

Evaluation of C-reactive protein, procalcitonin and the PCR/PCT index as indicators of mortality in abdominal sepsis

Evaluación de la proteína C reactiva, la procalcitonina y el índice PCR/PCT como indicadores de mortalidad en sepsis abdominal

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Abstract

Background: Biomarker combinations can improve timely diagnosis and survival. **Objective:** To determine the usefulness of serum procalcitonin concentration (PCT), C-reactive protein (PCR) and the PCR/PCT index as predictors of mortality. **Method:** Retrospective study of patients diagnosed with abdominal sepsis during the period from April 2017 to February 2018. **Results:** We included 182 cases. In the survivors, the mean PCR was 170 and procalcitonin (PCT) 10.5. In the deceased, the mean of C-reactive protein (CRP) was 328 and that of PCT was 17.6. When applying the student's t-test for independent samples, it was found that these differences were significant for PCR ($p = 0.001$); however, for PCT it was not significant ($p = 0.460$). Afterwards, the PCR/PCT index was studied, as a predictor of mortality, in the deceased cases a PCR/PCT score of 7534 (standard deviation [SD]: 19,303) and for survivors of 538 (SD:805) ($p = 0.001$) was obtained. **Conclusion:** CRP is associated with mortality, serum PCT does not correlate with mortality. The PCR/PCT index seems to be a better indicator to predict mortality in patients with abdominal sepsis due to secondary peritonitis.

Key words: Mortality. Procalcitonin. Reactive protein C. Sepsis.

Resumen

Antecedentes: Las combinaciones de biomarcadores pueden mejorar el diagnóstico oportuno y la supervivencia. **Objetivo:** Determinar la utilidad de la concentración sérica de procalcitonina (PCT), la proteína C reactiva (PCR) y el índice PCR/PCT como predictores de mortalidad. **Método:** Estudio retrospectivo de pacientes con diagnóstico de sepsis abdominal durante el periodo de abril de 2017 a febrero de 2018. **Resultados:** Se incluyeron 182 casos. En los sobrevivientes, la media de los valores de PCR fue de 170 y la de PCT fue de 10.5. En los fallecidos, la media de los valores de PCR fue de 328 y la de PCT fue de 17.6. Al aplicar el estadístico t de Student para muestras independientes se obtuvo que estas diferencias resultaron significativas para la PCR ($p = 0.001$), pero no para la PCT ($p = 0.460$). Posteriormente se estudió el índice PCR/PCT como predictor de mortalidad: en los fallecidos se obtuvo un valor de 7534 (desviación estándar [DE]: $\pm 19,303$) y en los sobrevi-

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vientes de 538 ($DE \pm 805$) ($p = 0.001$). **Conclusión:** La PCR se asocia con la mortalidad, mientras que la PCT no guarda relación con la mortalidad. El índice PCR/PCT parece ser un mejor indicador para predecir la mortalidad en los pacientes con sepsis abdominal por peritonitis secundaria.

Palabras clave: Mortalidad. Procalcitonina. Proteína C reactiva. Sepsis.

Introduction

Sepsis is a life-threatening condition that arises when the host responds to infection and damage to its organs¹. There is an unmet need for diagnostic tools. Although several biomarkers have been proposed, no single clinical or biological sepsis indicator has gained general acceptance². The most widely studied biomarkers in patients with suspected sepsis are C-reactive protein (CRP) and procalcitonin (PCT). Both CRP and PCT are commonly used in clinical practice, but they have limited capacity to distinguish bacterial sepsis from other inflammatory conditions³. PCT advantage lies in its high specificity, with minimal or no increase in viral infection, cardiogenic shock and non-infectious systemic inflammatory response syndrome⁴⁻⁶. CRP is one of the most widely used indicators as acute phase reactant. Serum CRP measurement can help differentiate inflammatory conditions from non-inflammatory diseases, and is useful to control patient disease because its concentration often reflects the response and the need for therapeutic intervention⁷.

Although PCT has an established role as a biomarker in septic patients, diagnostic accuracy of its systematic measurement has been questioned due to variable and inconsistent results depending on disease and infection severity in the studied patient population⁸⁻¹⁶.

In view of the substantial importance of timely diagnosis and accurate treatment of abdominal sepsis, we undertook the present study to determine CRP and PCT diagnostic value. Furthermore, we determined the discriminatory power of combining both these biomarkers, the former as an inflammatory marker and the latter as a marker of bacterial infection, as a single index in the diagnosis of abdominal sepsis.

Method

A retrospective, observational, correlational, analytical, cross-sectional study was carried out to collect data from patients admitted and operated on by the Abdominal Sepsis Comprehensive Care Clinic of

the Emergency Department of General Hospital of Mexico "Dr. Eduardo Liceaga", between April 2017 and February 2018, who were attended to with a diagnosis of abdominal sepsis and who underwent surgery to correct the abdominal infectious focus. Patients of both genders, older than 18 years, whose medical records contained data to determine CRP and PCT values, were selected. Patients with kidney failure, liver failure, metabolic or endocrine diseases, with chronic diseases that could modify the immune status, those with a history of cancer, chronic inflammatory diseases, chronic organ failure, who had received treatment with chemotherapy or radiotherapy, who had taken food supplements or other type of supplements within the previous 6 months, and those who voluntarily were discharged from the hospitalization department were excluded. Patients with death of undiagnosed cause were censored from the study. In all cases, the development of organ failure and mortality was determined, serum CRP and PCT concentration was measured, and the CRP/PCT index was determined. The sample was divided in two groups: survivors and non-survivors. As for organ failure, patients were separated in cases with or without organ failure. Subsequently, the groups were compared using 2 x 2 tables, and frequencies were assessed using Student's t-test for independent samples, with a p-value < 0.05 being established as significant.

Results

One-hundred and eighty-two patients were included (96 women and 86 men), with a mean age of 44.1 years (standard deviation [SD]: ± 18.9). Among the causes that gave rise to abdominal sepsis, acute appendicitis was the main cause (34.6% of cases), followed by lesions of the small intestine (22.5%), colon (7.7%), stomach (1.1%), bile ducts (24.2%), uterus and adnexa (4.9%), pancreas (3.3%), kidney (2.0%) and others (1%). There was localized peritonitis in 128 cases (70.3%) and generalized in 54 (29.7%). Twenty patients (11%) died and 162 (89%) survived. There was organ failure in 104 patients (57.1%). CRP and PCT

measurement showed a mean of 199.8 (SD: ± 175.93) and 9.76 (SD: ± 24.63), respectively. When the usefulness of CRP as mortality predictor was assessed, a mean CRP of 170 (SD: ± 149) was found in survivors, while in the deceased subjects it was 328 (SD: ± 226). When Student's t test was applied for independent samples, differences were found to be significant ($p = 0.001$). When PCT was evaluated as mortality predictor, a mean value of 10.5 (SD: ± 31.5) was obtained for survivors, and 17.6 (SD: ± 32.6) for deceased subjects. These differences turned out to be not significant ($p = 0.460$) when Student's t-test was applied. Subsequently, the CRP/PCT index was examined to assess its role in the discrimination between septic and non-septic subjects, and its role as mortality predictor. For septic cases, a mean CRP/PCT index of 246 (SD: ± 508) was found, and for non-septic cases, 1944 (SD: ± 8155), while in the deceased cases, a CRP/PCT index of 7534 was obtained (SD: ± 19303), and in survivors, 538 (SD: ± 805), with statistically significant differences in both cases ($p = 0.001$) (Table 1).

Discussion

In this study, CRP and PCT values and CRP/PCT index were compared in patients with abdominal sepsis. Both these biomarkers are useful to control patient disease because their concentration often reflects the response to and the need for therapeutic intervention⁷; however, CRP and PCT values were not well correlated in a previous study¹⁷. Another previous study found that PCT was better than CRP in a group of adult patients, with an area under the curve of 0.925 versus 0.677 for sepsis diagnosis. Sequential Organ Failure Assessment Score (SOFA) values were found to be associated with PCT values ($r = 0.73$), while the association with CRP was much lower ($r = 0.41$)¹⁸. Another study in critically ill neonates and children arrived to the same conclusion¹⁹.

In a 2007 meta-analysis, which included 18 studies published between April 1996 and November 2005, it was concluded that PCT does not allow to discriminate between sepsis and systemic inflammatory response syndrome²⁰.

Biomarkers may be more helpful for ruling out sepsis than to diagnose it. Pierrakos and Vincent², in a review of 178 different biomarkers that were assessed in 3370 studies, identified three with a high negative predictive value for ruling out sepsis: PCT (99% with a cut-off value of 0.2 ng/mL)²¹, partial thromboplastin

Table 1. C-reactive protein (CRP), procalcitonin (PCT) and CRP/PCT index values in alive and deceased patients

Variable	Outcome		p	OR
	Alive, Mean (SD)	Deceased, Mean (SD)		
CRP	170 (149)	328 (226)	0.001	0.104
PCT	10.5 (31.5)	17.6 (32.6)	0.460	9.75
CRP/PCT	538 (805)	7534 (19 303)	0.001	5.2
CRP/PCT*	246 (508)	1 944 (8155)	0.001	4.2

OR: odds ratio; SD: standard deviation.

*CRP/PCT index usefulness in septic and non-septic patients.

time waveform (96%)²² and fibrin degradation products (100% for gram-negative organisms-associated sepsis by enzyme-linked immunosorbent assay [ELISA])²³.

In our sample, the organ that most often caused abdominal sepsis was the appendix (44.4% of cases), which correlates with other studies^{24,25}.

In our study there was a mortality of 11%. When the data were analyzed, PCT showed no statistical significance to predict mortality, but blood CRP values and the CRP/PCT index do correlate with death.

We emphasize that CRP/PCT index showed statistical significance when it was compared between septic and non-septic patients.

PCT measurement had a mean of 9.76 ng/mL. Our sample shows high dispersion; this is an observation, and some values do not correlate with the literature, and patients with values > 200 ng/mL were therefore excluded. According to reports in the literature, values higher than 10 ng/mL are indicative of a high probability of severe sepsis or septic shock²⁶. Finally, PCT was not initially reported as a marker of abdominal sepsis, and thus, our study will serve as the basis for further research.

Conclusion

Serum CRP concentrations are associated with mortality in patients with abdominal sepsis, PCT is not related to mortality, and the CRP/PCT index is a better indicator to predict mortality and it is even a tool to differentiate between septic and non-septic patients.

Conflict of interests

The authors declare that there are no conflicts of interest.

Ethical disclosures

Protection of people and animals. The authors declare that no experiments were performed on humans or animals for this research.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained informed consent from the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

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