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Agreement Between Quantitative Cultures of Postintubation Tracheal Aspiration and Plugged Telescoping Catheter, Protected Specimen Brush, or BAL for the Diagnosis of Nosocomial Pneumonia*

Christophe Clec'h, MD; Françoise Jauréguy, PharmD; Lilia Hamza, MD; Philippe Karoubi, MD; Jean-Philippe Fosse, MD; Aïcha Hamdi, MD; François Vincent, MD; Frédéric Gonzalez, MD; and Yves Cohen, MD

Background: The diagnosis of ventilator-associated pneumonia relies on protected specimen brush (PSB), BAL, and plugged telescoping catheter (PTC) procedures. In the particular setting of nosocomial pneumonia (NP) occurring in non-mechanically ventilated patients, no consensus exists on their use. When mechanical ventilation (MV) becomes mandatory, postintubation tracheal aspiration (PITA) could be a simple, fast, and cheap diagnostic tool. Our aim was to compare the diagnostic accuracy of PITA to that of PSB, BAL, or PTC in patients requiring MV for suspected NP.

Methods: Patients with a prior hospital stay of ≥ 48 h who required MV for suspicion of NP were prospectively enrolled in the study. PITA was performed by sterile suction. Within 2 h, pulmonary samples were obtained by PSB, BAL, or blinded PTC, which are referred to hereafter as “reference methods” (RMs). The definite diagnosis of NP was made using a composite item of clinical, radiologic, and bacteriologic (ie, blood or pleural fluid cultures) patterns. The agreement between the quantitative microbiological results obtained with PITA and those of the RMs was assessed by the \( \chi^2 \)-statistic. The sensitivity, specificity, and positive and negative likelihood ratios of PITA and RMs were calculated taking the definite diagnosis of NP as the reference.

Results: There were 44 cases (63.8%) of confirmed NP. The \( \chi^2 \)-statistic was 0.71. The sensitivity, specificity, and positive and negative likelihood ratios were 77%, 84%, 4.80, and 0.27, respectively, for PITA, and 75%, 88%, 6.25, and 0.28, respectively, for RMs.

Conclusions: PITA may be a reliable alternative to RMs in the particular setting of NP in newly mechanically ventilated patients.

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Key words: diagnosis; intensive care; nosocomial pneumonia

Abbreviations: APACHE = acute physiology and chronic health evaluation; MV = mechanical ventilation; NP = nosocomial pneumonia; PITA = postintubation tracheal aspiration; PSB = protected specimen brush; PTC = plugged telescoping catheter; RM = reference method; TA = tracheal aspiration; VAP = ventilator-associated pneumonia

Nosocomial pneumonia (NP) is a common issue in the ICU, accounting for approximately one fourth of all nosocomial infections. An early and accurate diagnosis of NP is of utmost importance because of its potential impact on antibiotic use and patient outcomes.

The diagnosis of NP is often clinically suspected. Yet, clinical features suggestive of NP are nonspecific. Consequently, bronchoscopic techniques such as protected specimen brush (PSB) and BAL with quantitative cultures of pulmonary samples are widely used to avoid the excessive diagnosis of NP, and subsequent antibiotic misuse and increased antimicrobial resistance. These techniques are currently viewed as the tests yielding the best combination of sensitivity and specificity. However, they...
have not gained universal acceptance since they may not be available on a 24-h basis in all ICUs, and may be associated with serious adverse events and higher costs.11–13 Blinded techniques such as plugged telescopic catheter (PTC) and tracheal aspiration (TA) have been developed to increase the availability of respiratory tract specimens with quantitative cultures and to reduce the costs of the procedure. They have both been shown to offer sensitivity and specificity that are similar to those of bronchoscopic techniques and can be considered to be reliable alternative diagnostic tools.14–16

Of note, all comparisons of TA with other techniques were in patients with ventilator-associated pneumonia (VAP). Nevertheless, NP occurring in non-mechanically ventilated patients (ie, those with non-VAP NP) is also a frequent issue associated with increased morbidity and mortality,17,18 and requiring an early diagnosis. Yet, there is no consensus regarding the best diagnostic strategy. The clinical features of community-acquired pneumonia may apply, but microbiological examination is undoubtedly necessary to guide antibiotic therapy. The accuracy of TA in this particular setting has never been assessed. Performed immediately after intubation of the trachea, TA could be thought of as a simple, fast, and cheap way to identify the microorganisms involved, and to achieve early adequate antibiotic therapy, together with the knowledge of local epidemiologic characteristics. The aim of the present study was to compare the diagnostic accuracy of postintubation TA (PITA) to that of PSB, BAL, or PTC in patients requiring mechanical ventilation (MV) for suspected NP.

Methods and Materials

Study Design and Setting

This prospective study was carried out in the medical and surgical ICU of the Avicenne Teaching Hospital (Bobigny, France).

*From the Service de Réanimation (Drs. Clech, Hamza, Karouhi, Fosse, Hamdi, Vincent, Gonzalez, and Cohen), and the Département de Bactériologie-Virologie-Hygiène (Dr. Jauréguy), Hôpital Avicenne, Bobigny, France.
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Correspondence to: Yves Cohen, MD, Service de Réanimation, Hôpital Avicenne, 125, route de Stalingrad, 93009 Bobigny Cedex, France; e-mail: yves.cohen@avc.aphp.fr

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Patients

All consecutive patients with prior hospital stays of ≥ 48 h and suspected of NP were eligible for inclusion. Patients who subsequently required MV via an endotracheal tube were enrolled in the study. The clinical suspicion of NP was based on the following usual criteria: purulent respiratory secretions; fever (temperature of ≥ 38.5°C) or hypothermia (temperature of ≤ 36°C); blood leukocyte count of > 12 × 10⁹ or < 4 × 10⁹ cells/L; and new or progressive infiltrates seen on a chest radiograph.

The local committee in charge of the infection control program approved the study. Respiratory tract secretion samples were obtained as described below. Since the obtaining of protected specimens is currently recommended in France in patients with suspected pneumonia and TA who are receiving MV is otherwise part of routine nursing care, informed consent was waived.

Data Collection

For each patient, the following data were recorded: age; gender; simplified acute physiologic scale II score; APACHE (acute physiology and chronic health evaluation) II score; McCabe class; ICU admission category; main reason for ICU admission; presence or absence of ongoing antibiotic therapy; time between admission to hospital and initiation of MV; length of MV; causative microorganisms; and vital status at ICU discharge.

Specimen Collection

Immediately after intubation of the trachea, tracheal aspirates (from PITA) were obtained by sterile suction using a mucus collector (Mucus extractor; Vygon; Ecouen, France). Within 2 h, pulmonary samples were obtained by PSB, BAL, or blinded PTC, which are referred to hereafter as “reference methods” (RMs). Sampling procedures were performed as described in detail elsewhere.16,19

Bacteriological Processing

Samples were transferred to the microbiology laboratory within 30 min for Gram stain and quantitative cultures. Vortexed, undiluted samples (1 mL) were used to prepare 10⁻² and 10⁻⁵ dilutions. From each dilution, 0.1 mL was plated for aerobic and anaerobic cultures on blood agar, selective blood agar with colistin (10 µg/mL), nalidixic acid (15 µg/mL), and isovitalex chocolate agar for culture in CO₂ (5%). Cultures were evaluated after 24 and 48 h at 37°C. The number of bacteria in the original sample was expressed in colony-forming units per milliliter of the original 1-mL sample. Bacteria were identified by conventional methods, and antibiotic susceptibility was determined on Mueller-Hinton agar by the agar diffusion method according to Comité de l’Antibiogramme de la Societe Francaise de Microbiologie standards.20

Definitions

The thresholds for positive cultures were 10³ cfu/mL for PTC and PSB, 10⁴ cfu/mL for BAL, and 10⁵ cfu/mL for PITA.14 The definite diagnosis of NP was made by a committee of three ICU senior physicians on the basis of a composite item of clinical, radiologic, and bacteriologic (ie, blood or pleural fluid cultures) patterns. The diagnosis of NP was retained when the clinical suspicion (as defined above) was associated with either positive
results of pleural fluid tests or blood cultures without any extrapulmonary focus. In case of disagreement, the diagnosis of NP was retained if two physicians deemed NP to be present.

**Statistical Analysis**

The data are shown as the mean ± SD or No. (%). Comparisons between patients were based on χ² tests for categoric data, and on Student t tests for continuous data. Cultures of microorganisms were classified as positive or negative.

The agreement between the quantitative microbiological results obtained with PITA and those obtained with RMs was assessed by the κ-statistic test: κ of < 0.00, poor agreement; κ between 0.00 and 0.2, slight agreement; κ between 0.21 and 0.4, fair agreement; κ between 0.41 and 0.60, moderate agreement; κ between 0.61 and 0.80, substantial agreement; and κ between 0.81 and 1, almost perfect.21

Sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio of PITA and the RMs were calculated according to standard formulas, taking the definite diagnosis of NP as the reference. Statistical analyses were performed using a statistical software package (SAS, version 9.1; SAS Institute; Cary, NC).

**RESULTS**

**Patients**

Sixty-nine patients were included in the study over a 1-year period (September 2004 to September 2005). The clinical suspicion of NP was confirmed in 44 cases (63.8%). When a diagnosis of NP was not retained, the alternative diagnosis was as follows: exacerbation of chronic bronchitis (n = 12); atelectasis (n = 8); edema (n = 4); and intraalveolar hemorrhage (n = 1).

Patients with microbiologically confirmed NP were older, had higher severity scores, had spent more time in the hospital before NP suspicion, and were more likely to die than patients without NP, although no difference reached statistical significance (Table 1). The RMs used were blinded PTC in 48 patients (69.6%), BAL in 17 patients (24.6%), and PSB in 4 patients (5.8%).

**Microbiology**

Overall, 58 microorganisms were recovered from PITA, PTC, PSB, or BAL cultures. The predominant microorganisms were *Staphylococcus aureus* and Enterobacteriaceae (Table 2).

NP was due to Gram-positive bacteria in 18 cases (41%), Gram-negative bacteria in 12 cases (27%), and to more than one microorganism in 14 cases (32%). The proportion of polymicrobial NP was identical with both PITA and RM.

**Quantitative Agreement Between Respiratory Specimen Cultures**

When the diagnosis of NP was retained, the findings of 29 paired cultures (65.9%) were positive.

| Table 1—General Characteristics of Study Patients* |
|---------------------------------|-----------------|-----------------|------|
| Characteristics                | Patients With NP | Patients Without NP | p Value |
| Age                            | 68.5 ± 12.7     | 63 ± 14          | 0.10 |
| Male gender                    | 26 (59.1)       | 15 (60)          | 0.98 |
| SAPS II score                  | 59.3 ± 19       | 51.5 ± 18        | 0.10 |
| APACHE II score                | 28.7 ± 8.7      | 26 ± 9.2         | 0.23 |
| McCabe scale                   |                 |                  |      |
| 1                              | 19 (43.2)       | 15 (60)          | 0.39 |
| 2                              | 16 (36.4)       | 7 (28)           |      |
| 3                              | 9 (20.4)        | 3 (12)           |      |
| Admission category             |                 |                  |      |
| Medical                        | 38 (86.4)       | 23 (92)          | 0.98 |
| Scheduled surgery              | 3 (6.8)         | 1 (4)            |      |
| Unscheduled surgery            | 3 (6.8)         | 1 (4)            |      |
| Main reason for ICU admission  |                 |                  |      |
| Septic shock                   | 11 (25)         | 6 (24)           | 0.87 |
| Hemorrhagic shock              | 4 (8)           | 2 (8)            |      |
| Respiratory failure            | 12 (27.2)       | 7 (28)           |      |
| Acute exacerbation of COPD     | 7 (16)          | 4 (16)           |      |
| Coma                           | 9 (20.5)        | 5 (20)           |      |
| Postoperative surveillance     | 1 (2.3)         | 0 (0)            |      |
| Acute renal failure            | 0 (0)           | 1 (4)            |      |
| Elapsed time between NP suspicion and hospital admission, d | 8.6 ± 9.5 | 5.4 ± 5.1 | 0.15 |
| Prior antibiotic therapy       | 22 (50)         | 12 (48)          | 0.80 |
| Length of mechanical ventilation, d | 13 ± 15.3   | 12.9 ± 16.5      | 0.98 |
| Mortality                      | 21 (47.7)       | 9 (36)           | 0.35 |

*Values are given as the mean ± SD or No. (%), unless otherwise indicated.*
In five cases (11.4%), PITA yielded a positive result while RM samples were sterile. In four cases (9.1%), PITA yielded a negative result while RM samples had positive results (in three cases, the same microorganism was identified by both techniques, but PITA cultures remained below threshold value; in one case, the microorganism involved, *Streptococcus pneumoniae*, was retrieved only in samples obtained by the RMs). In six cases (13.6%), both PITA and RM yielded a negative result (ie, cultures were below threshold values).

When the diagnosis of NP was rejected, 21 paired cultures (84%) were sterile. In one case (4%), PITA yielded a positive result while the RM samples were sterile. In three cases (12%), both PITA and RM yielded a positive result. Accordingly, the κ-statistic was 0.71.

**Diagnostic Value of PITA and RM**

The sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio of PITA were 77%, 84%, 4.50, and 0.27, respectively. The sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio of the RMs were 75%, 88%, 6.25, and 0.28, respectively.

**DISCUSSION**

In this study, we observed a substantial agreement between quantitative cultures of PITA and RMs, and either technique had a similar diagnostic value in terms of sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio. Thus, PITA may be a reliable alternative to bronchoscopic samplings and blinded PTC in the particular setting of non-VAP NP.

Pneumonia is the leading cause of nosocomial infection in the ICU. Since several studies have reported a high rate of inappropriate early antibiotic therapy associated with increased morbidity and mortality, physicians used to often prescribe broad-spectrum antibiotics before obtaining specimens, which is a practice that is responsible for the subsequent confounding of the interpretation of culture results and difficult antibiotic management.

In this context, there was a need for diagnostic tests allowing early adequate antibiotic therapy while avoiding the overprescribing of antibiotics. Such tests (ie, quantitative cultures of blinded PTC and TA) have been validated for the diagnosis of VAP. In the particular setting of non-VAP NP, however, no consensus exists.

To the best of our knowledge, we performed the first study evaluating the diagnostic accuracy of PITA and showed that it may be suitable as a routine diagnostic tool. The RMs provided similar sensitivity and specificity. Nevertheless, bronchoscopic samplings are not always available on a 24-h basis, and such a procedure may be poorly tolerated in severely hypoxemic patients. Blinded PTC may be performed at any time and allows as early a diagnosis as PITA, but it is not as simple and cheap. Availability, harmlessness, simplicity, and low cost are the main advantages of PITA over the RMs.

One may be concerned about the composite item of clinical, radiologic, and bacteriologic patterns (excluding the results of PITA and the RMs) used to define NP, since it could be held responsible for an overdiagnosis of NP, leading to the biased interpretation of microbiological results. The use of the clinical pulmonary infection score could actually have been interesting. However, this score has low sensitivity and specificity for diagnosing NP, a considerable interrater variability, and a low concordance with bronchoscopic techniques.

Taking our composite item as the reference, the specificity of PITA and the RMs was very good. So, a biased conclusion was very unlikely. Of note, there were only three cases of positive PITA and RM results associated with the absence of NP. In these cases, pulmonary condensation was due to atelectasis. Positive culture results were considered to reflect colonization. No antibiotics were given, and all patients were discharged from the ICU alive. In six cases, the diagnosis of NP was retained despite the negative results of both PITA and the RMs. This is consistent with the fact that the sensitivity of these techniques for the diagnosis of NP is not 100%.

That almost half the patients were already receiving antibiotic therapy on the day of sampling might also be regarded as a potential bias because it could have led to a high rate of false-negative results. Nonetheless, we found reasonable sensitivity values (ie, 77% for PITA and 75% for RM), which were consistent with those of a previous report that
ongoing antibiotic therapy does not necessarily alter the diagnostic yield of respiratory specimen cultures. Yet, when cultures are negative while clinical suspicion of NP is high, repeated sampling might be advisable.

Two other potential limitations merit consideration. First, it may be argued that the main RM was PTC, and that results could have been different with BAL or PSB as the main RM performed. But, either technique offers equivalent diagnostic performance.14,16 Second, having chosen a diagnostic threshold for PITA of < 10^4 or > 10^5 cfu/mL might have changed the results. However, the best diagnostic threshold for TA remains unclear, probably ranging from 10^4 to 10^6 cfu/mL.30,31 The intermediate threshold of 10^5 cfu/mL was chosen in this study because it yields a good diagnostic accuracy and is routinely used by our microbiology laboratory.14

Finally, the impact of PITA results on antibiotic therapy adequacy and patient outcomes was not assessed. No recommendation for antibiotic management based on PITA results could be made before validation of the technique, which was precisely the purpose of this study. This issue represents an important outcome measurement for future investigations. In conclusion, quantitative cultures of PITA can be thought of as a simple and reliable tool for the early diagnosis of non-VAP NP.

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