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BIOMARKERS AND EMPIRIC ANTIBIOTIC THERAPY APPROPRIATENESS IN CRITICALLY ILL SEPTIC PATIENTS: ROLE OF PRESEPSIN

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Introduction. The outcome of critically ill patients with sepsis strongly depends on early and appropriate empiric antibiotic therapy. Therefore, early indicators of the adequacy of first-line antibiotic therapy are of great clinical value. Presepsin (PSEP) is a soluble fragment of the cluster of differentiation (CD) marker protein (CD14) released during monocyte activation upon the recognition of lipopolysaccharide (LPS) from infectious agents. The potential role of presepsin as a marker of appropriateness of antibiotic therapy has been recently suggested by retrospective studies.

Purpose. To evaluate the relationship between PSEP levels and empiric antibiotic therapy appropriateness at an early stage of sepsis in critically ill patients.

Methods. A prospective, observational study on adult critically ill patients with sepsis was performed. Exclusion criteria were trauma and surgery within the first 72 hours, and renal replacement therapy. Age, Charlson Index, APACHE II score, sepsis severity, source and etiology of infection were collected. Moreover, PSEP (PathFast® Presepsin assay for sCD14) levels and Endotoxin Activity (Smartline EAA diagnostic®) were assessed on days 1, 2, and 3. Appropriateness of antibiotic therapy was based on microorganisms isolated in cultures. Data are median and IQ range or number and percentage. Statistical analysis was performed by chi-square and Mann-Withney U tests and by linear regression analysis.

Results. Twenty-five patients with sepsis (28%), severe sepsis (40%) and septic shock (32%) due to pneumonia (60%), intra-abdominal (16%), urinary tract (12%) and bloodstream infections (12%) were enrolled. Patients aged 59 (51-70) years, APACHE II score was 18 (14-24) and Charlson Index was 2 (1-3.5).

On day 1, PSEP levels were 1,402 (924-2,277) pg/ml. In patients who received appropriated first-line antibiotic therapy (n = 16) PSEP levels dropped from 1,701 (1,401-2,419) pg/ml on day 1 to 1,181 (653-1,849) on day 2, and to 1,009 (571-1,511) on day 3 ($p < .05$),

while in those treated by unappropriated therapy PSEP levels were 935 (752-2882) pg/ml on day 1, 1068 (928-3588) on day 2 and 1495 (1031-2767) on day 3. Of note, in patients with EA = > 0.6 on day 1 PSEP levels were 2,105 (1390-6078) pg/ml, as compared to 912 (708-1422) pg/ml observed in patients with EA < 0.6 ($p < 0.05$) (fig).

Moreover, a significant correlation was found between PSEP levels and EA ($r = 0.52$; $p < 0.0001$) (fig).

Finally, in patients with later documented etiology by Gram negatives, PSEP levels on day 1 were 1903 (1370-5720) pg/ml, significantly higher than levels of 875 (689-1308) pg/ml observed in patients with sepsis by Gram positives ($p=0.003$).

Conclusions. Early assessment of presepsin levels may be a useful strategy to monitor the adequacy of the empiric antimicrobial therapy. High PSEP levels at the onset of sepsis, by strongly supporting Gram negatives as etiologic agents, could help clinicians to improve first-line antibiotic therapy appropriateness.