Neurología. 2016;31(1):9—17

NEUROLOGÍA

www.elsevier.es/neurologia

ORIGINAL ARTICLE

Ability of procalcitonin to predict bacterial meningitis in the emergency department☆

M.I. Morales Casado[a], F. Moreno Alonso[b], A.L. Juárez Belaunde[a], E. Heredero Gálvez[c], O. Talavera Encinas[b], A. Julián-Jiménez[b,*]

[a] *Servicio de Neurología, Complejo Hospitalario de Toledo, Toledo, Spain*
[b] *Servicio de Urgencias, Complejo Hospitalario de Toledo, Toledo, Spain*
[c] *Servicio de Microbiología, Complejo Hospitalario de Toledo, Toledo, Spain*

Received 21 January 2014; accepted 30 July 2014
Available online 27 November 2015

KEYWORDS
Procalcitonin;
C-reactive protein;
Biomarkers;
Acute meningitis;
Bacteraemia;
Emergency department

Abstract
Introduction: The aim of this study was to analyse and compare procalcitonin (PCT) and C-reactive protein (CRP) as tools for detecting bacterial meningitis and predicting bacteraemia.
Methods: Prospective, observational, and descriptive analytical study of 98 consecutive patients aged ≥15 years and diagnosed with acute meningitis in an emergency department between August 2009 and July 2013.
Results: We analysed 98 patients with AM (66 males [67%]); mean age was 44 ± 21 years. The diagnosis was bacterial meningitis in 38 patients (20 with bacteraemia); viral meningitis in 33; probable viral meningitis in 15; and presumptively diagnosed partially treated acute meningitis in 12. PCT had the highest area under the ROC curve (AUC) (0.996; 95% CI, 0.987—1; $P < .001$). With a cutoff of ≥0.74 ng/ml, PCT achieved 94.7% sensitivity, 100% specificity, negative predictive value (NPV) of 93.9%, and positive predictive value (PPV) of 100%. The mean levels for PCT were11.47 ± 7.76 ng/ml in bacterial meningitis vs 0.10 ± 0.15 ng/ml in viral meningitis ($P < .001$). The AUC for CRP was 0.916 and a cutoff of ≥90 mg/L achieved 67.5% sensitivity, 86.3% specificity, PPV of 89.2%, and NPV of 90.4%.

As a predictor of bacteraemia in bacterial meningitis, only PCT delivered a significant difference (14.7 ± 7.1 ng/mL vs 4.68 ± 3.54 ng/mL, $P < .001$). A cutoff of ≥1.1 ng/mL achieved 94.6% sensitivity, 72.4% specificity, NPV of 95.4%, and PPV of 69.2%; the AUC was 0.965 (95% CI, 0.921—1; $P < .001$).
Conclusions: PCT has a high diagnostic power for acute meningitis in emergency department patients. PCT outperforms CRP in the detection of bacterial aetiology and is a good predictor of bacteraemia in bacterial meningitis.

☆ Please cite this article as: Morales Casado MI, Moreno Alonso F, Juárez Belaunde AL, Heredero Gálvez E, Talavera Encinas O, Julián-Jiménez A. Capacidad de la procalcitonina para predecir meningitis bacterianas en el servicio de urgencias. Neurología. 2016;31:9—17.

* Corresponding author.
E-mail addresses: agustinj@sescam.jccm.es, agustin.jj@wanadoo.es (A. Julián-Jiménez).

PALABRAS CLAVE
Procalcitonina;
Proteína C reactiva;
Biomarcadores;
Meningitis aguda;
Bacteriemia;
Servicio de Urgencias

Capacidad de la procalcitonina para predecir meningitis bacterianas en el servicio de urgencias

Resumen
Introducción: El objetivo del estudio fue analizar y comparar la capacidad de la procalcitonina (PCT) y proteína C reactiva (PCR) para detectar meningitis bacteriana (MB) y para predecir la existencia de bacteriemia.
Métodos: Estudio observacional, prospectivo, descriptivo y analítico de pacientes adultos (≥15 años) diagnosticados de meningitis aguda (MA) en un servicio de urgencias (SU) desde agosto de 2009 hasta julio de 2013.
Resultados: Se incluyeron 98 casos diagnosticados de MA con una edad media de 44 ± 21 años, el 67% varones (66). De ellos 38 fueron MB (20 con bacteriemia), 33 meningitis virales (MV), 15 probable MV y 12 posibles MA decapitadas. La PCT obtiene la mayor área bajo la curva ROC (ABC-ROC), de 0,996 (IC 95%:0,987−1, p < 0,001) y con un punto de corte ≥ 0,74 ng/ml se consigue una sensibilidad del 94,7%, especificidad del 100%, un VPN de 93,9% y un VPP del 100%. Los valores medios al comparar la PCT en MB y MV fueron 11,47 ± 7,76 vs. 0,10 ± 0,15 ng/ml, p < 0,001. La PCR consigue un ABC-ROC de 0,916 y con punto de corte ≥ 90 mg/L una sensibilidad de 67,5%, especificidad de 86,3%, VPP 89,2% y VPN: 90,4%.

Para la predicción de bacteriemia en las MB solo la PCT consigue diferencias significativas (14,7 ± 7,1 vs. 4,68 ± 3,54 ng/ml, p < 0,001) y con un PC de 1,1 ng/ml una sensibilidad de 94,6%, especificidad 72,4%, VPN 95,4% y VPP 69,2% y un ABC de 0,965 (IC 95%: 0,921−1, p < 0,001).
Conclusiones: En los pacientes con MA en SU la PCT consigue un gran rendimiento diagnóstico para sospechar la etiología bacteriana, mayor que la PCR, y para predecir la existencia de bacteriemia en las MB.

Introduction

Bacterial meningitis (BM) is an inflammatory process involving the leptomeninges. Typical findings in cerebrospinal fluid (CSF) are marked pleocytosis (> 500-1000 leukocytes/mm^3, predominantly polymorphonuclear), elevated protein levels, and low glucose levels.[1] BM is not among the 10 most frequent infectious processes seen in adult patients in emergency departments (ED) or among patients requiring hospitalisation and antimicrobial agents.[2] Likewise, it is not listed in the 10 most common causes of EDs requesting a consultation with the on-call neurologist.[3] However, BM is the infectious process that most frequently meets criteria for sepsis, severe sepsis, and septic shock in EDs, which reflects its severity and clinical relevance.[2,4] Furthermore, the associated complications and mortality rates, even in the ED or within 24 hours of admission, are high considering the low incidence of BM, although it is not ranked among the 10 most common causes of death in the ED.[5] Remaining alert to potential bacterial aetiology of acute meningitis (AM), and confirming this, are therefore essential steps. Nonetheless, the situation still poses a challenge since microbial cultures and tests must be used to determine the bacterial or viral aetiology.[6] The aetiology of BM tends to differ by age group. In younger adult patients, *Streptococcus pneumoniae* (*S. pneumoniae*) and *Neisseria meningitidis* (*N. meningitidis*) *B* are the most frequently isolated pathogens, but other pathogenic agents frequently found in patients aged 50 and older include *Listeria monocytogenes* (*L. monocytogenes*), *Haemophilus influenzae* (*H. influenzae*), and gram-negative bacteria.[1,6]

Non-specificity of clinical manifestations increases with age and is greater in immunodepressed patients, diabetic patients, and others likely to experience severe infections. In these patients, normal signs and symptoms do not provide optimal sensitivity and specificity for distinguishing between potential BM and viral meningitis (VM).[1] EDs therefore need accurate and quick-acting tools enabling discrimination between bacterial and viral meningitis.[6] Biomarkers of infection and inflammation have been proving themselves useful for more than a decade,[7–12] and they can even reduce the chances of inappropriate administration of antimicrobials in EDs, and their subsequent adverse effects.[13] In recent years, researchers have published several studies and reviews on the diagnostic utility of these biomarkers, especially for discriminating between infectious agents and other causes of fever, or for identifying sepsis, severe sepsis, or septic shock.[7,9,14] However, few of these studies specifically addressed distinguishing between BM and VM in adult patients. Most analysed small samples or used semiquantitative techniques for measuring the biomarkers of infection and inflammation,[11,12,14–17] and these techniques are less sensitive than the ones available at present.[7]

Measuring the C-reactive protein (CRP) released in response to inflammation and bacterial infection in BM is less sensitive and specific than measuring procalcitonin (PCT). Likewise, the kinetic properties of the former are less favourable: CRP levels do not rise until 12 to 24 hours after bacterial infection and they remain high for several