

Follow-up of a clinical pathway for varicella-zoster virus infection

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CONFLICT OF INTEREST:

None

Background: Evaluation, follow-up and healthcare professional acceptance are critical issues in the implementation of a clinical pathway (CP).

Aims: To evaluate the performance of a varicella-zoster virus (VZV) pathway in different Emergency Departments (ED).

Design: Observational prospective multicenter study in 49 EDs (local, reference and intermediate EDs). The subjects of the study were patients older than 14 years with a clinical diagnosis of varicella or herpes who were assisted at all EDs during the whole study period (Feb-Jul 2007). Data on demographic, clinical characteristics and application of CP were recorded. Acceptance of CP was assessed by survey.

Results: The study included 929 herpes and 427 varicella patients. Our VZV cases had a higher admission and complication rates than the cases reported on previous publications, which reflects higher severity. CP recommendations were applied in 75% of varicella and 85,3% of herpes cases. Reference and local EDs had higher rates of CP application (95%, 87.7%) than intermediate EDs (72.9%) ($P < 0.01$). Ninety five percent of responders evaluated information and treatment on CP as "useful or very useful". The most appreciated feature of CP was information.

Conclusions: The level of acceptance of VZV CP is high. The severity of certain cases requires to adjust the recommendations. [Emergencias 2008;20:87-92]

Key words: Clinical Pathway. Varicella-Zoster Virus. Emergency.

Introduction

Infections caused by the varicella zoster virus (VZV), though normally benign, can occasionally cause severe conditions such as varicella-induced pneumonia or herpes encephalitis¹. The effective treatments currently available require early identification of the disease in order to achieve optimum results. Patients are identified and treated at hospital emergency departments (HED), as well as primary care centres. This must be taken into account when analysing the true incidence of the infection and at the start of treatment.

The variability in patient handling translates into differences in clinical results. Reduction of variability via the application of clinical pathways helps to improve service quality supported by quality clinical data^{2,3}. The application of clinical pathways is often difficult and very few pathways

are easily implemented. Follow-up of use is part of the development and implementation methodology of clinical pathways, in order to enable identification of modifications and improvement of the monitoring process⁴⁻⁷. This study aims to quantify the extent of clinical pathway follow-up of infections caused by VZV and the degree of acceptance of the pathway by HED professionals, in addition to identifying the potential differences between the various types of HEDs. Lastly, patient characteristics and VZV infection patterns were also recorded.

Design

An observational, prospective, multicentre study was designed to achieve the study objectives. No patient interventions other than those

already established in each centre were carried out.

The scope of the study included HEDs and the populations of patients over the age of 14 diagnosed with a VZV infection. The participating centres and the extent of each in terms of coverage are shown in Table 1. Three different HED levels were established according to the population covered by each: district hospitals, attending over 60,000 inhabitants; intermediate hospitals, attending more than 120,000 inhabitants; and reference hospitals, attending greater than 300,000 inhabitants. This selection of 49 participating centres (25 district, 13 intermediate and 11 reference centres) covered an estimated total population of 5 million, equal to 11% of the total Spanish populations (Table 1).

All patients over the age of 14 diagnosed with VZV infection and eligible for application of the clinical pathway were considered in the study, which was undertaken from February to July 2007.

Variables of interest were taken from clinical pathway guidelines⁸, specifically in terms of recommendations of location, information, treatment and tests proposed by the pathways. Treatment guidelines are included in Appendix 1. The demographic characteristics (gender and age), time distribution, presentation and risk factors (diabetes, immunosuppression and recent surgery) were also recorded.

In order to add data on the perceived usefulness of the clinical pathway, a questionnaire with the following closed questions was provided to each of the participating centres: "Do you consider the clinical pathway to be useful in improving the treatment of varicella zoster? (possible answers: very useful, useful, not very useful, not useful); "What do you think of the clinical data collected in the clinical pathway?" (possible answers: very adequate, adequate, not very adequate, inadequate); "To what extent do you believe the clinical pathway has helped you carry out your normal work?" (possible answers: it has helped me a lot, it has helped me, it has not helped much, it has not been of any help); "What aspects of the pathway have you found most useful?" (possible answers: the clinical information, the treatment information, information on complications, all the above, none of the above); and finally, "Can the clinical pathway be used as a teaching tool?" (possible answers: very suitable, suitable, not very suitable, unsuitable).

The calculation of the sample size in order to define the extent of pathway follow-up assuming

Table 1. Participating centres

Participating Centres	Herpes cases included	Varicella cases included
District hospital		
H. Calahorra	7	3
H. Campo Arañuelo	24	4
H. Can Misses	12	22
H. Cieza	11	21
H. Costa del Sol	12	3
H. de Antequera	3	5
H. de Barbanza	11	5
H. de Ceuta	2	1
H. de Guadix	5	7
H. de Igualada	8	8
H. de Laredo	3	5
H. de Poniente	7	5
H. de Vendrell	19	14
H. de Zumárraga	19	12
H. del Bierzo	19	–
H. García Orcoyen	8	5
H. Los Arcos	25	18
H. Mateu Orfila	12	1
H. Medina del Campo	21	5
H. Rafael Méndez	10	1
H. Royo Villanova	8	6
H. San Eloy	15	6
H. Santa Tecla	14	12
H. Valdeorras	7	1
H. Virgen del Castillo Yecla	12	2
Intermediate Hospitals		
Complejo H. Univ. Albacete	76	15
H. Carmen y Severo Ochoa	15	7
H. General Ciudad Real	8	13
H. General Lanzarote	11	–
H. La Moraleja	25	8
H. Mancha Centro	1	6
H. Morales Meseguer	55	22
H. Móstoles	13	18
H. Ntra. Sra. del Prado	17	7
H. Santiago Apóstol	20	10
H. Virgen de la Concha	25	6
H. Virgen de la Luz	18	11
H. Virgen de la Salud	23	6
Reference Hospitals		
H. 12 de Octubre	11	5
H. Clinic	11	10
H. Clínico San Carlos	24	7
H. Clínico Valencia	95	–
H. de Cruces	60	39
H. del Bellvitge	10	4
H. General Alicante	2	10
H. Gregorio Marañón	18	2
H. La Paz	20	15
H. Universitario de Salamanca	60	31
H. Xeral Cies	15	3

H: Hospital.

global follow-up of 60% with 5% precision and beta error rate of 10% resulted in a total of 800 patients in each of the infections caused by VZV. Data analysis was performed using the SPSS 11.0 programme. Results are shown as absolute and relative proportions for discrete variables and as measures of central tendency and dispersion for continuous variables. Student t test was used for proportion comparison. Differences were considered significant when p was lower than 0.05.

Results

The number of cases recorded during the study period was 1,354 of VZV infection of which 427 were varicella cases and 929 were herpes zoster cases. District, intermediate and reference centres respectively contributed 172, 129 and 126 varicella cases and 311, 292 and 326 herpes cases. The mean age of the varicella patients was 32.4 + 12.6 versus 58 + 19 for herpes patients with 51% of varicella cases being male versus the herpes cases in which a moderate predominance of women (54%) was observed. Thirteen percent of the patients diagnosed with herpes had previously presented at HED, and 15% repeated the consultation.

The distribution of the herpes location is shown in Table 2. Among the possible factors triggering the herpes episode were; immunosuppression in 83 patients (8.9%), diabetes in 156 patients (16.8%) and recent surgery in 26 patients (2.8%). Thirty-seven percent of the HZ cases included none of the risk factors considered (including age above 60). Varicella presentation forms are shown in Table 3. The time distribution of varicella cases over the study period yielded 31 cases in February (7%), 81 in March (19%), 122 in April (29%), 82 in May (19%), 74 in June (17%) and 29 in July (7%) ($p < 0.001$), whereas the distribution of herpes cases remained uniform throughout the study period.

The overall follow-up of the clinical pathway for herpes patients was of 75.8% (80% in district hospitals, 55% in intermediate hospitals and 90% in reference hospitals) ($p < 0.001$). No differences were found in the follow-up of herpes cases in patients with or without risk factors. With regard to varicella patients, the overall follow-up of the clinical pathway was of 85.3% (87.7% in district, 72.9% in intermediate and 95% in reference hospitals) ($p < 0.001$). The comparison between the different levels of clinical pathway follow-up for herpes and varicella in each of the areas of interest is shown in Table 4. A significantly higher degree of follow-up of treatment guidelines was observed only in patients diagnosed with varicella ($p < 0.001$).

The questionnaire regarding the perceived usefulness of the clinical pathway was answered by 29 of the 49 participating centres (59%). For the questions as to the usefulness of the pathway in treatment management, 95% considered it to be adequate or very adequate. In terms of how helpful the pathway was, 70% believed it had been of great help. Clinical information and treatment we-

Table 2. Locations of herpes zoster lesions

Herpes location	N (%)
Chest-abdomen	483 (52.0)
Ophthalmologic	217 (23.4)
Facial	170 (18.33)
Encephalitis	3 (0.3)
Other*	94 (10)

*Other locations include: upper and lower limbs, ears, genitals, Ramsay-Hunt syndrome and others unidentified (81 cases). Percentage is above 100% due to co-existence with other locations.

Table 3. Forms of varicella presentation

Varicella presentation	N (%)
Cutaneous (exclusively)	404 (96.7)
Pulmonary	25 (6.4)
Encephalic	3 (0.8)
Other	6 (1.6)

Percentage is above 100% due to co-existence with other locations.

re the pathway aspects deemed to be most useful (in 65% of centres). The pathway was also acknowledged to be a suitable or very suitable teaching tool in 95% of the questionnaires.

Discussion

The general characteristics of the series used to evaluate varicella clinical pathway follow-up in terms of age and period of presentation were similar to others in the literature⁹⁻¹¹, as was the case in the herpes series¹⁰⁻¹³.

Incidence rates cannot be derived from this study due to differential recording problems between the various centres, with the values obtained having been clearly underestimated and representative of a higher severity subpopulation due to the study scope having been the emergency services. In the case of herpes, it fails to reach the rate of 15% estimated in other publications for the populations covered during the six study months. From a theoretical population of 5 million inhabitants covered, 7500 cases would be expected over a period of 6 months (3 per 1000 years), whereas we have only recorded 929 (14.8%), which was expected in light of deficiencies in the recording process and selection of a higher severity subpopulation. In the case of varicella, the benignity and seasonality of this condition render the HED not ideal for estimating incidence rates. Varicella cases showed a typical distribution in the springtime, with an age pattern matching characteristics of VZV infections, whereas the herpes distribution did not show this seasonal quality¹⁴.

Table 4. Clinical pathway follow-up

	Varicella N(%)	Herpes N(%)	<i>p</i>
Location	159 (41)	335 (39)	0.72
Treatment	290 (73.4)	713 (76.7)	< 0.001
Tests	205 (52.4)	425 (51.8)	0.47
Information	354 (88.9)	730 (78.6)	0.08

Amounts represent number & percentage of cases in which clinical pathway guidelines have been applied.

The number of hospital admissions due to VZV infection in our study show that the annual rates for herpes are double those for varicella¹⁵. The ratio found in our study (2%/7%) shows higher values for varicella due to the characteristics of the cases over the age of 14. The admission rate for varicella patients was 7%, which is higher than that referred in other studies¹¹ and may be explained by the higher rate of patients developing pneumonia due to varicella (6%). Varicella-induced pneumonia is the most frequent complication in patients admitted with varicella¹⁶, and in our series showed a higher percentage than that reported in the literature. Nevertheless these rates are similar to those included in studies performed in HEDs¹⁷ suggesting the greater severity of the patients attended in these areas¹⁸.

The distribution of the herpes location among the recorded patients showed a higher number of ophthalmic and cranio-facial herpes as opposed to chest herpes in comparison with other publications^{19,20}, which may again be due to the greater severity of the herpes patients attended in HEDs, a characteristic previously identified in other publications²¹. This distribution of higher severity cases could be due to the characteristics of the centres to which such patients are referred, equipped with specialist areas such as ophthalmology. The number of patients with a herpes diagnosis presenting a known risk factor was high (63%). However, these data cannot be compared with those of other studies because of the lack of sufficient data, only using the risk factors as trigger agents for the development of post-herpetic neuralgia²²⁻²⁴.

The follow-up of the different pathway sections showed a high degree of application of the treatment and information guidelines which was lower in the location and tests section. Researchers may encounter difficulties in evaluating guideline follow-up in terms of patient location given that the guidelines are lax and allow the patient to be placed in any medical department that can meet different patient care requirements. The answers refer more to suitability than to the actual physical location where medical care has been given. In

the case of varicella, a location problem might ensue when attempting to follow the rules regarding respiratory isolation.

In the section of performance and monitoring of pathway recommended tests, the centres showed a low level of guideline follow-up. Pathways are restrictive in terms of use of complementary tests and the normal practice possible involves performance of a greater number of tests. Special consideration must be given to the performance of chest radiography in the cases of adult varicella, which the pathway recommends only in the event of a history of respiratory conditions. Given the percentage of cases of varicella-induced pneumonia (6%) and the possibility of this number being even higher in light of few clinical symptoms, the appropriateness of broadening this recommendation should be considered.

A higher degree of guideline follow-up was not observed for risk factor patients in herpes cases, whereas district and reference hospitals followed up recommendations more than intermediate hospitals. This data matches that of other studies in the case of district hospitals which normally show better follow-up rates, but not in the case of reference hospitals, which normally show lower rates of compliance.

Evaluation of the usefulness of the clinical pathways was high according to the questionnaires sent to the professionals, although the rate of response (29/49 centres) must be taken into account, with evident bias towards positive pathway appraisal. Within emergency departments, the role of the pathways as a teaching tool proves to be of great interest, in light of the extent of turnover of professionals in such departments and the difficulties faced in terms of information transfer and handover, which make it a very positive evaluation.

Centre selection bias and case selection bias are limitations of this study. The latter is evident in the variability shown in the number of cases recorded in each of the centres of a similar coverage, which points to a selection of patients on which clinical pathway has been applied, and not including the total number thereof. The non-use of period or progression of the condition when evaluating guideline follow-up is also a major limitation. Lastly, the lack of evaluation of the clinical results or patient perception has been excluded from this study.

In summary, we can conclude that the series shown in this study exhibits a higher rate of severity than that of the general population with VZV

infection. Clinical pathway follow-up in some areas was low which points to possible reconsideration of some guidelines.

Lastly, the questionnaire evaluating usefulness by professionals showed a positive appreciation in all aspects.

Appendix 1. Antiviral treatment in VZV infections as shown in the clinical pathway

Antiviral treatment for varicella

Medication dosage and treatment duration

Oral Aciclovir 800 mg 5 times per day for 7 days
 IV Aciclovir 5-7.5 mg/kg 3 times per day for 7 days
 IV Aciclovir¹ 8-10 mg/kg 3 times a day for 7-10 days
 Oral Famciclovir² 250 mg 3 times a day for 7 days or 750 mg once a day for 7 days
 Oral Brivudine oral² 125 mg Once a day for 7 days
 Oral Valaciclovir oral² 1.000 mg 3 times a day for 7 days

Antiviral treatment for zoster

Medication dosage and treatment duration

Oral Aciclovir oral 800 mg 5 times a day for 7 days
 IV Aciclovir 5-7.5 mg/kg 3 times a day for 7 days
 IV Aciclovir 8-10 mg/kg 3 times a day for 7-10 days
 Oral Brivudine³ 125 mg Once a day for 7 days
 Oral Famciclovir 250 mg 3 times a day for 7 days or 750 mg once a day for 7 days
 Oral Valaciclovir 1.000 mg 3 times a day for 7 days

¹In immunosuppressed patients.

²Used in practice. No guideline approval in respective technical data profiles.

³Does not require dose adjustment in the event of renal failure. Brivudine must not be administered together with 5-fluorouracil 5, including its topical versions or pro-medications, as well as other fluoropyrimidines 5.

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Seguimiento de las vías clínicas en la infección por el virus varicela zóster

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Objetivos: La implantación de una vía clínica precisa de la evaluación de su seguimiento y del nivel de aceptación por los profesionales. Tras la implantación de la vía clínica para las infecciones por el virus varicela-zóster (VVZ) se investiga el grado de aplicación y aceptación.

Método: Se realiza un estudio observacional, multicéntrico con la participación de 49 servicios de urgencias hospitalarios (SUH) de referencia, intermedios y comarcales. Se incluyen como casos los pacientes mayores de 14 años con el diagnóstico clínico de varicela y herpes, atendidos durante el periodo de estudio de febrero a julio 2007. Se registran las características de los pacientes y el grado de seguimiento de la vía, el grado de aceptación por los profesionales se evalúa mediante encuesta.

Resultados: Se registraron 929 casos de herpes y 427 de varicela. En la presente serie se registró, tanto en los casos de varicela como en los de herpes, un mayor porcentaje de ingresos y complicaciones que en las publicaciones existentes. El grado general de seguimiento de la vía del herpes fue del 75% y de la varicela el 85%. Únicamente en el apartado de tratamiento fue superior el seguimiento del herpes (82%) con respecto a la varicela (73,4%) ($p < 0,001$). El 95% de las encuestas valoraron como útil o muy útil el contenido y el tratamiento. El aspecto mejor valorado de la vía fue la información. Se detectaron mayores grados de seguimiento tanto para el herpes como la varicela en los SUH comarcales (87,7%) y de referencia (95%) con respecto a los intermedios (72,9%) con $p < 0,001$.

Conclusiones: La vía clínica para infecciones VVZ en general presenta un buen seguimiento y aceptación. El perfil de los pacientes atendidos en urgencias tiene una mayor gravedad, por lo que habría que adaptar las recomendaciones. [Emergencias 2008;20:87-92]

Palabras clave: Vía clínica. Varicela. Zóster. Urgencias.