Pancreatic Insulin Secretion in Critically Ill Patients

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Objective
- Glucose-insulin pharmacokinetic-pharmacodynamic (PK-PD) models can be used for improved glycemic control of critically ill patients.
- A key component of glucose-insulin PK-PD models is pancreatic insulin secretion.
- There is limited data in the literature quantifying insulin secretion in critically ill patients at physiologic levels.
- Using prospectively collected data, this study creates a model of pancreatic insulin secretion in critically ill patients to improve glucose-insulin system modeling.

Subjects
- 19 patients from the Christchurch Hospital ICU enrolled in a prospective clinical trial studying sepsis.
- 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.
  - Suspected sepsis or SIRS score ≥ 3.
- No diagnosed Type I diabetic patients were included.

Samples
- Each patient had two sets of arterial blood samples taken, where each set consisted of 4 separate samples.
  - The first set of samples was taken at the commencement of the SPRINT TGC protocol.
  - The second set was taken when the patient consistently met less than 2 of the SIRS criteria
- Insulin and C-peptide concentrations were determined using immunometric assays.
- Blood glucose levels were measured with a bedside glucometer at t = 0 and t = 60 mins as per normal clinical practise.

Methods
- Pancreatic insulin secretion rates were deconvolved from C-peptide data using the model and population constants of van Cauter et al.
- Data from literature suggested a maximum secretion rate of 16U/hr.
- A minimum rate of 1U/hr was also adopted.
- Model fitting was performed by minimising the sum of the geometric means of the squared deviations in each dimension

Results
- The best model for insulin secretion, in terms of both fit to data and simplicity is the 1-dimensional model based on blood glucose (BG) concentration alone.
- The clear separation between non-diabetic (ND) and T2DM patients suggests two separate models for insulin secretion (Uen):
  - ND: \( U_{en} = 893 \times BG - 2996 \) constrained to [1000-16000] mU/hr
  - T2DM: \( U_{en} = 296 \times BG - 1644 \) constrained to [1000-16000] mU/hr
- Model fits achieve coefficients of variation of \( R^2 = 0.61 \) and \( R^2 = 0.69 \) for ND and T2DM, respectively.
- The model slopes compare well with published data for healthy and diabetic individuals

<table>
<thead>
<tr>
<th>N</th>
<th>19</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>68 [57-75]</td>
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<tr>
<td>Gender (M/F)</td>
<td>10/9</td>
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<tr>
<td>APACHE II score</td>
<td>22.0 [18.3-26.8]</td>
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<tr>
<td>Confirmed sepsis</td>
<td>79%</td>
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<tr>
<td>Hospital mortality (L/D)</td>
<td>13/6</td>
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<tr>
<td>Diagnosed T2DM</td>
<td>3</td>
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</tbody>
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Endogenous secretion

Renal clearance

Plasma

Interstitial fluid

2-compartment C-peptide model

Sampling scheme