

Cost-effectiveness of sputum culture for patients infected with HIV and community-acquired pneumonia in the emergency department

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Objectives: To assess the diagnostic cost-effectiveness of sputum culture (SC) for microbiological diagnosis of community-acquired pneumonia (CAP) in HIV-infected patients in the Emergency Department.

Patients and methods: Two-year and six month prospective study conducted in a third level referral Academic Hospital. All the HIV-diagnosed patients with CAP were included in the study. A sample of sputum was collected from every patient. If the sputum sample was of good quality according to Murray's criteria, the culture was done. The study variables were: gender, number of CD4 lymphocytes, viral load, C-reactive protein (RCP), number of leukocytes, APACHE scale values in admission and highly active antiretroviral treatment (HAART). Statistical analysis was performed with the SPSS statistical package (SPSS, version 14.0).

Results: A total of 120 consecutive HIV-patients with CAP were enrolled and in 91 of them sputum culture was done. Organisms were present in 25 samples. The species isolated were: *S. pneumoniae* in 20 cases, *H. influenzae* in 4, and *S. aureus* in one case. There was no significant associations between the study variables and SC positivity.

Conclusion: The cost-effectiveness of SC for etiological diagnosis of CAP in HIV-patients is similar to the reported in previous literature. The positivity of SC is independent from the analyzed variables. SC is a useful test in HIV-patients with CAP. Among patients with positive test results the prevalence of *S. pneumoniae* is higher. [Emergencias 2008;20:256-259]

Key words: Sputum. Community-acquired. Infectious. Pneumonia. HIV. Emergency Medical Services.

Introduction

Respiratory infection is one of the most frequent problems in patients with infection by the human immunodeficiency virus (HIV). Following the introduction of highly active retroviral treatment (HAART), the incidence of pneumonia by *Pneumocystis jiroveci* (PJP) has considerably declined in par with an increase in bacterial aetiology mainly by *Streptococcus pneumoniae* which is currently the first cause of community-acquired pneumonia (CAP)¹. In a study carried out by our group, *S. pneumoniae* was the first aetiological cause of pneumonia (47% of all the episodes) representing an incidence of 12 episodes per 100 ad-

missions^{2,3}. Thus, early aetiological diagnosis in HIV-infected patients may lead to a better choice of empiric antibiotic therapy with a consequent reduction in morbimortality of these patients.

To achieve this objective, several diagnostic tests are available and, although some require hospital admission, others may be performed in the Emergency Department (ED). Among the latter tests, sputum culture (SC) may be used, although its utility in the general population for the aetiological diagnosis of CAP is controversial⁴. Similarly, neither is the cost-effectiveness of SC in the immunosuppressed population (particularly in HIV-infected patients) conclusive. This may explain the scarce literature available, with reports only

referring to immunosuppressed patients of any aetiology¹ or with pulmonary tuberculosis⁵. Thus, the aim of the present study was to determine the diagnostic cost-effectiveness of SC collected in the ED for the microbiological diagnosis of CAP in HIV-infected patients and evaluate the relationship between SC results and the immune status of the patient.

Methods

A two and a half-year prospective study (June 2005 to December 2007) was undertaken. All patients with HIV infection who attended the ED of a third level 850-bed university hospital and were diagnosed with CAP were consecutively included in the study. CAP was defined based on the criteria of the Infectious Diseases Society of America (IDSA)⁶. Exclusion criteria were: patients with high suspicion of PJP and/or tuberculous infection based on clinical manifestations, radiology and/or Ziehl of sputum or those who had previously received antibiotics. Sputum was collected following the usual method used in the ED with no strict protocol. If the sputum obtained was of good quality according to the Murray criteria, the culture was performed. Positivity or negativity of the SC was considered as a dependent variable. The independent variables analysed were: sex, age, number of CD4 lymphocytes (last count prior to admission), viral load (VL; last count prior to admission), C-reactive protein (CRP), the number of leucocytes (LEUC), APACHE II score at admission and HAART treatment.

Categorical variables were expressed as frequencies and percentages and were compared with the Chi-square or the Fisher exact test when necessary. Continuous variables were expressed as means and were compared with the non parametric Mann-Whitney U test. A bilateral $p < 0.05$ was considered significant. All the statistical analyses were performed with the SPSS version 14.0 (Chicago IL, USA).

Results

A total of 120 episodes of CAP fulfilling the IDSA criteria were diagnosed in HIV-infected patients using SC in 91 cases. Sputum culture was not obtained in the remaining 29 patients either because the patient did not expectorate (25 cases) or because immediate mechanical ventilation was re-

quired (4 cases). During the same period, 40 PJP and 25 tubercloses were diagnosed in HIV patients.

Of the 91 SC obtained, 53 (58.3%) corresponded to males and 38 (41.7%) to females. The mean age was 41 years. The empiric antibiotic most frequently used was the combination of cephalosporin-macrolide in 39 cases (43%) followed by quinolones in 17 (19%), cephalosporins in 13 (15%), cephalosporins-levofloxacin in 12 (13%) and other antibiotics in 19 (15%). Sputum was considered to be of good quality in 68 patients (74%). In total 25 out of the 91 SC were positive (27%) (Figure 1). The bacteria most frequently isolated were *S. pneumoniae* in 20 cases, followed by *Haemophilus influenzae* and *Staphylococcus aureus* with 4 and 1 isolations, respectively. Of the 25 cases in whom microbiological isolation was achieved, in 24 cases (96%) the empiric antibiotic administered in the ED was adequate as shown by the posterior antibiogram obtained.

Analysis of the different independent variables did not detect any significant association in relation to having a positive SC (Table 1).

Discussion

The clinical presentation of CAP in HIV patients is similar to that of the general population⁷. The present study evaluated the cost-effectiveness of SC carried out in the ED. Most ED are overcrowded^{8,9} and can only perform the collection of samples which do not require invasive techniques. Among these, the most common is SC. However, the use of SC in the aetiological diagnosis of CAP is controversial for many authors due to the difficulty in collecting samples of good quality¹⁰. This is often not possible due to difficulties in expectoration on behalf of the patient. However, comparative studies carried out with respiratory samples collected using invasive techniques and good quality SC demonstrated similar results^{4,11}, thereby favouring the reliability of SC. In the present study, the SC in HIV patients with CAP was diagnostic in 27% of the cases, being a percentage close to the 34% described by other authors⁴. Urgent Gram staining of sputum is not routinely performed in our centre because of a yield of only 14% which is clearly inferior to the SC¹². This yield in HIV patients is similar to that achieved in the general population in which positive SC are of around 39% based on the quality of the sputum collected¹³. It has been observed that the result of the SC is independent of the number of CD4 lymphocytes

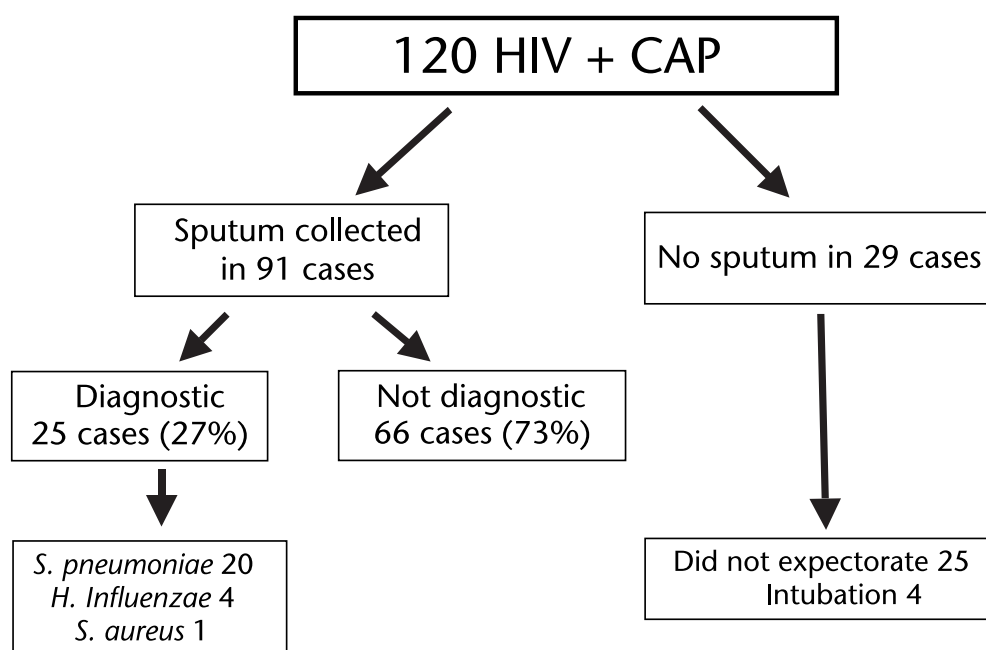


Figure 1. Distribution of the patients included in the study. CAP: community-acquired pneumonia.

presented by the patient, the logarithm of viral load or treatment with or without HAART. This lack of association between the immune status of a patient with the result of the diagnostic test is similar to the results obtained on isolation of respiratory virus in HIV patients with CAP with nasopharyngeal swab and posterior processing with a real time PCR technique¹⁴. Nonetheless, from the cost-effectiveness point of view, our results support the need to request SC in all HIV patients with CAP.

Another aspect evaluated in this study was the utility of SC when determining the most appropriate antibiotic treatment to be implemented. Thus, of the 25 positive SC, 4% required a change in antibiotic because of insufficient coverage. This scarce utility at the therapeutic level is similar to that of blood cultures in CAP in general with the difference that the latter have a much lower yield than sputum (7%) and its use

in the ED in patients with CAP is currently under debate¹⁵. The yield of blood cultures in CAP may be greater in the HIV population with CAP in which the pneumococcal aetiology (which is also known to have 50% of bacteraemia)¹⁶ predominates. Therefore, the current empiric antibiotic strategy of the ED which is based on the use of cephalosporins-macrolides or quinolones may be considered valid and does not seem to require modification in view of the results presented herein.

In summary, it can be concluded that sputum collection should be carried out in the ED because of its epidemiological relevance showing cost-effectiveness in the CAP in HIV similar to that of the general population. However, the repercussion which SC has for treatment of a particular patient in the ED is scarce, despite occasionally allowing modification of the empiric treatment administered.

Table 1. Univariate analysis of the influence of the different variables on the result of sputum culture

	CAP positive N = 25	CAP negative N = 66	P
Male sex (%)	16 (64%)	37 (56%)	0.92
Mean CD4 (cells/mm ³)	266 ± 201	331 ± 313	0.34
Viral load (log RNA copies/mm ³)	3.8 ± 1.5	3.5 ± 1.4	0.38
Use of HAART	11 (44%)	31 (47%)	0.50
CRP (mg/dL)	17.3 ± 14	16.7 ± 11.8	0.83
Leucocytes (cells/mm ³)	8.9 ± 6.2	9.9 ± 5.9	0.55
APACHE II	11.8 ± 4.1	12 ± 5.0	0.84

SC: sputum culture; HAART: highly active retroviral therapy; CRP: C-reactive protein.

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Rentabilidad del cultivo de esputo en la consulta de urgencias de los pacientes infectados por el VIH y neumonía comunitaria

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Objetivo: Determinar la rentabilidad diagnóstica del cultivo de esputo (CU), recogido en el servicio de urgencias (SU) en el diagnóstico microbiológico de la neumonía adquirida en la comunidad (NAC) en el paciente VIH.

Pacientes y método: Estudio prospectivo de 2 años y medio de duración realizado en un hospital universitario de tercer nivel. Se incluyeron todos los pacientes VIH diagnosticados de NAC en los que se procedió a la recogida de esputo. Si éste era de buena calidad, según los criterios de Murray, se procedía al cultivo del mismo. Se analizaron las siguientes variables: sexo, número de linfocitos CD4, carga viral, proteína C reactiva (PCR), número de leucocitos, valor de la escala de APACHE II al ingreso y tratamiento antirretroviral de gran actividad (TARGA). Todos los cálculos estadísticos se calcularon con el paquete SPSS versión 14.0.

Resultados: Se incluyeron un total de 120 episodios consecutivos de NAC de los cuales se cursó CU en 91 casos. Se obtuvo aislamiento microbiológico en 25 (27%) casos: 20 *S. pneumoniae*, 4 *H. influenzae*, 1 *S. aureus*. En cuanto a las variables analizadas no se objetivó ninguna asociación significativa entre su valor y la positividad del CU.

Conclusión: El rendimiento en el diagnóstico etiológico de la NAC en el paciente VIH mediante el CU es similar al descrito en la literatura. La positividad del CU es independiente de las variables analizadas. El CU es una prueba útil que, cuando es positivo en los pacientes VIH con NAC, el germen predominante es *S. pneumoniae*. [*Emergencias* 2008;20:256-259]

Palabras clave: Cultivo de esputo. Neumonía adquirida en la comunidad. VIH. Urgencias.