MAJOR ARTICLE

Acute Pain in Herpes Zoster and Its Impact on Health-Related Quality of Life

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Although the effects of postherpetic neuralgia on physical and emotional functioning have been examined in a number of studies, the impact of acute pain in herpes zoster ("shingles") on health-related quality of life has been neglected. We describe the characteristics of herpes zoster pain and examine its relationship to physical, role, social, and emotional functioning in 110 patients with herpes zoster. When we controlled for relevant covariates, we found that greater pain burden, as assessed by the product of pain intensity and duration, was associated with poorer physical functioning, increased emotional distress, and decreased role and social functioning. The results demonstrate that herpes zoster pain has broad effects on the daily lives of patients and on their emotional health. The increasing incidence of herpes zoster that can be anticipated as the population ages requires that clinical trials that examine interventions to prevent or treat herpes zoster pain be given a high priority.

Herpes zoster ("shingles") is caused by reactivation of the varicella-zoster virus after a period of latency that follows primary infection [1, 2]. A prodrome of dermatomal pain typically precedes the appearance of the characteristic rash, which is accompanied by moderate-to-severe acute pain in a majority of patients [3]. Pain that continues after the rash has healed is termed "postherpetic neuralgia" (PHN), a chronic neuropathic pain syndrome. Chronic pain has substantial adverse effects on physical and emotional functioning [4, 5], and physical disability and emotional distress are common in PHN [6]. PHN is often refractory to existing treatments, and recent clinical trials have examined whether various pharmacologic treatments improve pain and health-related quality of life in patients with PHN [7].

However, no randomized clinical trials of treatments for acute pain in herpes zoster have been conducted, and only one previous study has evaluated the impact of herpes zoster pain on health-related quality of life [8, 9]. This is surprising, given that herpes zoster occurs in ~500,000 people in the United States each year, during the lifetimes of as much as 20%–30% of the population, and in as many as 50% of those living until at least 85 years of age [1, 10–12]. Because herpes zoster has a high incidence, systematic evaluation of its adverse effects on health-related quality of life is needed. If these effects are substantial, they will provide a compelling basis for undertaking randomized clinical trials of treatments for herpes zoster pain.

The current study had 3 objectives: to describe acute pain in herpes zoster through use of a comprehensive assessment of pain intensity, quality, and duration; to examine associations between herpes zoster pain and the core domains of physical, role, social, and emotional functioning [5]; and to determine the impact of herpes zoster pain on these domains of health-related quality of life, after controlling for demographic and clinical covariates.

METHODS

Subjects and procedures. A sample of 129 patients with herpes zoster was recruited from the dermatology

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clinic and faculty practice at a university medical center and from community physicians. Eligible patients had received a diagnosis of herpes zoster from a physician, were at least 18 years old, and spoke English. Patients with a history of no more than 1 previous episode of herpes zoster were enrolled in the study if this episode had occurred ⩾5 years earlier. Nineteen patients were excluded from all data analyses because their assessments were conducted >30 days after the onset of rash, which can be considered to be the end of the acute phase of herpes zoster [13–16]; this left a sample of 110 patients with herpes zoster.

All patients provided informed consent and were interviewed in person by a clinical psychologist as soon as possible after referral to the study by the diagnosing physician. Patients were asked to provide the names of same-sex acquaintances of approximately their own age who might participate in the study as comparison subjects. A sample of 68 subjects without a history of herpes zoster was formed that included these acquaintances of patients, as well as individuals recruited from a medical center research-subject pool.

Assessments. Acute pain intensity was assessed using 4 measures: ratings of average and worst shingles pain on a numerical rating scale (NRS) of 0 to 100 (i.e., ratings of "no pain" to "pain as bad as it can be"), and ratings of average and worst shingles pain on the McGill Pain Questionnaire (MPQ) Present Pain Intensity (PPI) verbal rating scale (i.e., ratings of no pain, or mild, discomforting, distressing, horrible, or excruciating pain) [17]. Because these 4 ratings were highly intercorrelated (range of Pearson *r*, 0.80 to 0.91) and the results of recent research indicate that composite measures of pain intensity have somewhat greater reliability and validity than single ratings [18], a composite measure of pain intensity was calculated. Specifically, the PPI ratings were coded as 0–5 and were multiplied by 20, the resulting 2 PPI scores of 0–100 were averaged with the 2 NRS scores, and the result was divided by 10, which yielded a pain intensity composite score that ranged from 0 to 10.

A fundamental feature of current theory and research on pain is the distinction between the sensory components of pain (i.e., those described with terms such as "sharp" or "burning") and the affective components of pain (i.e., those described with terms such as "tiring" or "terrifying"), which are considered integral components of an individual's response to pain that should be assessed separately [17, 18]. These components of pain were assessed using the MPQ sensory and affective subscales, which have been shown to distinguish the sensory qualities of pain from its affective qualities in acute postoperative pain and birth-labor pain [17].

Overall pain duration and pain episode duration were assessed using modifications of items from the Medical Outcomes Study Pain Index [19]. The overall burden of acute pain in patients with herpes zoster reflects both the duration of pain and its intensity. Measures of pain burden that reflect the area under the pain intensity–pain duration curve [9, 20] were calculated by multiplying the pain intensity composite scores and the sensory and affective pain scores by the estimated number of days with pain (we could not directly assess the number of days with pain since the onset of rash, because the number of days after the onset of rash at which patients' initial assessments were conducted varied). The number of days with pain was estimated by the overall pain duration item, in which responses were weighted by the duration of herpes zoster in days (zoster duration), as follows: responses of "None" were coded as 0 days; "One or two days" as 1.5 days; "A few days" as 4 days or as $0.3 \times$ zoster duration, whichever was less; "About half the time" as $0.5 \times$ zoster duration; "Most days" as $0.8 \times$ zoster duration; and "Every day" as $1.0 \times$ zoster duration.

Premorbid physical, role, and social functioning during the week before the onset of herpes zoster were retrospectively assessed with the Medical Outcomes Study Short-Form General Health Survey [21]. The impact of herpes zoster pain on physical, role, and social functioning was assessed using modifications of items from the Medical Outcomes Study Pain Index [19]. In addition, 4 measures of emotional functioning were administered: the Beck Depression Inventory [22]; the Spielberger State-Trait Anxiety Inventory, state version [23]; the Mental Health Inventory emotional well-being scale [24]; and the Personality Disorder Questionnaire (revised version) impairment/distress scale [25].

Statistical analysis. Descriptive statistics, *t* tests, and Pearson correlation coefficients were calculated to characterize the samples of patients and comparison subjects and to examine the relationships between the measures of herpes zoster pain and the demographic, clinical, and health-related quality of life variables. A series of multiple regression analyses was conducted to determine the independent effects of pain burden on health-related quality of life, after we controlled for the demographic and clinical variables that were either significantly associated with health-related quality of life or that were considered potential covariates on biomedical or psychosocial grounds. Each measure of physical, role, social, and emotional functioning that was significantly associated with at least 1 measure of pain burden served as a separate criterion variable.

Relevant covariates were entered in the first 2 blocks of the regression models, with demographic covariates (i.e., age, sex, race, education level, and marital status) in the first block, and clinical covariates (i.e., herpes zoster duration, immune status, and the corresponding measure of premorbid functioning in the analyses of physical, role, and social functioning to control for patients' disability before their zoster infection) in the second block. The measures of overall, sensory, and affective pain burden were then entered simultaneously in the third block of the models to identify the specific aspects of herpes zoster pain

Table 1. Demographic and clinical characteristics of patients with herpes zoster (HZ) and of comparison subjects in a study of health-related quality of life in herpes zoster.

Characteristic	Patients with HZ (N = 110)	Comparison subjects (N = 68)
Age		
Mean ± SD, years	59.6 ± 15.0	56.2 ± 15.7
⩾50 years	72.7	57.4
Female sex	54.5	54.4
White race	89.1	82.4
Completed college	50.9	39.7
Married	57.3	50.0
Premorbid functioning, mean ± SD	0.39 ± 0.6	0.24 ± 0.4
HZ duration, mean days ± SD	17.1 ± 6.9	…
Immunocompromised	8.2	…
HZ location		…
Face or scalp	21.8	…
Other	78.2	…
Prodrome present	47.3	…

NOTE. Data are % of subjects, unless indicated otherwise.

burden that made independent contributions to each of the domains of health-related quality of life, after controlling for the demographic and clinical covariates.

RESULTS

Demographic and clinical characteristics of the patients with herpes zoster and the comparison subjects are presented in table 1. There were no statistically significant demographic differences between the patients and the comparison subjects. Almost three-quarters of the patients were ⩾50 years of age, approximately half had a prodrome before their rash appeared, and slightly more than 20% had trigeminal zoster. Approximately 50% of the patients were women, and almost 90% were white (5 patients reported their racial or ethnic identification as African American, 2 as Asian American, and 4 as Latino/a). Nine patients were immunocompromised as a result of HIV infection or concurrent chemotherapy or radiation treatment for cancer. On average, initial assessments occurred 17 days after the onset of rash (SD, 6.9; range, 0–30 days).

Characteristics of pain in herpes zoster. Descriptive statistics for the measures of pain intensity, quality, and duration are presented in table 2. The pain intensity composite and the sensory and affective pain scores were significantly intercorrelated (Pearson r values ranged from .71 to .97; all P values were < .01), as were the measures of overall, sensory, and affective pain burden (Pearson r values ranged from .74 to .90; all P values were < .01). On average, patients reported experiencing moderate pain that was present much of the time. However, there was great variability in pain intensity, with 4% of patients denying any herpes zoster pain on the pain intensity composite but 42% reporting that their worst zoster pain was "horrible" or "excruciating." Patients generally endorsed more of the sensory descriptors of pain quality than they did the affective descriptors, and one-quarter did not endorse any of the affective descriptors at all, which suggests that herpes zoster pain has minimal emotional impact in some patients. Three-quarters of the patients reported having had pain at least half of the time since their shingles began, and a majority reported that they had experienced pain during most days or every day. Although one-quarter of the patients reported that when they had pain, it lasted a few minutes, just as many reported that their pain lasted the whole day.

Relationships between the demographic and clinical variables and overall, sensory, and affective pain burden are presented in table 3. As can be seen, overall and sensory pain burden

Table 2. Assessments of acute pain in patients with herpes zoster in a study of health-related quality of life.

Assessment, by type	Value
Group score or value, mean ± SD (median)	
PIC score[a]	5.3 ± 2.7 (5.5)
MPQ sensory pain score	17.8 ± 9.2 (18)
MPQ affective pain score	3.3 ± 3.4 (2)
Estimated duration of pain, days	10.8 ± 6.9 (9.9)
Pain burden[b]	
Overall	67.6 ± 55.6 (61.9)
Sensory	222.8 ± 196.4 (180.0)
Affective	42.3 ± 56.8 (19.0)
Duration of pain reported, % of patients	
Overall	
No pain	2.8
1 or 2 days	5.6
A few days	17.8
About half of the time	15.0
Most days	14.0
Every day	44.9
Per episode	
No pain	2.8
A few minutes	25.6
Several minutes to an hour	17.4
Several hours	13.8
Most of the day	17.4
Whole day	22.9

NOTE. NRS, numerical rating scale; MPQ, McGill Pain Questionnaire; PIC, pain intensity composite; PPI, McGill Pain Questionnaire Present Pain Intensity scale.

[a] 0–10: standardized mean of 4 NRS and PPI measures.

[b] Overall pain burden was defined as PIC score × no. of days with pain; sensory pain burden was defined as MPQ sensory pain score × no. of days with pain; and affective pain burden was defined as MPQ affective pain score × no. of days with pain.

Table 3. Relationships between demographic and clinical variables and pain burden in patients with herpes zoster (HZ).

Variable	Pain burden		
	Overall	Sensory	Affective
Pearson *r*			
Age	−0.04	−0.03	−0.08
Education, years	−0.19[a]	−0.15	−0.28[b]
HZ duration	0.36[b]	0.31[b]	0.14
Average premorbid functioning[c]	0.15	0.18	0.18
Mean pain scores[d]			
Sex			
Male	69.1	221.4	35.6
Female	66.5	224.5	47.9
Race			
White	65.7	218.1	40.8
Other	89.7	278.3	59.5
Marital status			
Married	72.0	226.0	46.2
Not married	64.5	220.6	39.4
Immune status			
Compromised	109.5[a]	339.8[a]	70.4
Noncompromised	63.8	212.1	39.8
HZ location			
Face or scalp	68.1	188.6	40.3
Other	67.5	232.2	42.9
Prodrome			
Absent	52.2[b]	171.6[a]	35.0
Present	85.2	281.3	50.7

[a] $P < .05$.
[b] $P < .01$.
[c] The averages of the physical, role, and social premorbid functioning measures were used in calculating these correlations.
[d] Significance based on *t* tests.

were significantly greater in those patients with herpes zoster who were immunocompromised and who had a prodrome, and overall and affective pain burden were significantly less in more highly educated patients. Patients who had had herpes zoster for a longer period at the time of their assessment reported greater overall and sensory pain burden but not greater affective pain burden.

Associations between acute pain and health-related quality of life. There was considerable variability among patients in the effects of their pain on functioning. Although approximately half of the patients denied the interference of pain with daily activities, a substantial number reported that shingles pain had interfered "quite a bit" or "extremely" with their physical, role, and social functioning (14.6%, 21.8%, and 26.3% of patients, respectively).

Correlations between overall, sensory, and affective pain burden and health-related quality of life are presented in table 4. As can be seen in the first 3 rows of the table, greater pain burden was significantly correlated with poorer physical, role, and social functioning. With respect to emotional functioning, greater pain burden as assessed by each of the measures was significantly associated with greater symptoms of depression. Greater affective pain burden, but not overall or sensory pain burden, was also significantly associated with greater psychological impairment. Neither anxiety nor emotional well-being was significantly associated with any of the pain burden measures.

Because the measures of the interference of pain with functioning were not administered to comparison subjects, patients with herpes zoster and comparison subjects could not be compared with respect to these measures. However, the 2 groups were compared with respect to emotional functioning, and patients with herpes zoster reported slightly greater depression and anxiety and significantly less emotional well-being than did comparison subjects ($t = 2.02$; $P < .05$).

Multivariate analyses. The results of the regression models that examine the impact of pain on physical, role, and social functioning are presented in table 5. After controlling for the demographic and clinical covariates and the corresponding measure of premorbid physical functioning, we found that sensory pain burden made a significant independent contribution to poorer physical functioning, and overall pain burden made an independent contribution to poorer role and social functioning.

The results of the regression models that examine the impact of pain on emotional functioning are presented in table 6. After controlling for the demographic and clinical covariates, we found that affective pain burden made an independent contribution to symptoms of depression and demonstrated a trend in accounting for psychological impairment. Neither overall

Table 4. Pearson correlation coefficients between pain burden and health-related quality of life (HRQL) in patients with herpes zoster.

HRQL domain	Pain burden		
	Overall	Sensory	Affective
Physical functioning	0.47[a]	0.57[a]	0.54[a]
Role functioning	0.52[a]	0.52[a]	0.50[a]
Social functioning	0.57[a]	0.54[a]	0.54[a]
Emotional functioning			
Depression symptoms	0.26[b]	0.23[b]	0.39[b]
Anxiety symptoms	0.19	0.16	0.18
Emotional well-being	−0.08	−0.08	−0.16
Psychological impairment[c]	0.16	0.15	0.25[d]

[a] $P < .001$.
[b] $P < .01$.
[c] The sample size for psychological impairment was 87 because of missing data.
[d] $P < .05$.

Table 5. Standardized β weights and significance levels for multiple regression models for physical, role, and social functioning.

Block, variable[a]	Physical functioning	Role functioning	Social functioning
Block 1			
Age	−0.02	−0.04	0.00
Sex	0.07	0.07	0.14
Race	0.12	−0.02	0.02
Education	−0.11	0.04	0.02
Marital status	−0.08	0.10	0.05
Block 2			
Zoster duration	−0.17	−0.32[b]	−0.19[c]
Immune status	0.02	−0.09	−0.02
Premorbid functioning[d]	−0.07	0.07	0.00
Block 3			
Overall pain burden	−0.21	0.52[b]	0.55[b]
Sensory pain burden	0.74[b]	−0.06	−0.12
Affective pain burden	0.07	0.23	0.27
F	6.00[e]	6.50[e]	6.21[e]
df	11, 97	11, 97	11, 97
Adjusted R^2	0.35	0.37	0.35

[a] Standardized β weights and their significance levels are presented for each variable; for sex, 0 = male, 1 = female; for race, 0 = white, 1 = other; for marital status, 0 = not married, 1 = married; for immune status, 0 = compromised, 1 = noncompromised.
[b] $P < .01$.
[c] $P < .05$.
[d] The corresponding measures of physical, role, or social premorbid functioning were entered in this block of the 3 models.
[e] $P < .001$.

nor sensory pain burden contributed independently to these measures of emotional functioning.

DISCUSSION

The sample of patients examined in this study was generally representative of individuals with herpes zoster. The results demonstrated that such patients generally suffer from pain that is moderate in intensity, but that there is considerable variability in pain intensity, and a substantial minority have severe pain that is present for most or all of the day. Our analyses focused on assessments of pain burden, that is, the area under the pain intensity–pain duration curve (it is important to note, however, that the results of a parallel set of analyses of overall, sensory, and affective pain intensity were very similar). The burden of herpes zoster pain was greater in patients who were immunocompromised and who had had a prodrome, and less in patients who were more highly educated.

Although the disability and distress associated with PHN is well recognized, the impact of herpes zoster pain on health-related quality of life has rarely been investigated. Accordingly, the major objective of our analyses was to examine the associations between pain in herpes zoster and physical, role, social, and emotional functioning. These 4 domains of health-related quality of life were chosen because it has recently been recommended that physical and emotional functioning should be considered to be core outcome domains in assessing chronic pain and that role and social functioning should be considered to be key supplemental outcome domains [5]. We found that greater acute pain burden in herpes zoster was significantly associated with poorer physical, role, and social functioning and greater emotional distress.

In multivariate analyses that examined the independent contributions of overall, sensory, and affective pain burden to health-related quality of life, sensory pain burden made an independent contribution to physical functioning, and affective pain burden made an independent contribution to symptoms of depression and psychological impairment. Overall pain burden, which includes the sensory and affective components of pain, made an independent contribution to both role and social functioning, 2 domains of health-related quality of life in which both physical and emotional processes play an important role. The independent contributions of sensory pain to physical functioning and affective pain to emotional functioning in our data are consistent with the results of research on chronic pain [4, 17, 18] and provide support for a multidimensional conceptualization of acute pain and its impact.

Although the patients and comparison subjects did not significantly differ in symptoms of depression, anxiety, and psy-

Table 6. Standardized β weights and significance levels for multiple regression models for emotional functioning.

Block, variable[a]	Depression symptoms	Psychological impairment
Block 1		
Age	−0.08	−0.13
Sex	0.01	0.03
Race	0.10	0.18
Education	0.03	−0.05
Marital status	−0.15	−0.17
Block 2		
Zoster duration	−0.14	0.05
Immune status	0.04	−0.13
Block 3		
Overall pain burden	0.16	−0.03
Sensory pain burden	−0.28	−0.15
Affective pain burden	0.55[b]	0.33[c]
F	3.07[d]	2.36[b]
df	10, 97	10, 98
Adjusted R^2	0.17	0.12

[a] Standardized β weights and their significance levels are presented for each variable; for sex, 0 = male, 1 = female; for race, 0 = white, 1 = other; for marital status, 0 = not married, 1 = married; for immune status, 0 = compromised, 1 = noncompromised.
[b] $P < .05$.
[c] $P = .06$.
[d] $P < .01$.

chological impairment, additional evidence of the impact of herpes zoster on emotional functioning was provided by the significantly lower levels of emotional well-being reported by the patients, compared with those reported by the comparison subjects. Considered together with the results of the analyses of the acute pain measures and their associations with health-related quality of life, these data suggest that the adverse impact of acute pain in herpes zoster is relatively modest when averaged across all patients but that it is considerably greater in those patients who suffer from more severe and longer lasting pain.

Our study had several important limitations. Foremost among these was the varying duration of time between the onset of rash and the assessments of pain and health-related quality of life. We limited our analyses to patients who were first assessed within 30 days after the onset of rash, which is a validated definition of the acute phase of herpes zoster [13–16]. Because we assessed patients only once during the acute phase of herpes zoster, their reports of acute pain and health-related quality of life reflected both recalled and current levels of these variables. Although there is evidence that current pain intensity influences reports of past pain, correlations between prospectively assessed pain ratings recorded daily in diaries during 1 or 2 weeks and ratings of recalled pain are generally very high and support both the reliability and validity of the pain ratings we collected [18]. A final limitation of our study was that the assessment of premorbid functioning was retrospective, and the impaired functioning associated with herpes zoster could bias such a retrospective assessment. However, the relationships between the measures of herpes zoster pain and these retrospective reports of premorbid functioning were not significant.

Our results establish that pain in herpes zoster can have substantial adverse effects on the daily lives of patients and on their emotional functioning. It has been predicted that the incidence of herpes zoster will increase in the coming decades both because of the aging of the population and as a consequence of childhood varicella vaccination [26, 27]. The broad impact of herpes zoster on health-related quality of life that was apparent in our data not only requires that research on the prevention and treatment of herpes zoster pain be given a high priority but also provides an initial basis for evaluating the cost-effectiveness of such interventions [28]. Studies of varicella vaccination to attenuate herpes zoster in older individuals are ongoing [29, 30], and, if such vaccination is efficacious, it may offset the anticipated increase in the incidence of herpes zoster [26]. However, because of the aging of the population, the occurrence of herpes zoster in younger individuals, and the lack of compliance of older individuals with vaccination programs, vaccination may be unlikely to appreciably reduce the incidence of herpes zoster below current levels [26].

Attention must, therefore, be paid to the treatment of herpes zoster pain and its adverse effects on health-related quality of life. Unfortunately, no randomized clinical trials of treatments for pain in herpes zoster have been conducted. Although there have been recent, major advances in the treatment of PHN and other chronic neuropathic pain syndromes [7, 31], it is unknown whether these treatments—which not only relieve pain, but also improve quality of life—are beneficial for patients with herpes zoster. Because there is no base of evidence for selecting treatments, it is very likely that pain in patients with herpes zoster is often inadequately treated in clinical practice. The demonstration that herpes zoster pain can be both physically disabling and emotionally distressing provides considerable justification for initiating efforts to identify safe and efficacious treatments.

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