(5):629–635.
28. Lipton RB, Liberman JN, Kolodner KB, et al. Migraine headache disability and health-related quality-of-life: a population-based case-control study from England. *Cephalalgia*. 2003;23(6):441–450.
29. Lipton RB, Stewart WF. Migraine in the United States: a review of epidemiology and health care use. *Neurology*. 1993;43(6 Suppl 3): S6–S10.
30. Lipton RB, Stewart WF, Diamond S, et al. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. *Headache*. 2001;41(7):646–657.
31. Lipton RB, Stewart WF, Reed M, et al. Migraine's impact today. Burden of illness, patterns of care. *Postgrad Med*. 2001;109(1):38–40.
32. Lipton RB, Stewart WF, Scher AI. Epidemiology and economic impact of migraine. *Curr Med Res Opin*. 2001;17(1):S4–S12.
33. Lofland JH, Johnson NE, Batenhorst AS, et al. Changes in resource use and outcomes for patients with migraine treated with sumatriptan: a managed care perspective. *Arch Intern Med*. 1999;159(8):857–863.
34. Lopez AD, Murray CC. The global burden of disease, 1990–2020. *Nat Med*. 1998;4(11):1241–1243.
35. MacGregor EA, Brandes J, Eikermann A. Migraine prevalence and treatment patterns: the global Migraine and Zolmitriptan Evaluation survey. *Headache*. 2003;43(1):19–26.
36. Mannix LK. Epidemiology and impact of primary headache disorders. *Med Clin North Am*. 2001;85(4):887–895.
37. McHorney CA, Ware JE Jr, Lu JF, et al. The MOS 36-item Short-Form Health Survey (SF-36): III. Tests of data quality, scaling assumptions, and reliability across diverse patient groups. *Med Care*. 1994;32(1):40–66.
38. McHorney CA, Ware JE Jr, Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Med Care*. 1993;31(3):247–263.
39. Menken M, Munsat TL, Toole JF. The global burden of disease study: implications for neurology. The ambulatory workload of office-based neurologists: implications of the National Ambulatory Medical Care Survey. *Arch Neurol*. 2000;57(3):418–420.
40. Murray CJL, Lopez AD. *The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020. Global burden of disease and injury series*. Cambridge, MA: Harvard School of Public Health on behalf of the World Health Organization and the World Bank; 1966.
41. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: Global Burden of Disease Study. *Lancet*. 1997;349(9064):1498–1504.
42. Osterhaus JT, Townsend RJ, Gandek B, et al. Measuring the functional status and well-being of patients with migraine headache. *Headache*. 1994;34(6):337–343.
43. Pesa J, Lage MJ. The medical costs of migraine and comorbid anxiety and depression. *Headache*. 2004;44(6):562–570.
44. Rapoport AM, Adelman JU. Cost of migraine management: a pharmacoeconomic overview. *Am J Manag Care*. 1998;4(4):531–545.
45. Rasmussen BK. Epidemiology and socio-economic impact of headache. *Cephalalgia*. 1999;25(2):20–23.
46. Smith R. Impact of migraine on the family. *Headache*. 1998;38(6): 423–426.
47. Solomon GD, Dahlöf C. Impact of Headache on the Individual Sufferer. In: Olesen J, Tfelt-Hansen P, Welch KMA, eds. *The headaches,* 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2000: 25–31.
48. Stang PE, Crown WH, Bizier R, et al. The family impact and costs of migraine. *Am J Manag Care*. 2004;10(5):313–320.
49. Steiner TJ. Headache burdens and bearers. *Funct Neurol*. 2000;3:219–223.
50. Steiner TJ, Scher AI, Stewart WF, et al. The prevalence and disability burden of adult migraine in England and their relationships to age, gender and ethnicity. *Cephalalgia*. 2003;23(7):519–527.
51. Stewart WF, Lipton RB, Dowson AJ, et al. Development and testing of the Migraine Disability Assessment (MIDAS) Questionnaire to assess headache-related disability. *Neurology*. 2001;56(6 Suppl 1):S20–S28.
52. Stewart WF, Lipton RB, Kolodner K, et al. Reliability of the migraine disability assessment score in a population-based sample of headache sufferers. *Cephalalgia*. 1999;19(2):107–114.
53. Stewart WF, Lipton RB, Kolodner KB, et al. Validity of the Migraine Disability Assessment (MIDAS) score in comparison to a diary-based measure in a population sample of migraine sufferers. *Pain*. 2000;88(1):41–52.
54. Stewart WF, Lipton RB, Simon D, et al. Reliability of an illness severity measure for headache in a population sample of migraine sufferers. *Cephalalgia*. 1998;18(1):44–51.
55. Stewart WF, Lipton RB, Simon D, et al. Validity of an illness severity measure for headache in a population sample of migraine sufferers. *Pain*. 1999;79(2-3):291–301.
56. Stewart WF, Lipton RB, Whyte J, et al. An international study to assess reliability of the Migraine Disability Assessment (MIDAS) score. *Neurology*. 1999;53(5):988–994.
57. Stronks D, Tulen J, Bussmann J, et al. Interictal daily functioning in migraine. *Cephalalgia*. 2004;24(4):271–279.
58. Tepper SJ, Dahlöf C, Dowson A, et al. Prevalence and diagnosis of migraine in patients consulting their physician with a complaint of headache: data from The Landmark Study. *Headache*. 2004;44:856–864.
59. Turner-Bowker DM, Bayliss MS, Ware JE Jr, et al. Usefulness of the SF-8 Health Survey for comparing the impact of migraine and other conditions. *Qual Life Res*. 2003;12(8):1003–1012.
60. Ware JE Jr, Kosinski M, Bjorner JB, et al. Applications of computerized adaptive testing (CAT) to the assessment of headache impact. *Qual Life Res*. 2003;12(8):935–952.
61. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care*. 1992;30(6):473–483.
62. Wells NE, Steiner TJ. Effectiveness of eletriptan in reducing time loss caused by migraine attacks. *Pharmacoeconomics*. 2000; 18(6):557–566.
63. The World Health Report: 2001. *Mental health: new understanding, new hope*. Geneva: World Health Organization.