Immune enhancing enteral nutrition reduced mortality and acquired infections in intensive care unit patients with sepsis


**QUESTION:** Among patients in the intensive care unit (ICU) with sepsis, is immune enhancing enteral feeding more effective than high protein enteral feeding for reducing mortality and subsequent episodes of bacteraemia?

**Design**
Randomised (unclear allocation concealment), unblinded controlled trial.

**Setting**
6 hospitals in Spain.

**Patients**
181 patients > 14 years of age who were admitted to the ICU, had sepsis (positively cultured or clinically diagnosed infection), and had an Acute Physiology and Chronic Health Evaluation (APACHE) II score ≥10. Exclusion criteria were pregnancy, previous radiotherapy, previous treatment with immune enhancing enteral or parenteral nutrition, treatment with immuno-suppressive drugs, AIDS, neoplasia, or metastases. Follow up was 97% (mean age 56 y, 73% men).

**Intervention**
Patients received enteral feeds by nasoenteric, nasogastric, gastrostomy, or jejunostomy tube. Feeds were started within 36 hours of the diagnosis of sepsis, and total intake of calorific needs was to be reached by the fourth day. 94 patients were allocated to an immune enhancing formula (Impact), which was enriched with arginine, mRNA, and n-3 fatty acids from fish oil. 87 patients were allocated to a high protein, control formula, Preciote Hiperproteico (Nutrodrip Protein). Both formulas had similar calorific distributions.

**Main outcome measures**
Mortality, acquired bacteraemia and nosocomial infection, digestive complications, and length of ICU stay.

**Main results**
Analysis was by intention to treat. Patients who received immune enhanced nutrition had a lower mortality rate and fewer acquired bacteremias than patients who received the control formula (table). Although the groups did not differ for the number of acquired nosocomial infections, fewer patients in the immune enhanced group acquired ≥1 nosocomial infection. The groups did not differ for digestive complications or ICU length of stay.

**Conclusion**
Immune enhancing enteral nutrition, compared with high protein enteral nutrition, reduced mortality and acquired infections in intensive care unit patients with sepsis.

**COMMENTARY**

The study by Galbán et al looks at several important patient outcomes in a very specific population of critically ill patients. The study focuses on the outcomes of mortality, bacteraemia, nosocomial infection, and length of ICU stay among septic patients receiving immune enhanced enteral nutrition compared with septic patients receiving non-immune enhanced enteral nutrition. In this particular population, the high cost of enhanced enteral nutrition is justified and balanced by the severity of the patient's illness. Whereas research has not settled the debate about the efficacy of immunonutrition, this study initiates a move in a positive direction.

The participants were from 6 hospitals in Spain, but given similarities among human nutritional needs and immune processes, it would not seem that the findings of this study would be limited geographically. One limitation, however, may be related to geographical variation in factors that determine length of ICU stay but may not be related to patient condition. Measurement of mortality and infection is much more objective, and these were the measures that yielded significant results.

As a multisite, randomised, experimental design, the study is strong. The sample inclusion criteria were specific and clear. Two issues that warrant consideration are that follow up did not extend past discharge from the ICU, and the physician investigators who provided care for the patients were not blinded to the type of feeding.

The results are relevant to ICU nurses who care for patients with sepsis. This study illuminates another path toward the enhancement of the immune systems of critically ill patients to improve outcomes related to mortality and infection rates. Given the finding of no group differences in the incidence of gastrointestinal complications, there is certainly no harm in enhancing a patient's enteral feedings. Although study limitations may have exaggerated the results, even if patient outcomes can be improved only incrementally, this intervention warrants thorough discussion and consideration by the healthcare team.

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<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Immune enhancing formula</th>
<th>Control formula</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>19%</td>
<td>32%</td>
<td>41% (1 to 65)</td>
<td>8 (4 to 637)</td>
</tr>
<tr>
<td>Acquired bacteraemia</td>
<td>8%</td>
<td>22%</td>
<td>64% (21 to 84)</td>
<td>8 (4 to 28)</td>
</tr>
<tr>
<td>≥1 acquired nosocomial infection</td>
<td>6%</td>
<td>20%</td>
<td>71% (29 to 89)</td>
<td>8 (5 to 23)</td>
</tr>
</tbody>
</table>

*Abbreviations defined in glossary: RRR, NNT, and CI calculated from data in article.*