Usefulness of Procalcitonin in the management of Infections in ICU

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CHU Sart Tilman Liège
Procalcitonin

- Peptide 116 AA
- Produced by parenchymal cells during « sepsis »:
  - IL1, TNF, IL6 : stimulators
  - Inf gamma: inhibitor
- Can differentiate bacterial meningitis from viral meningitis (Gendrel CID 1997)
Procalcitonin

- marker of the severity of infection?
- tool for tailoring the antibiotherapy?
- prognostical factor for the outcome?
PCT as a marker of sepsis

- Brunkhorst et al ICM 2000 26: S148-152
  185 consecutive patients with suspicion of sepsis
Harbarth et al AJRCCM 2001;164: 396-402

• 78 consecutive patients with suspicion of sepsis
• SIRS 18, Sepsis 14, Severe sepsis 21, Septic shock 25
• ability to differentiate between SIRS and septic patients: cut-off value of 1.1 ng/ml
• AUC = 0.92
Meta-analysis (Tang et al)  
The Lancet 2007

• Distinction between « Sepsis » et « SIRS »
• 18 studies out of 672 abstracts
• « Procalcitonin cannot reliably differentiate sepsis from other non-infectious causes of SIRS » (se and sp = 71%)
PCT and non infectious states

- Trauma
- Surgery
- Cardiac arrest
- Hypothermia
- Acute coronary syndrome
Decrease in antibiotic consumption

- Respiratory infections (out-of-hospital setting) Christ-Crain Lancet 2004
- Length of treatment in CAP Christ-Crain AJRCCM 2007
- COPD exacerbation Stolz Chest 2007
Christ-Crain et al, Lancet 2004

Procalcitonin

< 0.1 ng/ml: No antibiotic
< 0.25 ng/ml: treatment discouraged
between 0.25 et 0.5 ng/ml: treatment recommended
> 0.5 ng/ml: treatment mandatory
Length of treatment?
Christ-Crain AJRRCM 2006

- Decision to stop treatment according to the same cut-off levels as for the beginning: on day 4, 6 and 8.
How about ICU?

- Nobre AJRCCM 2008, 177: 498-505
  282 patients in severe sepsis
  203 excluded
  79 randomized
  68 analyzed: 31 PCT
  37 Ctrl
Exclusion criteria

• Infections caused by *P aeruginosa*, *A baumannii*, *Legionella*, *Pneumocystis*, BK

• Severe parasitic or viral infections

• Infections requiring prolonged treatment: endocarditis, deep abscesses

• Chronic infections

• Immunocompromised patients
Nobre et al 2008

- Daily measurement of PCT from D0 till D10
- At D5: consider stopping AB if
  PCT dropped more than 90%,
  PCT < 0.25 µg/l, baseline > 1
  PCT < 0.1 µg/l, baseline < 1 µg/l
- If blood culture was positive: at least 5 days of treatment
HR: 1.9 (1.2-3.1)  
$p = 0.009$
• All patients suspected to be infected on admission or during ICU stay (621 patients from 7 ICUs from 5 hospitals)
• PCT used to start the treatment
• PCT used to stop the treatment: when < 20% of the baseline or < 0.5 ng/ml
Procalcitonin levels

- If $< 0.25 \, \mu g/l$: no antibiotics
- If $0.25 < X < 0.5 \, \mu g/l$: treatment discouraged
- If $0.5 < X < 1 \, \mu g/l$: treatment suggested
- If $> 1 \, \mu g/l$: treatment highly encouraged
## Types of patients

<table>
<thead>
<tr>
<th></th>
<th>PCT (307)</th>
<th>Control (314)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>61</td>
<td>62.1</td>
</tr>
<tr>
<td>Medical</td>
<td>90%</td>
<td>89%</td>
</tr>
<tr>
<td>Emergency admission</td>
<td>47%</td>
<td>54%</td>
</tr>
<tr>
<td>Cancer</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Immunodef</td>
<td>15%</td>
<td>16%</td>
</tr>
<tr>
<td>SAPS II</td>
<td>47.1</td>
<td>46.9</td>
</tr>
<tr>
<td>SOFA</td>
<td>8</td>
<td>7.7</td>
</tr>
<tr>
<td>Septic shock</td>
<td>17%</td>
<td>18%</td>
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</table>
## Types of Infection

<table>
<thead>
<tr>
<th></th>
<th>PCT (307)</th>
<th>Contrôles (314)</th>
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<tbody>
<tr>
<td>Pulmonary</td>
<td>71%</td>
<td>74%</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>9%</td>
<td>6%</td>
</tr>
<tr>
<td>Skin and soft tissue</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Intraabdominal</td>
<td>5%</td>
<td>7%</td>
</tr>
<tr>
<td>CNS</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Catheter related</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Primary bacteremia</td>
<td>3%</td>
<td>4%</td>
</tr>
<tr>
<td>Other</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td></td>
<td>PCT</td>
<td>CTRL</td>
</tr>
<tr>
<td>------------------</td>
<td>-----------</td>
<td>-----------</td>
</tr>
<tr>
<td>Death 28 days</td>
<td>21.2%</td>
<td>20.4%</td>
</tr>
<tr>
<td>Death 60 days</td>
<td>30%</td>
<td>26.1%</td>
</tr>
<tr>
<td>Recurrence</td>
<td>6.5%</td>
<td>5.1%</td>
</tr>
<tr>
<td>Superinf</td>
<td>34.5%</td>
<td>30.9%</td>
</tr>
<tr>
<td>LOS</td>
<td>15.9j</td>
<td>14.4 j</td>
</tr>
<tr>
<td>MDR bact</td>
<td>17.9%</td>
<td>16.6%</td>
</tr>
</tbody>
</table>
Antibiotic consumption

- Antibiotic free days
  14.3 days vs 11.6 days \( p < 0.0001 \)

- Days of treatment:
  65.3 days vs 81.2 days/100 hospitalisation days
  \( p < 0.0001 \)
Comments:

- No a posteriori confirmation of the diagnosis
- No data on the number of infections /patient
- No data on the reason for prolonged treatment
- Was the rule the same for all kinds of infections?
- Duration of VAP treatment is now 7-8 days
Diagnosis of infection

- Study in Liège in 505 patients
- Prospective, randomized study
- From April 2008 till December 2008
- 5 ICUs in the same hospital
- Inclusion criteria:
  - patients with LOS > 2 days
  - informed consent
  - > 18 years old
Design of the study

• Measurement of procalcitonin level for each clinically suspected infection.

• PCT results were blinded for 50% patients

• Clinicians were asked to take into account the Procalcitonin level in the intention to treat

• Charts were reviewed by ID specialist at the end of ICU stay
Aim of the study

• Reduction of number of wrong diagnosis?
• Reduction in antibiotic consumption?
<table>
<thead>
<tr>
<th>Types of suspected Infections</th>
<th>PCT group</th>
<th>Ctrl group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory</td>
<td>229</td>
<td>225</td>
</tr>
<tr>
<td>Intraabdominal</td>
<td>33</td>
<td>28</td>
</tr>
<tr>
<td>Urinary</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>Soft tissue</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td>Catheter related</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Others</td>
<td>60</td>
<td>71</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>353</strong></td>
<td><strong>314</strong></td>
</tr>
</tbody>
</table>
Area under ROC curve = 0.6661
## Consumption of antibiotics

<table>
<thead>
<tr>
<th></th>
<th>PCT</th>
<th>Ctrl</th>
</tr>
</thead>
<tbody>
<tr>
<td>DDD/100 ICU days</td>
<td>151%</td>
<td>158%</td>
</tr>
<tr>
<td>days of treatment</td>
<td>62 %</td>
<td>62 %</td>
</tr>
</tbody>
</table>
Diagnosis of VAP
Jung et al ICM 2010

• Proven by quantitative cultures on BAL (cult>10000 CFU/ml)
• Comparison between
  CPIS
  CPIS + previous endotracheal culture
  CPIS + BAL exam
  PCT
• 86 BAL in 57 patients, 56% with pos cult
Diagnostic of VAP
Jung et al ICM 2010

• Bacteriological data
  – From previous endotracheal samples
  – From direct exam of BAL

were more useful than the PCT level
PCT as a prognostic marker

- F Bloos et al Crit Care 2011 multicentre study on respiratory tract infections (CAP, HAP, VAP) requiring mechanical ventilation
- PCT measured daily for 14 days in 175 patients
- Initial PCT, max PCT correlated with maxSOFA and with mortality but in the same proportion as APACHE II did
PCT in severe sepsis

- Karlsson et al Crit Care 2010
- 4-month study in 24 ICUs in Finland
- 242 adult patients with severe sepsis
- 15% had low levels of PCT!
- PCT levels did not differ between hospital survivors and non survivors, but mortality was lower in patients in whom PCT decreased >50% over 72 h.
Figure 4 Change in procalcitonin (PCT) concentration (ΔPCT/PCT on day 0) in hospital survivors and nonsurvivors. Asterisks refer to difference in PCT change. Positive change is defined as decreasing concentrations.
Conclusions

• PCT measurements cannot replace the infectious diagnostic strategy, nor the evaluation of severity
• PCT has a place in the emergency room; in the ICU, the data are still limited
• The available studies allow us to treat patients for a shorter time
• To become part of the routine blood analysis, cost of measurement should be much cheaper.