The clinical performance of a point of care assay for measurement of Presepsin in patients with bacteremia

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Background

Sepsis remains to be a cause of the poor outcome. In order to treat sepsis appropriately, it is important to reach diagnosis of sepsis early during the course and start antibiotic treatment.

“Gold standard” of sepsis diagnosis is blood culture but have issues with its sensitivity along with contamination.

Soluble CD 14 subtype (sCD14st: renamed as presepsin) is a N-terminal fragment of CD14, the receptor for lipopolysaccharide (LPS)/LPS binding protein (LBP) complexes.

Presepsin is reported to increase in sepsis patients. Few studies examined presepsin levels among neutropenia or fungemia. In this study, we evaluated the specificity, clinical effectiveness of presepsin in patients with bacterial and fungal infection.
Methods

The study population was 43 sepsis patients in Kochi health sciences center between January 2009 and September 2009. We investigated the clinical performance of presepsin using compact automated enzyme immunoanalyzer PATHFAST (Mitsubishi Chemical Medience Co., Japan) and other biomarkers (procalcitonin: PCT, CRP, WBC) on the day of bacteremia or fungemia. Sepsis was diagnosed according to the American College of Chest Physicians/ Society of Critical Care Medicine (ACCP/SCCM) criteria.
Table 1
Background of 43 cases with blood culture test positive

<table>
<thead>
<tr>
<th>Blood Culture</th>
<th>Gram-Positive bacterial infection</th>
<th>Gram-negative bacterial infection</th>
<th>Fungal infection</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median)</td>
<td>3-88(75)</td>
<td>43-87(70)</td>
<td>63-74(64)</td>
<td>3-87(72)</td>
</tr>
<tr>
<td>Male/Female</td>
<td>10/10</td>
<td>10/9</td>
<td>2/2</td>
<td>22/21</td>
</tr>
<tr>
<td>Admission～Blood Cululture positive Days (median)</td>
<td>1-37(5)</td>
<td>1-134(1)</td>
<td>1-55(6)</td>
<td>1-134(3)</td>
</tr>
<tr>
<td>Focus of infection ①/②/③/④/⑤/⑥</td>
<td>1/4/1/4/2/8</td>
<td>3/6/7/1/1/1</td>
<td>0/0/1/3/0/0</td>
<td>4/10/9/8/3/9</td>
</tr>
<tr>
<td>Infection/Sepsis/Severe sepsis/Septic shock</td>
<td>2/14/4/0</td>
<td>3/12/3/1</td>
<td>0/4/0/0</td>
<td>5/30/7/1</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>19</td>
<td>4</td>
<td>43</td>
</tr>
</tbody>
</table>

①Respiratory ②Intra abdominal ③Urinary tract ④CV catheter ⑤Others ⑥Unknown
Fig. 1
Distribution of presepsin, PCT, CRP and WBC in patients with gram-negative bacterial infection (n=19), gram-positive bacterial infection (n=20) and fungal infection (n=4)
Fig. 2
Distribution of presepsin, PCT, CRP and WBC in patients with infection (n=5), sepsis (n=30) and severe sepsis (n=7)
Fig. 3
Case 1: 50y M. AML Pyrogenic neutropenia (1)

<table>
<thead>
<tr>
<th>CNS</th>
<th>CNS</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCFG</td>
<td>VCM</td>
</tr>
<tr>
<td>CLDM</td>
<td>MEPM</td>
</tr>
</tbody>
</table>

Blood culture positive

CNS: Coagulase Negative Staphylococcus
Fig. 4
Case 2: 3y M. neuroblastoma  Pyrogenic neutropenia (2)

Bacillus cereus

Blood culture positive

- PIPC
- MEPM
- AMK
- ABPC
Fig. 5
Case 3: 64 M. esophageal cancer  Systemic fungal infection

Blood culture positive

Blood culture positive

Candida parapsilosis

Candida parapsilosis

CRP (mg/dL)

Presepsin (pg/mL)

PCT (ng/mL)

WBC (mm3)
Results

1) There were 19 patients with Gram-negative bacterial (GNB) infection, Gram-positive bacterial (GPB) infection in 20 patients and fungal infection in 4 patients, respectively. (Table 1)

2) There were no difference between GNB group, GPB group and fungal infection groups in presepsin levels. (Fig 1)

3) Presepsin levels were only significant difference between sepsis/ infection group and severe sepsis group (p<0.05). (Fig 2)
4) Two pyrogenic neutropenia patients who indicated over 800 pg/ml in presepsin had Bacillus or CNS infection. No changes in PCT level were observed during bacteremia. (Fig 3.4.)

5) We newly observed that presepsin increased in patient with systemic fungal infection (Fig 5).
sCD14-ST (Presepsin)

- Soluble CD14 is a pattern recognition receptor of LPS binding protein. It is considered to activate human endothelial cell / epithelial cells.
  
  Pugine et al Proc Acad Sci USA 1994

- One of the production mechanisms of presepsin is related to the phagocytosis process and cleavage of membrane CD14 with lysozomal enzymes of granulocytes.
  
  Naitoh K et al SEPSIS 2010, Poster P-19

- Serum levels of Presepsin reflect the APACHE II and SOFA scores.
  
  Kojika et al Med Postgra 46. 2010

- The PATHFAST Presepsin assay reveals its result within 17 min using whole blood.
  
  Okamura et al Clinica Chimica Acta 2011
Discussion

We have measured presepsin levels in bacteremia and fungemia patients.

Among the 2 pyrogenic neutropenia cases in this study, only presepsin increased on the day of bacteremia.

Measurement of presepsin level had made it possible to diagnose sepsis at the early stage.

High presepsin level was thought to predict the severity of sepsis in neutropenic and also fungemia patients.
Conclusion

Presepsin was a useful biomarker for the diagnosis of sepsis and reflected clinical severity even in patients with neutropenia and fungemia.