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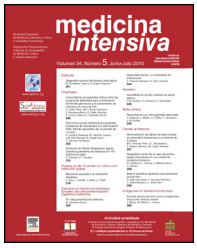

ORIGINAL

Role of plasma procalcitonin in the diagnosis of ventilator-associated pneumonia: Systematic review and metaanalysis☆

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KEYWORDS
Ventilator-associated pneumonia;
Procalcitonin;
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Abstract
Objective: To determine the role of plasma procalcitonin (PCT) levels in diagnosing ventilator-associated pneumonia.
Design: A systematic review of publications prospectively assessing the diagnostic role of PCT in ventilator-associated pneumonia was carried out. The search was performed using Medline, Embase, the Cochrane Collaboration and MEDION, with reviewing of the references of retrieved articles. We extracted data that allowed the calculation of sensitivity, specificity, likelihood ratios and diagnostic odds ratio.
Intervention: Metaregression was performed to determine whether exposure to previous antibiotic treatment, the time to occurrence of ventilator-associated pneumonia and the type of patients had an impact upon the diagnostic performance of procalcitonin.
Results: Seven studies were considered (373 patients, 434 episodes). We found no publication bias or threshold effect. High plasma PCT levels were associated to an increased risk of suffering ventilator-associated pneumonia (OR: 8.39; 95% CI: 5.4–12.6). The pooled data on sensitivity, specificity, positive and negative likelihood ratio, and diagnostic odds ratio found were 76% (69–82), 79% (74–84), 4.35 (2.48–7.62), 0.26 (0.15–0.46) and 17.9 (10.1–31.7), respectively. Diagnostic yield was modified by prior exposure to antibiotics (rDOR 0.11, 0.02–0.069), but not by the type of critically ill patient or the time to occurrence of ventilator-associated pneumonia.
Conclusions: Our results suggest that PCT provides additional information on the risk of VAP. Inclusion of PCT in diagnostic algorithms could improve their effectiveness.

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PALABRAS CLAVE
Neumonía asociada a ventilación mecánica;
Procalcitonina;
Diagnóstico;
Metaanálisis de pruebas diagnósticas

Papel de la procalcitonina plasmática en el diagnóstico de la neumonía asociada a ventilación mecánica: revisión sistemática y metaanálisis

Resumen
Objetivo: Determinar el papel de los niveles plasmáticos de procalcitonina (PCT) en el diagnóstico de neumonía asociada a ventilación mecánica.
Diseño: Revisión sistemática y metaanálisis de los trabajos originales que evalúan el papel de PCT en el diagnóstico de neumonía asociada a ventilación mecánica. La búsqueda de trabajos se llevó a cabo en Medline, Embase, Colaboración Cochrane y MEDION y tras revisión de las referencias de los artículos obtenidos. Se extrajeron datos que permitieron el cálculo de la sensibilidad, la especificidad, las razones de verosimilitud y la *odds ratio* diagnóstica.
Intervención: Metarregresión para determinar si la exposición a tratamiento antibiótico previo, el tiempo de desarrollo de neumonía y el tipo de paciente crítico tienen impacto en el rendimiento diagnóstico de la procalcitonina.
Resultados: Se incluyeron 7 estudios (373 pacientes, 434 episodios). No encontramos sesgos de publicación ni efecto umbral. Las cifras elevadas de PCT plasmática se asocian a un mayor riesgo de padecer neumonía (OR 8,39; IC 95% 5,4-12,6). Los datos agrupados de sensibilidad, especificidad, razón de verosimilitud positiva y negativa y *odds ratio* diagnóstica encontrados son, respectivamente, 76% (69-82), 79% (74-84), 4,35 (2,48-7,62), 0,26 (0,15-0,46) y 17,9 (10,1-31,7). El rendimiento diagnóstico se ve modificado por la exposición previa a antibióticos (rORD 0,11, 0,02-0,069), no así por el tipo de paciente crítico o el tiempo de desarrollo de neumonía.
Conclusiones: Nuestros resultados muestran que la PCT aporta información adicional respecto al riesgo de sufrir neumonía asociada a ventilación mecánica. Su inclusión en los algoritmos diagnósticos podría mejorar la capacidad de los mismos.

Introduction

Ventilator-associated pneumonia (VAP) is a serious problem in critically ill patients. Despite great efforts to prevent VAP, it remains very common and is regarded as one of the main quality of care indicators, since it accounts for up to 25% of all nosocomial infection episodes seen in Departments of Intensive Care Medicine.[1] No less important is the high risk of recurrence (in the order of 25%), particularly associated to the development of septic shock or adult respiratory distress syndrome,[2] and its impact upon patient mortality. Indeed, VAP has been associated with a mortality risk of 35%, which proves even higher when associated among other factors to inappropriate treatment, the development of severe sepsis or bacteremia, or when VAP is late in manifesting or causes respiratory failure.[3]

The diagnosis of VAP presents still unresolved problems that complicate early and adequate antibiotic treatment capable of reducing the risk of life-threatening situations in the Department of Intensive Care Medicine. The diagnosis is fundamentally clinical, combining radiological criteria (appearance of new infiltrates or progression of already existing infiltrates), evidence of respiratory deterioration (PO_2/FiO_2), and signs of both local (purulent bronchorrhea) and systemic inflammatory reaction (fever/hypothermia, leukopenia/leukocytosis).[4] An adequate diagnosis requires microbiological confirmation, however, and this may take 3–5 days. From the microbiological perspective, gram staining of the respiratory secretions and anticipative rapid cultures can help establish both the diagnosis and the treatment strategy–thereby shortening the response times.[5]

Procalcitonin (PCT) is a soluble protein composed of 116 amino acids with a sequence identical to that of the calcitonin prohormone, produced under normal conditions by the C cells of the thyroid gland secondary to internal PCT proteolysis. The basal circulating levels are very low (<0.05 ng/ml).[6] Situations of sepsis, bacterial infections or severe inflammatory reactions increase expression of the CALC-1 gene, favoring the production of PCT in all tissues (including lung, liver, kidney, adipocytes and muscle), and in all differentiated cells of the body. The levels increase quickly 2–3 h after the triggering stimulus,[7] remaining stable both in vivo and in vitro, and laboratory assay based on immunoanalytical methods allows reliable determination of the plasma concentrations.

Procalcitonin is used in the diagnosis of sepsis, for differentiating bacterial infections from other causes of systemic inflammatory reaction, as a severity marker, and as a prognostic element in the evaluation of the impact of antibiotic treatment and in certain organic infections.[8–10] The role of PCT in the diagnosis of VAP has been investigated in a limited number of studies, with conflicting results.[11] The joint utilization of clinical criteria, preliminary microbiological data and plasma PCT levels could allow early diagnosis and treatment, thereby contributing to lessen the impact of VAP.

The present study was carried out to determine the usefulness of the plasma PCT levels in diagnosing VAP and to identify possible factors capable of modifying the diagnostic performance of the molecule.