New sepsis cocktail – thanks for the new marik protocol

Mini Review

Sepsis mortality is still remarkably high and according to the latest surviving sepsis campaign guidelines, sepsis related mortality is around 15% while septic shock is associated with 40% in-hospital mortality.1 Thousands of interventions have been tried over decades failed to improve sepsis survival.

Even drugs that was able to reduce mortality in one study, failed to do so in another study. The best example was the recombinant activated protein C, which didn’t show any survival benefits in PROWESS-Shock trial while was associated with decreased mortality in PROWESS Trial.2,3

Also Annane et al.,4 able to prove that sepsis is associated with high incidence of relative adrenal insufficiency and usage of steroid in septic shock was associated with significant reduction in mortality.4 While CORTICUS and ADRENAL Trials failed to reveal any benefits related to using steroid in septic shock.5 So it sounds that, the problem is the difficulty to find a magic drug to work effectively alone in septic shock.

Dr. Marik and his group used a very intelligent idea. They used mixture of drugs assuming their perfect synergism and looked at their effect on sepsis mortality.7

Study design

They used a retrospective approach to compare the outcome of their cocktail in sepsis and septic shock before and after clinical study.

a) Control Group: received a standard of care.

b) Treatment Group: received IV Vitamin C, Thiamine and Hydrocortisone within 24 hours of their admission to ICU.

Outcome

i. Primary outcome: Hospital mortality.

ii. Secondary outcome:

i. Mean duration of vasopressor therapy.

ii. Requirement for renal replacement therapy in patients with AKI.

iii. PCT clearance (initial PCT minus PCT at 72 hours divided by the initial PCT multiplied by 100).

iv. The 72-hour delta SOFA score (difference between subsequent scores).
**Marik cocktail**

i. All given Intravenous.

ii. Vitamin C and Thiamine given for 4 days or until ICU discharge.

iii. Hydrocortison given for 7 days or until ICU discharge.

**Results**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Control Group</th>
<th>Treatment Group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital Mortality</td>
<td>19/47 (40.4%)</td>
<td>4/47 (8.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICU LOS (days)</td>
<td>4 – 10</td>
<td>3-5</td>
<td>------</td>
</tr>
<tr>
<td>Time on Vasopressors (hrs)</td>
<td>54.9(+/-28.4)</td>
<td>18.3(+/-9.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CRRT for AKI</td>
<td>11/30 (33%)</td>
<td>3/31(10%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Delta SOFA at 72hrs</td>
<td>0.9 (+/-2.7)</td>
<td>4.8 (+/-24)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Delta PCT Cleanance at 72hrs</td>
<td>33.97(62.4 – 64.3)</td>
<td>86.47 (80.1 – 90.8)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Conclusion**

It sound that the Marik cocktail works perfectly in sepsis based on the study result, which showed that early use of IV Vitamin C, Thiamine and Corticosteroids may be useful in reducing in-hospital mortality as well as preventing organ dysfunction e.g. AKI requiring CRRT and speed up shock reversal in patients with sepsis/septic shock. Despite the result is very promising but it has to be taken very carefully because of many limitations in the study which includes, small sample size, retrospective, single center and non RCT. So we are awaiting to see soon a large prospective RCT to confirm that sepsis cocktail does work effectively without any safety concerns.

**References**