Endogenous insulin secretion and suppression during and after sepsis in critically ill patients: Implications for TGC protocols

C.G. Pretty¹, P.D. Docherty¹, J. Lin², L. Pfeiffer², U. Jamaludin¹, G.M. Shaw³, A.J. Le Compte¹ & J.G. Chase¹

1. Centre for Bioengineering, Department of Mechanical Engineering, University of Canterbury
2. Christchurch School of Medicine and Health Sciences, University of Otago, New Zealand
3. Department of Intensive Care Medicine, Christchurch Hospital, New Zealand

INTRODUCTION

OVERVIEW:
Insulin infusions over 2 U/hr have been shown to suppress endogenous insulin secretion in healthy subjects 30-45% [1]. Most tight glycemic control (TGC) protocols deliver insulin via infusion. This study examines the impact of bolus delivery of insulin in TGC on the endogenous insulin secretion of critically ill patients.

This study uses data collected prospectively from 16 patients enrolled in a clinical trial studying sepsis at the Christchurch Intensive Care Unit (ICU). C-peptide measurements taken during the study can be used to estimate endogenous insulin secretion following a bolus of insulin.

GOALS:
A better understanding of the body’s response to exogenous insulin delivery during critical illness will help improve the performance and safety of TGC protocols. Bolus insulin may provide more effective TGC as unsuppressed endogenous insulin supplements the exogenous dose, possibly lowering the required doses and the risk of hypoglycemia.

METHODS

Each patient had two sets of blood samples taken. The first set of samples were taken at the commencement of the SPRINT TGC protocol. The second set were taken when the SIRS score was consistently below 2. Bolus size was dictated by the SPRINT protocol, but was in the range 2-5 units.

RESULTS

SUPPRESSION:
Median (IQR) level of suppression during the first sampling period (sepsis samples) was 1.03 [0.95-1.20], showing little or no suppression for most patients during suspected sepsis. Suppression during the post-sepsis, recovery samples was 0.89 [0.78-1.07], indicating limited suppression outside c-peptide assay error of 9%.

On an individual patient basis there is no definite tendency towards increased suppression with the recovery samples. Thus, these results reflect a shift in the overall cohort distribution.

PATIENTS

16 patients from the Christchurch Hospital ICU enrolled in a prospective clinical trial studying sepsis each had two sets of blood samples assayed for insulin and C-peptide. Patients were included in the study if they met all of the following criteria:

- Age ≥ 16 years.
- Expected survival ≥ 72 hours.
- Expected ICU length of stay ≥ 48 hours.
- Entry to the SPRINT TGC protocol (2 sequential BG measurements ≥ 8 mmol/L).
- Suspected sepsis OR SIRS score ≥ 3.

Where suspected sepsis indicates that they received treatment for sepsis with antibiotics. Patients with a known history of diabetes were subsequently excluded from this analysis.

The table below shows an outline of the patient characteristics.

<table>
<thead>
<tr>
<th>N</th>
<th>16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>66 [56-74]</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>7/9</td>
</tr>
<tr>
<td>APACHE II score</td>
<td>22 [16-26]</td>
</tr>
<tr>
<td>Confirmed sepsis</td>
<td>81%</td>
</tr>
<tr>
<td>ICU mortality</td>
<td>25%</td>
</tr>
</tbody>
</table>

CONCLUSIONS

- Bolus delivery of insulin appears to cause limited suppression of endogenous insulin secretion, particularly during the early stages of critical illness with suspected sepsis.
- Bolus insulin may provide more effective TGC as unsuppressed endogenous insulin supplements the exogenous dose, possibly lowering the required doses and the risk of hypoglycemia.
- These results suggest a comparative study between bolus and infused insulin in TGC.

REFERENCES