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Economic Burden of Herpes Zoster ("culebrilla") in Latin America

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ABSTRACT

Background: Herpes zoster (HZ) is characterized by debilitating pain and blistering dermatomal rash. The most common complication of HZ is postherpetic neuralgia (PHN), a persistent pain that can substantially affect patients' quality of life. HZ has significant impact on patients' lives with considerable implications for healthcare systems and society. The purpose of this study was to evaluate the healthcare resource utilization (HCRU) and medical costs associated with HZ in Latin America.
Method: We conducted a pooled-analysis of three prospective cohort studies of HZ patients ≥50 years of age in Argentina (n = 96); Brazil (n = 145) and Mexico (n = 142). Patients were recruited at different time-points during their HZ episode and were followed for six months. The incidence of PHN was defined as a worst ZBPI pain score of ≥3, persisting or appearing more than 90 days after the onset of rash. Work effectiveness was measured on a 100-point Likert scale where 100 was described as completely effective (able to work like before HZ began) and 0 as not effective at all. Direct costs included costs due to use of antiviral medications and all medical services used to treat HZ. Indirect cost was based on foregone earnings from patients due to work loss and presenteeism, and work loss by family caretakers. One-way sensitivity analysis was performed to assess the impact on total costs. All costs are reported in 2015 USD currency.
Results: 383 HZ patients were included and PHN incidence was 38.6%. The most commonly used resources were visits to the doctor's office (79.1% of patients), the emergency room (48.8%) and a specialist (37.9%); hospitalization was reported for 5.7% of patients. The overall direct cost per case was $763.19 USD, indirect cost was $701.40, for a total of $1,464.59 per HZ episode in Latin America. Total cost associated with HZ in patients with PHN was markedly higher compared to patients without PHN ($2,001.13 vs. $867.72, respectively) with indirect costs accounting for the most part of this difference. The sensitivity analysis was generally robust to changes in the assumptions made.
Conclusion: HZ and its sequelae impose a substantial economic burden in Latin America which is expected to rise as the population ages and the number of HZ cases increases. The results support the need for early intervention, preventative strategies and improved disease management to reduce the HZ-associated disease burden in Latin America.

Introduction

Herpes zoster (HZ) is caused by reactivation of latent varicella-zoster virus (VZV) in sensory ganglia and is typically characterized by painful, blistering dermatomal rash.[1] The most common complication of HZ is post herpetic neuralgia (PHN), which is characterized by pain persisting or appearing months after the rash heals. PHN can cause physical disability, emotional distress and

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interference with daily activities and sleep.[2,3] The incidence, severity, and duration of PHN increases with age, particularly in adults aged 50 years and older.[4] HZ may also cause neurological sequelae, HZ opthalmicus (HZO) with eye involvement or disseminated disease.[5] Complications of HZ have been reported in 13-26% of HZ cases.[6,7]

The annual incidence of HZ has been reported to range from 1.2 to 4.8 cases per 1,000 inhabitants/year in North America, Europe and Asia-Pacific.[5,8,9] The greatest challenge in reporting incidence rates in Latin American countries is the scarcity of available information.[10]In the available literature, the incidence rate in Latin America ranges from 3.6-6.5.[5,11–13] Suggesting a higher burden of disease in Latin American, compared to the previously mentioned countries.

However, there is a paucity of data detailing the economic burden in Latin American countries[9] which may be due to the lack of mandatory reporting and active surveillance systems in these countries. The decision to introduce a new vaccine in a national immunization program is not only made on the basis of clinical data but is also influenced by health economic parameters. The purpose of this study is to address this literature gap and provide a better understanding of the healthcare resource utilization costs associated with HZ and its complications in Latin America.

Methods

Study Design and Population

Data from the observational prospective cohort MASTER (Monitoring and Assessing Shingles Through Education and Research) study, conducted in Argentina, Brazil and Mexico, using similar methods to those described in other MASTER studies,[2,14,15] were pooled.

Male and female patients aged ≥ 50 years at the date of onset of the HZ rash, with a physician-confirmed diagnosis of HZ, and capable of completing the study questionnaires were eligible for the study. Of the 383 patients included, 96 were from Argentina, 145 from Brazil and 142 from Mexico. Patients were recruited at different time-points during their HZ episode and were followed for up to 6 months to assess HZ-associated burden of illness. PHN was defined as a "worst pain in the last 24 hours" score of ≥3, as assessed with the Zoster Brief Pain Inventory (ZBPI),[16] appearing or persisting after ≥90 days since rash onset. All patients signed an informed consent form and the study was approved by local Institutional Review Boards in each country.

Health Care Resource Utilization and Cost Sources

The societal perspective was utilized comprising HZ-related direct costs associated with outpatient care, hospital expenditures, and drug/treatment use, and indirect costs associated with work days lost by the patients and/or family caregivers and patient work effectiveness.

Patient reported healthcare resource utilization associated with HZ and impact on employment were assessed with a customized questionnaire and the work and productivity questionnaire, respectively. The following healthcare resources were considered in estimating direct costs: visit to a general practitioner/family doctor or specialist, use of ambulance services, visit to the emergency room, hospitalization, admission to a long-term care facility, use of nursing services, visit to a physiotherapist/rehabilitation, consultation of a psychiatrist/psychologist/counsellor, and use of medications or non-pharmacological treatments to treat HZ. Work effectiveness was measured on a 100-point Likert scale; patients were asked to rate their work effectiveness during a shingles episode, 100 being completely effective (able to work like before shingles began) and 0 not effective at all.

The unit costs for the medical care services and pharmaceuticals (Supplemental Table 1) were obtained from country specific official registries in Argentina,[17–19] Mexico[20] and Brazil.[21,22] If costs were not available, information was obtained from literature searches with service fee data and was validated by local expert opinion. The cost per unit of antivirals was derived by taking the mean unit cost of treatment for HZ using the generic acyclovir (200 mg, 25 capsules), valacyclovir (500 mg, 10 capsules), and famciclovir (125 mg, 10 capsules) in the respective countries. The unit cost for famciclovir was unavailable for Mexico, therefore the unit cost of acyclovir was applied as 96.3% of patients took acyclovir. In addition, the weighted unit cost of government reimbursed non-generic valacyclovir and government reimbursed generic acyclovir was used for Mexico. Unit costs from previous years were converted to current costs using the Consumer Price Index (CPI) for the respective countries[23] and were converted, for the purpose of the analysis, from local currencies to USD using current exchange rates on October 23, 2015 as follows; 1 Brazilian real = 0.258 USD, 1 Argentine peso = 0.105 USD and 1 Mexican peso = 0.060 USD. No discount rate was applied, as the mean disease duration and follow-up period were less than 1 year.[24]

The unit cost of work/productivity loss by patients was based on the national average salary at each country; for Argentina, the age-weighted national average salary for the age groups 50-59, 60-69 and ≥70 years was used as age-specific information was available. No transfer payments for work days lost were applied. The cost of family caregiver lost work days was calculated using the unit costs based on the overall national average salary. Mean productivity loss of the 6-month follow-up period was assessed on a 0-100% productivity scale (100% being completely effective; able to work like before shingles began).

Statistical Analysis

All results are reported for the overall population and by PHN status. Summary statistics were utilized to describe the study sample including measures of central tendency (mean) and dispersion (standard deviation) for continuous variables, and frequency distributions and odds ratios (OR) with the respective 95% confidence intervals (CI) for categorical variables (patients experiencing PHN as compared to those without). A one-way sensitivity analysis was performed by increasing and reducing the direct and indirect unit costs by 25% to determine the impact on total cost per HZ case. Statistical analyses were carried out using SPSS 21.0 (SPSS Inc., Chicago, IL) and SAS 9.4 (SAS Institute, Cary, NC).

Results

A total of 383 patients were included in the analysis. Of 363 patients with available PHN information, 140 (38.6%) developed PHN. Table 1 summarizes the patient characteristics at baseline by PHN status and overall. The mean (SD) age at onset of disease was 67.7 (11.2) years and the majority of patients were female (64.2%). Approximately 50.0% of patients reported 20 lesions or less in the primary and adjacent dermatome at the time of enrolment and the majority (73.6%) had experienced severe prodromal pain (worst pain score ≥7). Overall, patients developing PHN were older (70.3 vs. 65.8 years) and had more severe rash at enrolment (20.2% vs. 11.4% of patients with available information had more than 50 lesions in the affected dermatomes) as compared to patients without PHN.

Table 2 describes the healthcare resource utilization associated with HZ in Latin America. The most commonly used resources used