



Best of Both Worlds

Industry-conducted patient registries not only offer commercial advantages but also benefit the public, argues Jean Siebenaler at Kendle



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Family Physicians and the American Academy of Pharmaceutical Physicians. She has authored articles, lectured and presented workshops on the design and operational logistics of late phase studies.

Patient registries are observational prospective studies conducted in 'real world' medical practices. There is typically no control over patient treatment or the number of patient visits, which differentiates these studies from randomised controlled clinical trials. However, correctly designed registries can inform physicians and the public regarding the effectiveness and safety of medical treatments, resulting in improved patient care and the promotion of best practices.

When conducted by industry, patient registries may also have commercialisation objectives, which include:

- ◆ Evaluation of long-term clinical utility of a treatment in a 'naturalistic' setting
- ◆ Evaluation of patient satisfaction and compliance with a treatment
- ◆ Evaluation of cost-effectiveness of a treatment
- ◆ Evaluation of 'off-label' use of a treatment
- ◆ Hypothesis generation for future clinical trials (for example to expand label indications)
- ◆ Strengthening physician and patient relationships

Therefore, well-designed industry-sponsored patient registries can result not only in improved commercial outcomes for the pharmaceutical company, but can serve the public well through the monitoring of long-term clinical practice patterns and trends, especially in diseases that are undergoing demographic and treatment changes. An example is Herpes Zoster (HZ).

CURRENT HERPES ZOSTER EPIDEMIOLOGY

The lifetime risk of getting Herpes Zoster (HZ) is estimated to be 10 to 20 per cent, with age (older than 50 years) being the most common risk factor (1). The goals of treatment are to reduce acute pain, accelerate skin lesion resolution and prevent acute and chronic complications, especially post herpetic neuralgia (PHN), which is the most common chronic ramification. PHN is a neuralgic pain that persists for months to years after the HZ skin lesions have healed and is reported to affect between eight and 70 per cent of those with HZ, with incidence and duration increasing with age (2). In one study, each one year increment over 50 years of age was associated with between nine and 12 per cent increases in the prevalence of PHN at 30 and 60 days respectively (3). Antiviral agents given within 72 hours of rash onset have proven to

be effective in reducing pain severity and duration of the rash, but have not entirely removed the risk of PHN.

Though HZ is primarily managed by general practitioners globally, there are substantial variations among countries in the management of the disease, with treatment guidelines being used to varying degrees (4). For example:

- ◆ In the UK and Germany, patients are generally aware of the disease and physicians tend to follow guidelines published by the UK Department of Health, British Society for the Study of Infection (BSSI) and the German Dermatological Society
- ◆ In Italy and Spain, patients tend to seek treatment at later stages and antiviral agents are not always prescribed according to local guidelines
- ◆ Some Eastern European countries have been hampered by an inability to prescribe antiviral medication for immunocompetent patients
- ◆ No US professional societies have issued formal HZ management guidelines (2)

Delays in treatment and the under-prescribing of effective therapy add to the high costs of healthcare for HZ, especially when the disease is severe or occurs in high risk groups like the elderly or immunocompromised who require hospitalisation. A recent study from Spain demonstrated that 78 per cent of hospitalisations for zoster occurred in adults older than 50 years of age (5).

In addition to the direct costs of HZ and PHN (for example, antiviral therapy, pain medication, physician costs, lab tests, hospitalisations and so on) there are negative effects on the quality of life that must be considered, such as the loss of ability to care for oneself, the loss of productivity and with psychological symptoms such as depression or concentration problems (6).

Despite the high incidence of HZ in the older patient population, which is rapidly increasing, and the high prevalence of acute and chronic pain associated with the disease globally, there have been few prospective observational cohort studies (that is patient registries) performed that provide a real-world analysis of the disease's epidemiology in this age group regarding:

- ◆ Natural history and risk factors
- ◆ Medication and procedural effectiveness and safety (such as antiviral drugs, pain medications and nerve blockades)

- ◆ Variations in physician management
- ◆ Cost drivers and cost comparisons
- ◆ Impact on quality of life
- ◆ Patient preferences and satisfaction

A review article examined 31 reports through 2003 that included population-based descriptive data for adults (7). Nineteen of these reports could be analysed for HZ incidence, and all but one study included both old and young people. Within all these populations, there was a steep rise in HZ incidence with age, but there was variation in incidence within each oldest age group examined, highlighting the need for more long-term incidence data in these higher age groups.

CHANGES IN FUTURE HERPES ZOSTER EPIDEMIOLOGY

The US instituted a mass childhood VZV vaccination strategy in 1995, but never required that varicella be a nationally-reported disease and therefore had little baseline epidemiologic data. Consequently, it is difficult to analyse the trends that have occurred in the disease since that time, including the medium- to long-term effects on the incidence of HZ and PHN (8).

It is assumed the risk of HZ in adulthood is reduced by re-exposure to the VZV virus, and thus there is concern that a lower rate of varicella would translate into higher rates of HZ in the older population. In a shingles prevention study in the US, morbidity associated with HZ and Post Herpetic Neuralgia (PHN) in the elderly was greatly reduced with one injection of an experimental, live attenuated varicella-zoster vaccine (Oka/Merck VZV vaccine) (9). This vaccine is expected to be approved by the FDA in 2006, and if adopted by the medical community and the older population should reduce the rates of HZ and PHN in the US.

European countries in general have taken a more targeted approach to varicella vaccination. More countries, though, are implementing or planning to implement mass childhood varicella, and presumably adulthood herpes zoster vaccination strategies (after the zoster vaccine is licensed and approved) into their immunisation programmes over the next decade. Consequently, the global epidemiology and management of HZ and PHN will continue to evolve, albeit without a global strategy for monitoring changes.

CURRENT SURVEILLANCE SYSTEMS FOR HZ AND PHN

Some countries do have their own individual zoster surveillance systems (10):

- ◆ Slovenia currently has primary care surveillance data for herpes zoster
- ◆ Slovakia has case-based mandatory notification of herpes zoster
- ◆ The Netherlands, Ireland and England/Wales have primary care sentinel surveillance data for both varicella and herpes zoster
- ◆ Spain has a hospital surveillance system from which hospitalised cases of HZ and PHN can be extrapolated
- ◆ The US has the Varicella Active Surveillance Project (VASP), funded by the Centers for Disease Control and Prevention (CDC) and implemented by the Philadelphia

Department of Public Health and the Los Angeles County Department of Health Services since 1995. The programme's purpose is to obtain population-based incidence rates for varicella and herpes zoster diseases (HZ was added to the active surveillance in January 2000) in two communities with established high varicella vaccination coverage rates, and evaluate the impact of current and future varicella vaccination practices and policies (8)

- ◆ Germany had plans for a sentinel surveillance scheme to be in place by 2005 for both varicella and herpes zoster

CONCLUSION

Without a well-designed global patient registry to systematically define, collect and analyse uniform data endpoints, we run the risk of being unable to draw valid scientific conclusions about the trends in outcomes, disease management and quality of life impact from diseases and their treatment regimens. Herpes Zoster is a perfect example of a common disease that affects millions of older people around the world, yet little is known about its natural history. As governments embark on varied immunisation strategies globally, we will be sure to see an evolution in the incidence of HZ and its chronic complications. Instead of relying on a patchwork quilt of individual surveillance systems around the world, a global patient registry would fulfil both commercialisation and public health goals in monitoring these changes. ◆

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