Enfermedades Infecciosas y Microbiología Clínica

Original article

Validity of procalcitonin for the diagnosis of bacterial infection in elderly patients

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A B S T R A C T

Introduction: PCT has been consolidated as a key tool in the diagnosis of bacterial infections in general population. Few studies have been conducted to determine the applicability of this test in elderly patients.
Methods: Study of validity of PCT on elderly patients. Two groups were formed; the first group was formed by patients aged 75 years or older, under bacterial infection criteria and PCT on the initial Lab test. The second group was formed by patients aged 75 years or older with any noninfectious disease; these patients were asked PCT in the initial Lab test. Sensitivity, specificity, positive and negative likelihood ratio were calculated.
Results: 161 patients were included, 95 with probable bacterial infection and 66 without infection. Patients with probable bacterial infection criteria, 72% of them had PCT >0.5 ng/mL. Patients without infection, 8% of the patients had PCT >0.5 ng/mL. Sensitivity and specificity of PCT to bacterial infection with the cutoff value of 0.5 ng/mL was 72% and 92%, respectively.
Conclusion: PCT can be used in elderly patients to diagnose bacterial infections because it has proved good sensitivity and high specificity.

Validez de la procalcitonina para el diagnóstico de infección bacteriana en pacientes ancianos

R E S U M E N

Introducción: La PCT se ha consolidado como una herramienta clave en el diagnóstico de las infecciones bacterianas en la población general. Pocos estudios se han realizado para determinar la aplicabilidad de esta prueba en pacientes ancianos.
Métodos: Estudio de validez de la PCT en población anciana. Se conformaron 2 grupos: un grupo con pacientes con edad igual o mayor de 75 años con criterios de probable infección bacteriana y a quienes se les hubiese realizado PCT en la analítica inicial. Otro grupo conformado por pacientes con edad igual o mayor de 75 años ingresados por patología no infecciosa; a estos pacientes se les solicitó PCT en la analítica de ingreso. Se calcularon: sensibilidad (S), especificidad (E), valor predictivo positivo (VPP), valor predictivo negativo (VPN), razones de verosimilitud positiva y el inverso de la razón de verosimilitud negativa (RVP y I-RVN).
Resultados: Se incluyeron 161 pacientes, 95 con probable infección bacteriana y 66 sin infección. De los pacientes con probable infección bacteriana, 72% tenían la PCT > 0,5 ng/mL. En el grupo sin infección, 8% tenían la PCT > 0,5 ng/mL. La S y E de la PCT fue de 72 y 92%, respectivamente.

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Conclusión: La PCT se puede utilizar en pacientes ancianos de forma fiable porque posee una buena sensibilidad y alta especificidad para el diagnóstico de infección bacteriana.

Introduction

Procalcitonin (PCT) has become a key tool in the diagnosis of bacterial infections and sepsis among other things due to its higher sensitivity, higher specificity and earlier response regarding other markers of inflammatory response[1,2] and good correlation with the response to antibiotic treatment.[3,4] In general population, it has been evaluated the usefulness of PCT and CRP as markers of bacterial infection and it has been found that the PCT has a greater ability to discriminate bacterial infection with a sensitivity and specificity of 88% and 81%, respectively, compared to CRP whose sensitivity and specificity are 75% and 67%, respectively.[5] However in the Department of Internal Medicine, Emergency and Infectious Diseases every day more elderly patients are admitted in which the inflammatory markers do not always behave the same as in the general population. In these patients the clinical manifestations usually are less clear, in part because of the lower activation of the immune system,[6] which makes the diagnosis and early treatment more difficult, leading to sepsis, which is one of the most common causes of death in the elderly. A recent meta-analysis on the utility of PCT for diagnosis of bacterial infection among the elderly population only found four studies that met the specifications adopted for the analysis,[7] demonstrating that unfortunately the different studies performed to evaluate the applicability of the diagnostic tests exclude elderly patients. Nonetheless one quickly extrapolates the use of these diagnostic tests to this age group.

Some diseases such as ischemic heart disease, heart failure (HF) and tumors can cause high levels of PCT in blood in absence of infection[8,9]; Therefore, considering that these illnesses are very common in elderly patients, it is important to carry out specific studies in elderly population in order to determine whether PCT can be used as a reliable tool for the diagnosis of bacterial infections and sepsis, as demonstrated in the general population.

Thus, the aim of our study is to establish whether the cut off of PCT (established 0.5 ng/ml) is also valid for the diagnosis of bacterial infection in the elderly population as it has been applied in the general population.

Materials and methods

We performed a study to evaluate the validity of the PCT on elderly population (75 years old or older). The study was conducted at San Pedro Hospital in Logroño (La Rioja, Spain). The San Pedro Hospital is a referral care center that provides services to a population of 310,000 inhabitants and serves approximately 95,000 persons in the Emergency Department annually. To collect the data, confidentiality forms of our hospital were signed. Two groups were formed. A first group formed retrospectively by patients aged 75 years or older treated in the Emergency Department for an infectious disease and with PCT on the initial Lab Test during the months of January to September 2013. Within this group we selected patients with probable bacterial infection criteria and sepsis[10] (patients with signs of systemic inflammatory response, elevated acute phase reactants, compatible clinical profile and clearly infectious focus demonstrated in laboratory tests, radiological and/or positive cultures) and excluded patients who were receiving antibiotic treatment. In this group

the differentiation between patients with criteria of sepsis, severe sepsis and septic shock[10] was performed. A second group was formed prospectively by patients aged 75 years or older admitted to the Internal Medicine Department for any non-infectious disease since September 1 to October 3, 2013. PCT was assessed in these patients in the initial Lab test. In this group those patients who presented fever, leukocytosis or positive cultures during hospitalization as well as those treated previously with antibiotics were excluded. PCT was conducted in our laboratory using Electrochemiluminescence and the range established as normal is 0.0–0.5 ng/ml. To assess the validity of the test, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) as well as the reasons for negative, positive likelihood ratio (positive LR and negative LR) and the inverse of the negative likelihood ratio was calculated (I-negative LR) were calculated. Data analysis was performed using SPSS 15.0 and 3.1 Epidat program.

Results

161 patients were included: 95 patients in the group with probable bacterial infection and 66 patients in the group without infection. The main characteristics of both groups are described in Table 1. The mean age was 84 years in both groups and the group with probable infection had 56% of male patients and the group without infection 52%. The major comorbidities in the group with probable bacterial infection were Neurological diseases, Diabetes Mellitus (DM) and Chronic Renal Insufficiency (CRI), while in the group without infection were HF, Neurological disease, DM and CRI. The main diagnoses were pneumonia and Urinary Tract Infection in the group with probable bacterial infection and HF, and cerebrovascular disease (stroke) in the group without infection. In the group with probable bacterial infection, 76% of patients had sepsis criteria (72 patients) and 48% of them fulfilled severe sepsis criteria (48%).

Among patients with probable bacterial infection criteria, 72% (68 patients) had PCT >0.5 ng/ml and 41% (28 patients) of them greater than 2 ng/ml. Meanwhile, in the group without infection, only 8% of patients had PCT >0.5 ng/ml, highlighting that all of them had in common a lower glomerular filtration rate of 60 ml/min/1.73 m^2. The sensitivity and specificity of PCT to determine the presence of probable bacterial infection with 0.5 ng/ml cut off was 72% (95% CI: 62–81) and 92%, respectively, (95% CI: 85–100). The PPV was 93% (95% CI: 82–97) and NPV of 70% (95% CI: 56–80%). The positive LR was 9 and the I-negative LR was 3. The sensitivity and specificity of PCT for the presence of sepsis with 1 ng/ml cut off was 67% (95% CI: 55–78) and 61% (95% CI: 39–83) respectively, while the sensitivity and specificity of PCT for the presence of sepsis with 2 ng/ml cut off was 46% (95% CI: 34–58) and 74% (95% CI: 54–94) respectively.

The main diagnoses in the group of patients with probable bacterial infection were the community-acquired pneumonia (33%), urinary tract infection (31%), sepsis of unknown origin (13%), gastroenteritis (6%), bronchoaspiration (4%), cholangitis (3%) and cholecystitis (2%). It should be noted that 81% of the patients with community-acquired pneumonia had PCT >0.5 ng/ml. Blood cultures were taken in 75 patients (79%) and were positive in only 14 patients. The microbiology findings and the correlation with PCT

Table 1
Clinical and epidemiological properties of elderly patients with and without bacterial infection.

Characteristics	With bacterial infection	No bacterial infection	P value
Age (years)	84. SD 5.8	84. SD 4.5	0.5
Sex (men, %)	56	52	0.5
Admission days (median/IQR)	6/7	6/5	0.1
Comorbidities (%)			
CRI	30	26	0.6
Cirrhosis	3	0	0.1
DM	34	26	0.2
COPD	17	3	0.006
HF	10	44	0.000
IHD	14	21	0.2
Neurological disease	36	29	0.2
Cancer	23	0	0.000
Death	20	5	0.005
Laboratory data			
CRP (mg/L)	140	50	0.000
PCT (ng/ml)	11	0.4	0.001
Leukocytes (cell per mm^3)	14,940	7910	0.000
Creatinine (mg/dl)	2	1.6	0.1
Glomerular filtration (mL/min/1.73 m^2)	42	45	0.4

SD, standard deviation; IQR, interquartile ratio; DM, diabetes mellitus; CRI, chronic renal insufficiency; COPD, chronic obstructive pulmonary disease; HF, heart failure; IHD, isquemic heart failure; CRP, C-reactive protein; PCT, procalcitonin.

are described in Table 2. Median PCT concentrations were 25 ng/ml (SD 41) in patients with positive cultures and 9.2 ng/ml (SD 22) in patients with negative cultures.

Finally, the patients without infection but with PCT >0.5 ng/ml (5 patients) all had GFR <60 ml/min/1.73 m^2. This elevation of PCT is because one-third is eliminated by kidney.

Discussion

The aging of the population causes difficulties in the early diagnosis of infectious processes by the ambiguity and poor expression of symptoms as well as atypical presentations of sepsis,[11] forcing medical staff to have a higher degree of suspicion and to creating the

Table 2
Microbiology findings and the correlation with PCT.

Micro-organism	Patients (%)	PCT values, ng/ml (median)
Blood cultures (14 patients)		
E. coli	6 (44)	35.95
E. coli BLEE	3 (21)	2.77
Pseudomonas aeruginosa	1 (7)	18.79
Stenotrophomona	1 (7)	7.98
Streptococcus mitis	1 (7)	1.84
Providencia stuarti	1 (7)	100
Salmonella tiphimuriun	1 (7)	1.26
Urinary culture		
E. coli	5 (36)	1.87
E. coli BLEE	3 (22)	2.09
Pseudomonas aeruginosa	2 (14)	0.11
Proteus mirabilis	1 (7)	4.58
Candida albicans	1 (7)	0.16
Enterococcus faecium	1 (7)	0.10
Candida parapsilosis	1 (7)	5.60
Other cultures		
Clostridium difficile (abscess)	1	100
Enterococcus faecalis (ulcer)	1	1.49

PCT, procalcitonin.

need of diagnostic tests with a high specificity and good predictive value.

In our study we show that the PCT has a high specificity for the diagnosis of bacterial infection (92%) and acceptable sensitivity but somewhat lower compared to the general population (72% vs 88%). However, comparing our results with other studies in the same population such as Stucker et al.[12] wherein the sensitivity and specificity was 24 and 92%, respectively, and Steichen et al.[13] in which a sensitivity and specificity of 64% and 39% was obtained, respectively, we can highlight that our study provides better results that could reliably be applied in daily clinical practice.

In our study, the PPV and NPV were 93% and 70%, respectively. However it is important to recall that predictive values depend on the prevalence of disease in the general population and so, if we consider that the prevalence of bacterial infection in emergency services is around 10–15%,[14–15] we would have a PPV and NPV of 61% and 95%, respectively, indicating that it is a useful tool for medical staff of the Emergency Department to rule out bacterial infection in those patients with nonspecific symptoms and clinical examination.

On the other hand, the positive likelihood ratio obtained in our study (positive LR of 9) is quite relevant because we have a high probability of finding a positive value of Procalcitonin in patients with bacterial infection compared to those without infection. Moreover the likelihood ratios do not change with the prevalence of the disease, which indicates that PCT can be used interchangeably in the Emergency Department, Internal Medicine, Infectious Diseases, etc. Regarding the capacity of the PCT to establish the risk of sepsis, the best result has been with the cut off of 1 ng/ml, however the values for sensitivity and specificity are low.

In view of the results of our study, we can say that Procalcitonin can be used in the elderly patients reliably for the diagnosis of bacterial infections because it has a good sensitivity and high specificity for the diagnosis of bacterial infection with 0.5 ng/ml cut off.

Conflict of interest

The authors declare no conflict of interest.

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