Herpes zoster: when do patients present and who gets antiviral treatment?

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ABSTRACT

INTRODUCTION: Herpes zoster and its sequelae can have a serious impact on quality of life, particularly in the elderly. The duration and severity of herpes zoster symptoms can be reduced with antiviral treatment. Early treatment is most effective.

AIM: To identify how soon after onset of herpes zoster symptoms adults presented to a suburban Dunedin general practice and to describe which patients received antiviral treatment.

METHODS: Adult herpes zoster cases were identified from a large suburban general practice from 2004 to 2009. Duration of symptoms at presentation and antiviral prescription were identified from medical records and described by patient characteristics.

RESULTS: We identified 278 incident cases. Approximately one-third presented within three days of symptoms, one-third after three days, and in one-third of cases the duration of symptoms was not documented. A higher percentage of patients with ophthalmic herpes zoster presented within three days (45%), while a lower percentage of men (24%) and patients from the lowest socioeconomic quintile (25%) presented within three days. Most incident cases received antiviral treatment. A higher percentage of patients with ophthalmic herpes zoster and patients who presented within three days of symptoms received antiviral treatment. Some patients who presented after seven days of symptoms also received treatment. Antiviral prescribing did not increase with patient age.

DISCUSSION: Despite many adults with acute herpes zoster presenting after three days of symptoms, most received antiviral treatment. It is not known why many presented late. It is not known whether late treatment is effective.

KEYWORDS: Antiviral treatment; general practice; herpes zoster virus; signs and symptoms

Introduction

Herpes zoster is generally experienced as a painful, vesicular rash with a unilateral dermatomal distribution. The rash is often preceded by prodromal symptoms, including pain in the region of the affected sensory nerve, fever and malaise.

Herpes zoster is caused by reactivation of the varicella zoster virus that has remained dormant in a cranial nerve or dorsal root ganglion since a primary infection (chicken pox). Precise triggers for reactivation are unknown, although herpes zoster is more common with increasing age and with immune-compromise.1 The annual rate of herpes zoster is about 3 to 4 cases per 1000, roughly doubling every decade after the age of 50 years.1,6 Studies suggest the incidence of herpes zoster is increasing.1 Vaccination has been shown to reduce the incidence of both herpes zoster and its complications, and is recommended for patients 60 years or older.7,8

Herpes zoster and its complications can have a serious impact on quality of life, and impose an economic burden on the health service and on society. It is estimated that herpes zoster costs the Australian health system about A$32.8...
The burden of herpes zoster in New Zealand is not known; herpes zoster is not mentioned in the recent Ministry of Health burden of diseases study.\(^9\)

Early antiviral treatment (within three days of onset of symptoms) has been shown to hasten rash healing and decrease the severity and duration of acute pain.\(^{1,11,12}\) Antiviral treatment is generally recommended for those at highest risk of complications from herpes zoster, including the elderly, the immune-compromised, and those with severe symptoms or eye or facial involvement.\(^{1,4,11,13}\) Other patients might also benefit from antiviral treatment, but their risk of complications is lower.

Valacyclovir and famciclovir are the preferred antiviral drugs because of ease of dosing and higher levels of antiviral drug activity.\(^{1,11}\) Acyclovir is less effective for reducing herpes zoster pain and must be taken five times a day, but it is well tolerated, generally safe, and relatively cheap.\(^{14}\) In New Zealand, acyclovir is the only fully funded antiviral for use in general practice—valacyclovir is funded with special authority, and famciclovir is not funded. A recent Cochrane review found that oral acyclovir does not significantly reduce the incidence of post-herpetic neuralgia (PHN), and that there is insufficient evidence to determine whether valacyclovir and famciclovir prevent PHN.\(^{15}\) Despite early antiviral treatment, many patients experience persistent pain and long-term reduction in health-related quality of life.\(^{16}\)

While early treatment is most effective, in clinical practice there are many barriers to early presentation and treatment, including delays in recognising the significance of prodromal symptoms, delays in making an appointment (perhaps because of cost or transport barriers), and delays in getting an appointment (especially if symptoms start on a Friday). There may be further delays in receiving antiviral treatment as prodromal pain may be misdiagnosed.

Patients may benefit when antiviral treatment is started after three days, but the efficacy of later treatment has not been systematically studied and there is no clear guidance on how to manage patients who present later. The controlled clinical trials of antiviral treatment have started treatment within three days of onset of symptoms—an arbitrary inclusion criterion that does not necessarily reflect the cessation of viral replication.\(^{11}\) The National Institute for Health and Care Excellence (NICE) recommends antiviral treatment up to one week after rash onset for those at higher risk of severe herpes zoster or complications;\(^{13}\) other experts recommend initiating treatment after three days if new skin lesions are still appearing, if complications are present, or if there is advanced age or severe pain.\(^{1,4,11}\) The manufacturer’s acyclovir datasheet on the Medsafe (New Zealand Medicines and Medical Devices Safety Authority) website recommends treatment ‘as soon as possible after the onset of infection’ to reduce the ‘acute symptoms and rash, for reduction of zoster-associated pain and for reduction of the incidence and duration of post-herpetic neuralgia’.\(^{17}\)

There is no New Zealand research showing how soon after onset of symptoms patients with acute herpes zoster present in general practice, or which patients receive antiviral therapy. The aim of this study was to identify how soon after on-
set of herpes zoster symptoms adults presented to their general practitioner in a suburban Dunedin general practice, and to describe which patients received antiviral treatment.

**Methods**

**Data source**

The study utilised the electronic medical records of a large suburban Dunedin general practice. The general practice uses the Medtech32 electronic practice management system (PMS). It is the policy of the general practice to code all diagnoses.

The general practice had 15 500 registered patients on average over the study years; 8% of the practice population were Maori or Pacific, the remainder mostly European: 48% were male and 52% female. Eight percent of the practice population were over 65 years, compared to 14% for the Otago District Health Board (DHB) region and 12% for New Zealand as a whole in the 2006 census. The breakdown of the practice population by the NZDep2006 index (an index of socioeconomic deprivation for each meshblock based on the 2006 census, where quintile 5 denotes the most socioeconomic deprivation and quintile 1 the least) is as follows: quintile 1 (18%), quintile 2 (23%), quintile 3 (23%), quintile 4 (20%), and quintile 5 (16%).

**Incident zoster cases**

LH liaised with the practice nurse who identified all patients with a new diagnostic Read code of herpes zoster or shingles between 1 January 2004 and 31 December 2009. We included data for all patients aged 18 years or older residing in their own home (i.e. those not in residential care), with a presenting complaint consistent with acute herpes zoster (i.e. we excluded those who presented with complications of herpes zoster, such as post-herpetic neuralgia or who were incorrectly coded). We excluded the records of patients living in residential care because we wanted to focus on herpes zoster in the community, and because the daily records of patients living in residential care settings were paper-based rather than electronic.

We obtained a printout of de-identified medical records for all incident cases. KR searched the daily record for days of symptoms at presentation (less than three days, between three and seven days, and more than seven days), affected dermatome (ophthalmic, other cervical, thoracic, lumbosacral), and antiviral prescription (yes or no), and entered these data onto an Excel spreadsheet, along with patient age at presentation, gender, socioeconomic quintile, pre-existing conditions and medications. ‘Days of symptoms at presentation’ was taken as that recorded in the daily record by the treating doctor. If, for example, the daily record stated ‘painful rash three days R upper thoracic region’, the case was coded as presenting between three and seven days, and the affected dermatome as thoracic.

**Data analysis**

We described duration of symptoms at presentation by patient characteristics, including age, sex, socioeconomic quintile and affected dermatome. We described antiviral prescription by patient characteristics and by duration of symptoms at presentation. No statistical analyses were conducted as the study was insufficiently powered.

None of the authors work or are patients at the general practice that provided the study data. Ethical approval for this study was provided by the Lower South Regional Ethics Committee, (Ref. LRS/10/EXP/020).

**Results**

**Adults with acute herpes zoster**

We identified 353 patients with a new diagnosis of herpes zoster during the six study years (2004–2009). After excluding cases that did not fit the inclusion criteria, there were 278 adult acute herpes zoster cases remaining. Most exclusions were for age under 18 years, while a few were for a diagnosis other than acute herpes zoster. Incident cases were aged up to 98 years, but most were younger than 65 years (75%). There were more women than men in our sample (58%).

**Duration of symptoms at presentation**

Table 1 summarises duration of symptoms at presentation by patient characteristics. One-third
of incident cases presented within three days of symptoms (92; 33%). A higher percentage of women (40%) than men (24%) presented within three days of symptoms. A higher percentage of patients with ophthalmic herpes zoster presented within three days (45%) than those with other dermatomal involvement, with the lowest percentage of early presentations for thoracic herpes zoster (28%). A lower percentage of patients from quintile 5 (most deprived) presented within three days of symptoms (25%) compared to other quintile groups. Age did not influence duration of symptoms at presentation.

**Antiviral treatment**

Table 2 summarises antiviral treatment by patient characteristics. Most of the 278 incident cases received antiviral treatment (82%). Acyclovir was the only antiviral prescribed. A higher percentage of patients with ophthalmic herpes zoster received antiviral treatment (97%) than those with other dermatomal involvement, with patients with thoracic herpes zoster least likely to receive antiviral treatment (75% of patients treated with antivirals). A higher percentage of patients presenting within three days of symptoms received antiviral treatment (96%), but almost one-third of patients who presented after seven days of symptoms also received antiviral treatment (32%). Antiviral prescribing did not increase with age.

**Discussion**

This study presents a single general practice audit assessing how soon after onset of symptoms adults with acute herpes zoster present to their general practitioner, and describing antiviral prescribing patterns. Previous research findings suggest 50–75% of patients present within three days of herpes zoster symptoms. In our study, approximately one-third of incident cases presented within three days of symptoms, one-third presented after three days, and in one-third, the duration of symptoms was not documented.
lower percentage of men (24%) than women (40%) presented within three days. It is not known why many patients in our study presented after three days. A lower percentage of patients from quintile 5 (25%) presented within three days, hinting that cost may be a factor. While a higher percentage of patients with ophthalmic zoster presented within three days (45%), it is concerning, given the potentially serious nature of ophthalmic herpes zoster, that nearly one-quarter of patients with ophthalmic herpes zoster presented after three days of symptoms, although numbers were small (8; 32%).

Despite many patients presenting after three days of symptoms, most patients in our study received antiviral treatment (82%). Previous research has found between 22% and 85% of adults receive antiviral treatment, with prescribing increasing with age. Antiviral prescribing did not increase with age in our study. We found that a higher percentage of patients with ophthalmic herpes zoster (97%) received antiviral treatment, as did those who presented within three days of symptoms (96%). We also found that approximately one-third of patients who presented after seven days of symptoms received antiviral treatment, which is surprising since it is not known whether treatment at this late stage is effective; it should be noted, however, that numbers were small (8; 32%).

Table 2. Proportion of adults with herpes zoster receiving antiviral treatment by patient characteristics and duration of symptoms at presentation

<table>
<thead>
<tr>
<th>Patient characteristic</th>
<th>Received antiviral treatment n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>117</td>
</tr>
<tr>
<td>Female</td>
<td>161</td>
</tr>
<tr>
<td>Age group (years)</td>
<td></td>
</tr>
<tr>
<td>18–49</td>
<td>126</td>
</tr>
<tr>
<td>50–64</td>
<td>82</td>
</tr>
<tr>
<td>65+</td>
<td>70</td>
</tr>
<tr>
<td>Dermatome</td>
<td></td>
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<tr>
<td>Ophthalmic</td>
<td>31</td>
</tr>
<tr>
<td>Cervical—other</td>
<td>78</td>
</tr>
<tr>
<td>Thoracic</td>
<td>122</td>
</tr>
<tr>
<td>Lumbosacral</td>
<td>38</td>
</tr>
<tr>
<td>Not stated</td>
<td>9</td>
</tr>
<tr>
<td>Socioeconomic deprivation quintile</td>
<td></td>
</tr>
<tr>
<td>Quintile 1</td>
<td>64</td>
</tr>
<tr>
<td>Quintile 2</td>
<td>55</td>
</tr>
<tr>
<td>Quintile 3</td>
<td>69</td>
</tr>
<tr>
<td>Quintile 4</td>
<td>46</td>
</tr>
<tr>
<td>Quintile 5</td>
<td>44</td>
</tr>
<tr>
<td>Duration of symptoms at presentation (days)</td>
<td></td>
</tr>
<tr>
<td>Less than 3</td>
<td>92</td>
</tr>
<tr>
<td>3–7</td>
<td>72</td>
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<tr>
<td>More than 7</td>
<td>25</td>
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<tr>
<td>Not stated</td>
<td>89</td>
</tr>
<tr>
<td>Total</td>
<td>278</td>
</tr>
</tbody>
</table>

Despite these limitations, the study provides new information about how soon after onset of symptoms patients with acute herpes zoster presented to their general practitioner in a suburban New Zealand general practice, and which patients received antiviral treatment. The study found that most adults with acute herpes zoster received antiviral treatment, despite many presenting after three days of symptoms. Further work is needed to confirm our findings, and to determine whether the high antiviral prescribing rate is indicative of prescribing in the wider New Zealand general practice context. Further work is also needed to understand the reasons for late presentation, and to learn how best to manage herpes zoster presenting after three days of symptoms. Since acyclovir is now known not to prevent PHN, the acyclovir datasheet should be updated to remove this indication.

The strengths of this study are that it is based in a large, fully computerised general practice that codes diagnoses; the dataset provided useful electronic data, including detailed daily records; and the analyses answered the two research questions. However, the study suffers from a number of limitations. The dataset was small, the clinical records incomplete (one-third lacked information about the duration of herpes zoster symptoms), and we may have missed incident herpes zoster cases that were not classified, all potentially introducing bias. Doctors may be more likely to classify herpes zoster cases when prescribing antiviral therapy because of the way the practice management system is set up, possibly explaining our high antiviral prescribing rate. We excluded patients in residential care, potentially explaining why the elderly were under-represented in our study (75% of incident cases were younger than 65 years).
References

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COMPETING INTERESTS
None declared.