Original Article

Sputum examination in the clinical management of community-acquired pneumonia*

Exame do escarro no manejo clínico dos pacientes
com pneumonia adquirida na comunidade

Leonardo Gilberto Haas Signori[1], Maurício Weyh Ferreira[1], Luiz Carlos Hack Radünz Vieira[1],
Karen Reetz Müller[1], Waldo Luís Leite Dias de Mattos[2]

Abstract

Objective: To evaluate the frequency of the use of sputum examination in the clinical management of community-acquired pneumonia (CAP) in a general hospital and to determine whether its use has an impact on mortality. **Methods:** The medical records of CAP patients treated as inpatients between May and November of 2004 at the Nossa Senhora da Conceição Hospital, located in Porto Alegre, Brazil, were reviewed regarding the following aspects: age; gender; severity of pneumonia (Fine score); presence of sputum; sputum bacteriology; treatment history; change in treatment; and mortality. **Results:** A total of 274 CAP patients (134 males and 140 females) were evaluated. Using the Fine score to quantify severity, we classified 79 (28.8%) of those 274 patients as class II, 45 (16.4%) as class III, 97 (35.4%) as class IV, and 53 (19.3%) as class V. Sputum examination was carried out in 92 patients (33.6%). A valid sample was obtained in 37 cases (13.5%), and an etiological diagnosis was obtained in 26 (9.5%), resulting in a change of treatment in only 9 cases (3.3%). Overall mortality was 18.6%. Advanced age (above 65), CAP severity, and dry cough were associated with an increase in the mortality rate. Sputum examination did not alter any clinical outcome or have any influence on mortality. **Conclusion:** Sputum examination was used in a minority of patients and was not associated with any noticeable benefit in the clinical management of patients with CAP treated in a hospital setting.

Keywords: Pneumonia/etiology; Sputum; Diagnosis.

Resumo

Objetivo: Este estudo retrospectivo avaliou a freqüência do uso da bacteriologia do escarro no manejo clínico de pacientes com pneumonia adquirida na comunidade (PAC) em um hospital geral, e se a utilização deste método modificou a mortalidade. **Métodos:** Os prontuários de pacientes internados no Hospital Nossa Senhora da Conceição, em Porto Alegre (RS) Brasil, para tratamento de PAC entre maio e novembro de 2004 foram revisados quanto aos seguintes aspectos: idade; sexo; gravidade da pneumonia (escore de Fine); presença de expectoração; bacteriologia do escarro; história de tratamento; resposta clínica; troca de tratamento; e mortalidade. **Resultados:** Foram avaliados 274 pacientes com PAC, sendo 134 do sexo masculino. Dentre os 274 pacientes, 79 (28,8%) apresentavam, de acordo com o escore de Fine, classe II; 45 (16,4%), classe III; 97 (35,4%), classe IV; e 53 (19,3%), classe V. Em 92 pacientes (33,6%), uma amostra de escarro foi colhida para exame bacteriológico. Obtivemos amostra válida em 37 casos (13,5%) e diagnóstico etiológico em 26 (9,5%), o que resultou em modificação do tratamento em apenas 9 casos (3,3%). A mortalidade geral foi 18,6%. Idade acima de 65 anos, a gravidade da PAC e a ausência de escarro associaram-se à maior mortalidade. A bacteriologia do escarro não influenciou o desfecho clínico, nem a taxa de mortalidade. **Conclusão:** O exame do escarro foi uma ferramenta diagnóstica utilizada na minoria dos pacientes, e não trouxe benefício detectável no manejo clínico dos pacientes com PAC tratados em ambiente hospitalar.

Descritores: Pneumonia/etiologia; Escarro; Diagnóstico.

Introduction

Community-acquired pneumonia (CAP) is defined as that which affects the patient out of the hospital environment or occurs within the first 48 h after admission. The incidence of CAP is approximately 12:1000 inhabitants.[1] In Brazil, according to data from the Ministry of Health, CAP led to 726,366 hospitalizations in 2005, at a cost of R$331,639,501.89 (in Brazilian reals).[2]

Mortality rates range from 1-5% for outpatients to approximately 12% for inpatients and up to 40% for patients in intensive care units.[1,3-5] In Brazil, in 2005, pneu-

monia was the cause of death in 37% of all deaths due to respiratory diseases, accounting for 6.7% of all deaths nationwide.[2]

Diagnostic tests to determine the etiology of CAP are performed for a number of reasons: to adjust antibiotic therapy and thereby obtain more efficacy at a lower cost and with lower toxicity; to rule out less common etiologies, such as *Mycobacterium tuberculosis* and endemic fungi; to select drugs that reduce selective pressure, preventing drug-induced bacterial resistance; to allow the identification of etiologies of epidemiological interest to the community, such as Legionnaires' disease and tuberculosis; and to gather information on the tendencies of bacterial resistance in the community.[4,5]

Sputum examination is one of the tools typically used in the etiological diagnosis of CAP. However, the benefit of its use in the initial management of CAP remains controversial.[6,7]

Some studies recommend sputum bacteriology as routine practice for patients with CAP.[5,8-10] Although most of these studies were not designed to calculate the cost-benefit ratio of sputum examination, some argue that reducing the spectrum of empirical treatment based on the sputum examination results would also lead to a significant reduction in costs.[8,11] However, other studies suggest that sputum bacteriology is a method with low sensitivity and specificity for the etiological diagnosis of CAP and does nothing to facilitate the management of these patients.[12-17] In addition, some authors argue that these diagnostic tests are not typically performed in clinical practice, and that most patients receive the treatment empirically, with satisfactory results.[18,19] The only controlled study designed to assess the efficacy of the use of diagnostic strategy in CAP failed to demonstrate differences in mortality between patients whose treatment was based on the identification of some pathogen and those whose treatment was empirical.[20]

The consensus of the Infectious Diseases Society of America of the American Thoracic Society, published in 2007,[5] recommends the routine performance of blood culture and sputum bacteriology in patients for whom hospital treatment has been indicated only when there is some clinical indicator of severity or increased risk of unusual pathogens of community-acquired infections. The guidelines established in 2004[1] by the Brazilian Thoracic Society do not recommend the routine use of sputum examination in patients with CAP.

The authors carried out this study with the objective of finding out whether sputum examination is part of the strategy adopted in the diagnosis of CAP in a general hospital, and assessing whether it affects mortality rates.

Methods

This study was conducted in a teaching hospital in Porto Alegre, with 800 inpatient beds and medical residency programs in all clinical and surgical areas, whose routine for hospital discharge requires that a computerized discharge summary be filled out, thereby allowing the system to be searched by cases, classified according to the tenth revision of the International Classification of Diseases (ICD-10). A search was carried out in the period from May 18 of 2004 to November 18 of 2004 for any diagnosis of pneumonia that met any of the descriptions of pneumonia standardized in the ICD-10 (J12, J13, J14, J15, J16, J17 and J18). All clinical charts selected (hospitalization notes, general medical charts, discharge summaries, radiological records and complementary test results) were reviewed by the authors. Cases were included upon confirmed diagnosis of CAP, which was defined as occurrence of the disease within to the first 48 h after hospital admission, previously undetected infiltrate now seen on X-rays and symptoms of acute respiratory disease (at least two of the following findings: cough; acute alterations in the quality of sputum; axillary temperature ≥ 37.8 °C; diffuse fine rales upon pulmonary auscultation; dyspnea; tachypnea; hypoxemia; and leukocytosis of >10,000 cells/mm^3 or containing >15% immature neutrophils).

A standardized chart was filled out in order to collect data regarding the following: age; gender; score and classification according to the Fine score[21]; sputum (absent, present/collected or present/not collected); culture for Koch's bacillus; HIV testing; antimicrobial treatment prior to hospitalization; initial prescription of antibiotics (identification of the drug); modification of the antibiotic regimen during hospitalization; attending physician report if the change in treatment was based on the result of the sputum examination; clinical response (cure or treatment failure); and outcome (discharge or death).

We found that sputum test results informed decisions regarding changing antibiotics if the change resulted from identification of the etiological agent in the sputum culture of a valid sample. Valid sputum samples were defined as those that contained <10 epithelial cells and >25 polymorphonuclear cells per low-power microscopic field (×100) on direct examination. Cultures were considered valid only when concordant with findings on direct examination. Treatment failure was defined as the absence of improvement or the worsening of symptoms, requiring that treatment be changed after at least 3 days of treatment. The protocol was approved by the ethics in research committee of the hospital. Logistic regression models were used in the statistical evaluation in order to evaluate the associations between the variables hospital discharge and presence of sputum (dependent) and a set of explanatory variables (independent), such as gender, age, previous treatment, HIV infection and change of therapeutic regimen. This multivariate analysis was carried out following a hierarchical model, and variables presenting $p \leq 0.20$ in the likelihood ratio test remained in the model. The data were organized using Microsoft Excel, version 2000, and were analyzed using the Statistical Package for the Social Sciences, version 10.2 (SPSS Inc., Chicago, IL, USA). A 95% confidence interval (95% CI) was adopted, and the level of statistical significance was set at $p < 0.05$.

Results

In the period studied, a total of 274 CAP patients were treated as inpatients (mean age, 60 years; range, 14-99 years) (Table 1). Using the Fine score to quantify severity, we classified 79 (28.8%) of those 274 patients as class II, 45 (16.4%) as class III, 97 (35.4%) as class IV, and 53 (19.3%) as class V. A total of 216 patients (78.8%) presented a history of expectoration, and 58 (21.2%) had a dry cough upon hospital admission. Testing for HIV was performed in 55 patients and was positive in 23 cases (8.4% of the total). We found that 34 patients (12.4%) had a history of use of antibiotics prior to hospitalization, 160 (58.4%) initiated treatment in the hospital, and no information regarding antibiotic use was available in the remaining 80 charts.

In 92 patients (33.6%), a sputum sample was collected for bacteriological tests, and 74 of these

Table 1 – Profile of the 274 patients evaluated.

Characteristic/event		
Age (years)	60.6 ± 20.9[a]	
Gender	n	%
Male	134	48.9
Female	140	51.1
Fine score		
Class II	79	28.8
Class III	45	16.4
Class IV	97	35.4
Class V	53	21.2
Sputum		
With sample collection	92	33.6
With valid sample	37	13.5
Etiological diagnosis	26	9.5
Modified initial treatment	131	47.8
Due to treatment failure	45	16.4
Death	51	18.6

[a]mean ± standard deviation.

were tested for acid-fast bacilli (positive in 1 case). Regarding the remaining 124 patients (45.2%) who reported productive cough, no sputum samples were collected prior to the first day of treatment, either due to patient inability to produce a sample or due to failure to order the test on the part of the attending physician. Of the patients whose sputum was collected, 37 (13.5%) produced a sample qualifying as valid on direct examination, and cultures revealed the etiological agent in 26 patients (9.5%): *Haemophilus* spp. in 13 samples; *Streptococcus pneumoniae* in 6; *Staphylococcus aureus* in 4; *Klebsiella pneumoniae* in 1; *Haemophilus* spp. and *Moraxella catarrhalis* in 1; and *Pseudomonas aeruginosa* in 1. Cultures were negative in the remaining 11 samples.

Many antibiotic therapy regimens were prescribed at treatment onset, which made it impossible to compare different antibiotics. Monotherapy was used in 160 patients (58.4%), 114 patients (41.6%) received combined therapy, and 111 patients (40.5%) received some antimicrobial treatment against atypical germs. In order of frequency, most typically used antibiotics were as follows: penicillin associated with ciprofloxacin; penicillin; amoxicillin; amoxicillin-clavulanate; piperacillin-tazobactam; cefuroxime; ciprofloxacin; and levofloxacin. Treatment was completed without any changes in the initial antimicrobial therapy in 143 patients (52.2%) and, in the remaining 131 patients (47.8%), treatment

was modified as follows: due to clinical diagnosis of treatment failure in 45 patients (16.4%); due to reduction in the spectrum of the antimicrobial treatment in 55 (20.1%); and due to the addition of a second antibiotic to the initial regimen in 31 (11.3%).

Considering these 131 patients whose treatment was modified, separately, we observed the following: 52 patients (39.7%) presented expectoration, but the sputum was not examined; sputum samples were collected for testing from 49 patients (37.4%); and 30 patients (22.9%) did not present expectoration of sputum at the time treatment was changed.

There were 51 deaths (18.6% mortality) among the 274 patients, regardless of gender, seropositivity for HIV or history of treatment. There were no significant differences among the various treatment regimens used. In addition, there was no significant difference between the group of patients that received monotherapy and the group that received combined therapy, nor was there any difference between those who received treatment against atypical germs and those who did not. Mortality among those who received monotherapy or combined therapy was 16.2% and 21.9%, respectively. Among those who received or did not receive treatment against atypical germs, mortality was 22.5% and 15.9%, respectively. The mortality rate was influenced by age and severity of pneumonia. Odds ratios (ORs) were used as a measure of the strength of the associations between the different variables and the risk of death. Patients over the age of 65 were at a 2-times greater risk of death (OR =1.99; 95% CI: 1.06-3.73; p = 0.03) when compared to those under 65. Considering as a reference the patients classified by the Fine score as class II, we found that the risk of death was 5.6-times greater for patients classified as class III (OR = 5.61; 95% CI: 1.03-30.14; p = 0.04), 15.4-times greater for patients classified as class IV (OR = 15.36; 95% CI: 3.28-71.81; p = 0.001) and 41.5-times greater for patients classified as class V (OR = 41.51; 95% CI: 8.18-210.41; p < 0.0001).

There were 19 deaths (32.7% mortality) among the 58 patients not presenting expectoration, 26 deaths (20.9% mortality) among the 124 who presented expectoration but from whom sputum samples were not collected for testing and 6 deaths (6.5% mortality) among the 92 patients whose sputum was collected for testing. Considering as a reference the group of patients whose sputum was collected, we found that the risk of death was 3.7-times greater in the group of patients presenting expectoration but from whom sputum samples were not collected for testing (OR = 3.78; 95% CI: 1.40-10.23; p < 0.01) and 8-times greater in the group of patients presenting no expectoration (OR = 8.01; 95% CI: 2.67-23.97; p < 0.0001). There was no statistically significant difference among these groups regarding the following: gender; age; history of antimicrobial treatment; severity of pneumonia classified by the Fine score; rate of treatment failure; and change of treatment regimen. This finding is independent of the qualification of the sample as valid or of its usefulness in guiding the treatment.

The initial treatment was changed based on the result of sputum bacteriology in only 9 patients (3.3%), and there was no statistically significant difference in mortality rates between this group of patients whose sputum examination result helped to guide the antibiotic therapy and the other groups (those not presenting expectoration, those presenting expectoration from whom sputum samples were not collected for testing and those whose sputum samples were collected but whose results were interpreted as not useful to guiding the treatment).

Discussion

Through the retrospective analysis of a series of CAP patients treated in a general hospital, the authors showed that sputum samples were routinely collected from approximately one-third of the patients. Valid samples were collected from one-sixth of the patients, and etiological diagnosis through sputum examination, which did not affect the prognosis of the patients, was obtained in less than one-tenth of these. Therefore, sputum examination was a tool used in a minority of the patients and did not result in any apparent benefit. Although we used a retrospective analysis which reflected local conditions of clinical practice, this seems to be the first Brazilian study that objectively evaluated the frequency of use and effectiveness of sputum bacteriology in the management of CAP in clinical practice.

The first difficulty in the interpretation of these data was related to the retrospective nature of clinical data collection. Therefore, we cannot ensure that these data reflect the level of efficacy of the method, since there is no confirmation as to the commitment of the professionals or as to whether proper instructions were followed during the collection of the sputum samples, which would prevent a lower yield than we could possibly have. However, we can confirm that the result was the best possible, considering the artificial environment of a study.

A meta-analysis published in 1996 showed that sensitivity and specificity of the microbiology of sputum range, respectively, from 15 to 100% and from 11 to 100%,[22] emphasizing the variability of the yield according to the characteristics of the patients and methodology of the studies, which can explain the risk we assume when we extrapolate the results of the assessment of this method from the medical literature to local clinical practice. A more recent retrospective study showed that sputum bacteriology provides a 21% diagnostic yield.[16] Prospective studies also revealed significant variability in the results of sputum bacteriology. Considering the diagnostic yield for all cases, regardless of the proportion of cases in which sputum samples were actually collected, one group of authors[17] identified the causal pathogen of CAP through sputum examination in only 5% of the cases. Three other groups of authors managed to do so in 9%,[14] 14%,[23,24] and 17%,[25] respectively, which reflects the difficulty in obtaining an etiological diagnosis using this test. One study reported a better yield (approximately 31%), although that study was based only on the presumptive diagnosis of sputum smear microscopy.[8] In a prospective case-series study conducted in Brazil, the etiological agent was identified through sputum bacteriology in 21.4% of the cases evaluated.[29] These data together suggest that this method, albeit ideal in theory, is applicable in clinical management in a small proportion of the cases.

A second aspect to be considered, regardless of the capacity to identify the etiology of CAP, is the percentage of patients whose treatment was effectively modified based on sputum evaluation, which further reduces the proportion of cases in which there is a noticeable benefit. In two different studies, it was reported that the treatment was modified in less than 1% and in 12%, respectively, of the cases

evaluated.[14,26] In our study, antibacterial treatment was modified in 9 patients (3.3%), and treatment with tuberculostatic drugs was started in one case.

Another possible approach to assess the beneficial potential of obtaining etiological diagnosis through sputum examination consists of the evaluation of the differences among the therapeutic approaches used in CAP. Some authors have not found any difference in mortality rates when comparing empirical treatment with that defined by etiology.[20] Two meta-analyses published in 2005[27,28] showed that there is no significant difference between therapeutic regimens with coverage for atypical agents and those without in terms of survival or clinical efficacy. If we consider that different treatment approaches do not result in significant differences in the outcomes evaluated, it is reasonable to question the advantage of investing in etiological diagnostic methods.

In our series of cases, we found an overall mortality rate of 18.6%. Regarding independent factors that increased the chance of death, we observed 32.7% mortality when there was no expectoration, 20.9% mortality when there was expectoration but there was no confirmation through sputum collection and 6.5% mortality when the sputum was examined. No difference in efficacy was found among the wide variety of antibiotics chosen for initial treatment. Due to the significant number of class IV and V patients (55% of the patients in our sample), overall mortality in our study was slightly higher than that observed in the literature.[3,4] However, we could not explain the apparent influence of the presence of expectoration or sputum collection as protective factors, since this had no effect on the therapeutic strategy in most cases. In addition, if we separately analyze the group of cases in which an etiological diagnosis was obtained, the only acceptable protection against death would be to offer potentially better treatment, since there was no significant difference among the groups regarding mortality. Variables that can interfere with the expectoration capacity of the patients, such as gender, age or severity of CAP, also had no influence on the results.

Although there are other reasons to implement the search for an etiological diagnosis, we need to determine whether this is actually achieved. If, in addition to not affecting mortality rates, the effectiveness of this method is low or uncertain and

cannot promote changes in treatment, thereby reducing costs, or establish diagnoses of epidemiological interest, this procedure seems to be unnecessary as a routine practice in the management of CAP. Information on the tendencies of bacterial resistance should be obtained from specific clinical protocols, which also does not imply that the use of this procedure is recommended in routine practice. An additional negative factor is the need to obtain sputum samples before instituting antibiotic therapy in order to enhance the yield of the method, since it is even less effective when the sample is collected after the introduction of antibiotic therapy. However, this is a noninvasive test of low operational cost, which can somewhat sustain the argument in favor of its use, even recognizing all of the limitations.

The data presented revealed that sputum examination was used as a diagnostic tool in a minority of the patients, without noticeable benefit in the clinical management of CAP inpatients. However, it is still possible that specific groups of patients identified as at risk for unusual pathogens of community-acquired infections can benefit from this method.

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