

Clinical and psychosocial correlates of acute pain in herpes zoster

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Abstract

Background: Acute and persistent pain are the most significant clinical manifestations of herpes zoster (HZ), but the characteristics of acute pain in HZ patients have been inadequately investigated.

Objectives: To correlate the severity of acute pain with clinical, demographic and psychosocial characteristics of HZ patients.

Study design: Five hundred thirty-three patients with acute HZ were recruited by 119 dermatologists who collected medical and demographic data at diagnosis, provided counselling and therapy where appropriate and asked the patients to complete the Short Italian Questionnaire designed for comprehensive evaluation of HZ patients.

Results: In a univariate analysis, greater acute pain severity was significantly associated with female gender, number of dermatomes affected, presence of prodromal pain, abnormal sensations (dysesthesia), education level, anxiety and depression. Quality of life, even if greatly reduced, did not correlate with the intensity of pain. In a multivariate model, the intensity of pain was independently associated with the extent of rash ($p = 0.042$), presence of prodromal pain ($p = 0.005$), dysesthesia, education level ($p = 0.040$), and depression ($p < 0.001$), but not with gender, anxiety or quality of life.

Conclusions: This study suggests that in patients with acute HZ the severity of the disease and depression at presentation are the main correlates of pain intensity.

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1. Introduction

Herpes zoster ([HZ]; ‘shingles’) results from the reactivation of latent varicella zoster virus (VZV) from the dorsal root and some cranial nerve ganglia. Although HZ is not a reportable disease, 200,000–250,000 cases are estimated to occur annually in Italy (di Luzio Paparatti et al., 1999).

Abbreviations: HZ, herpes zoster; PHN, postherpetic neuralgia; VZV, virus varicella zoster

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In immunocompetent persons, the most notable manifestations of shingles are rash, acute neuralgia (pain occurring within 30 days of disease onset) and persistent pain, termed postherpetic neuralgia (PHN). Social, psychological, and environmental factors can influence a patient’s perception of pain and their ability to cope with pain and discomfort (Johnson, 2002). All of these factors should be addressed in order to provide optimal care.

The effects of PHN on physical and emotional functioning have been examined in several studies and it has been established that, other than older age, the best supported risk factor for developing PHN is the severity of acute pain accompanying HZ (Schmader et al., 1990; Dworkin et al., 1992; Dworkin and Portenoy, 1996; Whitley et al., 1999; Dworkin

and Schmader, 2001; Nagasako et al., 2002; Thyregod et al., 2004). However, acute pain in HZ patients has been less well investigated (Tyring et al., 1995; Dworkin et al., 2001; Chidiac et al., 2001; Katz et al., 2004). The present study examines the demographic, clinical and psychosocial correlates of pain that were present in a large sample of patients when first seen with HZ.

2. Materials and methods

2.1. Patients

Five hundred and thirty-three patients with a clinical diagnosis of acute HZ were recruited by 119 dermatologists in private practices nationwide from April to October 2001. At diagnosis, patients were asked to participate in a study of HZ and to complete a short questionnaire. Informed consent was obtained from all the patients who accepted. The dermatologists also collected medical and demographic data and provided counselling and therapy where appropriate.

2.2. Data collection

Each patient completed the Short Italian Questionnaire at the physician's office. This previously validated questionnaire was designed to evaluate the intensity of pain, psychological profile and quality of life (Serafini et al., 2003). It elicits information about anxiety or depression and the perceptions that an individual has about their pain and quality of life (worst pain over last week, physical and social functioning, vitality, physical and emotional role, psychological distress and well-being). Each item was scored between 0 (negative) and 10 (maximum). At the visit the physician collected the following information from the patient: demographic data, medical history, history of present disease, distribution of manifestations, clinical expression of disease and treatments.

2.3. Statistical analysis

Statistical analyses and data processing were performed using SAS software—version 8.2 for WindowsTM. All two-sided statistical tests were performed with a 5% significance level.

Quantitative variables were analyzed by descriptive statistics including mean values, standard deviation, median, minimum and maximum. Clinical and demographic characteristics were analyzed as categorical variables, whereas intensity of pain, anxiety, depression and quality of life were analyzed as continuous variables. Pearson's correlation coefficient was used to investigate the relationship between pain intensity and the other variables. Multivariate analysis of variance (MANOVA) was used to analyze pain intensity in relation to gender, age, education level, rash extension, abnormal sensations (such as pruritus, tingling, and allo-

dynia), prodromal pain, anxiety, depression and quality of life.

3. Results

Five hundred thirty-three subjects were enrolled in the study within 6 months. They were all Caucasian Italians and were evenly distributed from various areas of the Country. Demographic and clinical characteristics of the patients are summarized in Table 1. The median age was 58 years (range

Table 1
Demographic and clinical characteristics of the 533 patients with acute HZ

	Number (%)
Total	533 (100)
Gender	
Male	237 (44.5)
Female	296 (55.5)
Age (years)	
<50	190 (36)
50–60	109 (20)
>60	234 (44)
Years of education	
Elementary	178 (33)
Secondary	118 (22)
High school/university degree	237 (55)
Geographic area	
North	199 (37)
Center	117 (22)
South	156 (29)
Islands	61 (12)
Onset of pain (time to observation) (range: 1–30 days)	
<3 days	247 (46.3)
3–7 days	212 (39.8)
>7 days	74 (14.9)
Onset of rash (time to observation) (range: 1–30 days)	
<3 days	294 (55.2)
3–7 days	190 (35.6)
>7 days	49 (9.2)
Prodromal pain	435 (81.6)
Duration of prodromal pain before rash (days) (range: 1–>3 days)	
1	71 (16.4)
2–3	224 (51.3)
>3	140 (32.2)
Localization of rash	
Cranial (including ocular)	101 (19)
Cervical	62 (11.6)
Thoracic	271 (50.8)
Lumbar	88 (16.5)
Extent of rash (dermatomes)	
1	355 (66.6)
2	145 (27.2)
>2	18 (3.4)
Abnormal sensations (including itch, tingle and allodynia)	162 (30.4)
Motor paralysis	12 (2.3)
Fever (>37.5 °C)	63 (12.1)

Table 2

Demographic, clinical and psychological correlates of the intensity of acute pain in 533 zoster patients

	N (patients)	Median pain intensity score (range)	Pearson correlation coefficients	p-Value	Multivariate analysis (p)
Gender					
Male	237	5 (1.5–10)	−0.093	0.05	Ns
Female	296	6 (1.5–10)			
Age (years)					
< 50	190	5 (1.5–10)	0.055	Ns	Ns
50–60	109	6 (2–10)			
>60	232	6.5 (1.5–10)			
Years of education					
Elementary	176	7 (1.5–10)	−0.106	0.015	0.040
Secondary	118	5 (1.5–10)			
High school/university	237	5 (2–10)			
Extent of rash (dermatomes)					
One	355	5.5 (1.5–10)	0.133	0.005	0.042
>One	163	6.75 (1.5–10)			
Prodromal pain					
Yes	435	6.1 (1.5–10)	0.110	0.005	0.005
No	98	5.4 (1.5–10)			
Abnormal sensations					
Yes	162	6 (0–10)	−0.544	<0.001	0.014
No	371	5 (0–10)			
Anxiety	533	5 (0–10)	0.115	0.008	Ns
Depression	533	5 (0–10)	0.390	<0.001	<0.001
Quality of life	533	5 (0–10)	−0.020	Ns	Ns

18–82) and subjects were well distributed by age. There were slightly more females than males (56% versus 44%). The majority of participants in the study were married (65%), and 45% had a high school education or university degree. In Italy, compulsory education was for 5 years until the early 1960's and thereafter for 8 years, starting from 6 years of age. Alcohol consumption was none or negligible in over 80% of the subjects.

Ninety-two percent of individuals with acute HZ had pain at presentation. Medical advice was sought by 46% of patients within 72 h of developing pain and by 54% within 72 h of rash appearance. Initial assessment occurred at a median time of 72 h after the onset of rash. More than 80% of the subjects reported prodromal pain, which in the majority of cases lasted 2 days or 3 days. Abnormal sensations, including itch, tingle and allodynia, were reported by 162 subjects (30%). Rash was limited to a single dermatome in the majority of patients (67%), and involved cranial dermatomes in 19% of cases and spinal dermatomes in the remainder (Table 1). Fever was unusual and motor paralysis was diagnosed only in 2.3% of patients. The mean of the scores for anxiety, depression, and quality of life were 5.06 ± 0.8 , 3.6 ± 1.7 , and 5.7 ± 1.3 , respectively. Antiviral therapy was prescribed in 94.2% of cases.

Demographic, clinical and psychological correlates of the severity of acute pain in HZ patients are shown in Table 2. The severity of the acute pain was significantly associated with female gender, fewer years of education, rash involving more

than one dermatome, presence of prodromal pain, abnormal sensations, anxiety and depression. A trend towards greater acute pain severity was also observed as a function of age. Quality of life, although greatly reduced, did not significantly correlate with the intensity of pain.

In a multivariate model, the extent of rash, prodromal pain, abnormal sensations, years of education and depression were significantly associated with the severity of pain, but not gender, age, anxiety or quality of life. Females were more anxious (5.1 ± 1.6 versus 4.4 ± 1.7 ; $p < 0.001$) and depressed than men (3.4 ± 1.7 versus 4.0 ± 1.6 ; $p < 0.001$). Anxiety was significantly correlated with depression (Pearson's correlation = 0.234; $p < 0.001$). In addition, people with less years of education were more anxious and depressed than their counterparts, without reporting differences in the quality of life scores (Table 2).

4. Discussion

Our study confirms that acute HZ pain is generally moderate to severe with considerable variability in its intensity, character and duration (Katz et al., 2004). Consistent with previous studies, we also observed that rash involving more than one dermatome and the presence of prodromal pain were associated with more severe acute pain (Dworkin et al., 2001; Katz et al., 2004). In addition, the presence of abnormal sensations was associated with a greater severity of acute pain

(Table 2). A trend correlating pain severity with age was also found, in accordance with previous reports (Schmader, 1998, 1999; Oxman et al., 2005).

Taking into account only the demographic characteristics of our HZ patients, the univariate analysis suggested that female gender and fewer years of education are associated with more severe acute HZ pain. Dworkin and Schmader (2001) recently reported similar results and did not find sex differences associated with other aspects of HZ. Based on previous studies suggesting that women generally report greater pain than men (Unruh, 1996), the authors concluded that it is likely that the observed gender difference reflected a general trend of greater pain severity in women, rather than resulting from some gender-specific aspect of the pathophysiology of HZ. Consistently, in our multivariate analysis gender difference was obscured by depression, which was found to be more severe and more frequent in women compared to men. Regarding the association between more severe acute HZ pain and a lower level of education, it could be speculated that people with less education have a worse perception and/or lower comprehension of their pathological condition, resulting in greater anxiety and depression.

The absence of an association between severity of acute pain and quality of life differs from a previous report (Katz et al., 2004). However, in that study approximately half of the patients denied that pain interfered with daily activities (Katz et al., 2004). A tentative explanation for this discrepancy is that due to an Italian cultural trait pain interferes with quality of life independently from its severity. A possible limitation of our study is that acute pain severity was rated on a single occasion within a wide window of time after the rash onset (Table 1). Peak pain was found to occur equally often before, at, and after the rash onset (Haanpää et al., 2000). A potential sampling bias is that patients presenting to dermatologists for diagnosis might differ from patients presenting to primary care physicians. In this regard, similar studies examining HZ patients on presentation to either dermatologists or general practitioners, did not report significant differences between the two groups (Chidiac et al., 2001; di Luzio Paparatti et al., 1999).

The results of the multivariate analysis (Table 2) indicated that the severity of acute HZ pain is significantly associated with the extent of rash, prodromal pain, abnormal sensations, fewer years of education, and depression. Thus, among psychosocial factors, only depression, and not anxiety and gender, was associated with more severe acute pain, in contrast to the results of the univariate analysis. Katz et al. (2004) also reported that acute HZ pain burden was significantly associated with greater symptoms of depression and greater psychological impairment, but not with anxiety and emotional well-being. In addition, previous studies showed that a considerable number of HZ patients, during the last 3 months prior to the onset of symptoms, experienced an important familial, personal or professional life event, which is described as negative by 80% of them

(Schmader et al., 1990, 1998; Chidiac et al., 2001). Hence, it is difficult to say whether depression precedes herpes zoster or is a consequence of it. The causal relationship of pain and depression has been the subject of a long-standing controversy, and numerous pain syndromes associated with depressive disorders can be regarded as dynamic systems within which the elements interact bidirectionally (Wörz, 2003). Unfortunately, the examination of our study patients only at presentation (i.e. only once during the acute phase of HZ) did not allow us to investigate this further. In addition, our observations and those of other authors, raise important questions on the meaning and/or the reciprocal influence of different psychological symptoms, such as anxiety and depression, on the patient's perception of quality of life; in fact, even though there is an implicit suggestion that these are separate domains of psychosocial functioning, tests measuring quality of life include "mental health" as well as physical functioning, thereby blurring individual contributions to pain perception by anxiety and depression.

In conclusion, our study strongly indicated that the severity of the disease at presentation and depression are the major correlates of pain burden in patients with acute HZ. These results, which were obtained in a large number of cases, confirm those reported previously by other authors (Katz et al., 2004). In addition, we showed that acute HZ pain may interfere with quality of life independently from its severity.

It has been predicted that the incidence of HZ will increase worldwide in the coming decades because of aging of the population and possibly as a consequence of childhood varicella vaccination (Schuette and Hethcote, 1999; Brisson et al., 2003; Oxman et al., 2005; Gialloreti et al., 2005). The demonstration that acute pain in HZ can be both disabling and emotionally distressing provides justification for developing evidence-based guidelines, including both pharmacological and emotional support, for the treatment of HZ in the acute phase. Additional studies addressing the relationship between baseline psychosocial and demographic measures and the experience of acute HZ pain are needed to inform the design of additional treatments of acute shingles. Optimal treatment during the acute phase of HZ might also prevent the occurrence of postherpetic neuralgia.

Conflict of interest

Authors do not have conflicts of interest in relation to the present manuscript.

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