C-peptide Correction Method to Determine Exogenous Insulin Levels in Pharmacokinetic Studies Using Technosphere® Insulin

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ABSTRACT

Introduction: Determining the concentration of exogenous insulin in pharmacokinetic studies usually requires the use of a potassium insulin or an insulin analog (type 1: aspart, degludec, glargine, or type 2: exenatide), but costs and methods differ. The objective of this study was to explore the use of C-peptide as a biomarker for determination of exogenous insulin. The relationship between C-peptide and insulin is one-to-one, and the C-peptide:insulin relationship is considered to be an exogenous insulin marker. C-peptide:insulin ratio is a useful tool for determining the presence of exogenous insulin.

Methods: Data from human trials were used to evaluate the C-peptide:insulin relationship. The relationship was analyzed with a linear mixed effect model using data from 60 healthy volunteers and subjects with COPD, and 1 study evaluated subjects with type 2 diabetes who inhaled GLP-1 as well as hepatic insulin extraction. The relationship was observed only with endogenous insulin, either prior to or during an insulin clamp procedure using a rapid acting insulin analogue, which can be distinguished from native human insulin in formulations is difficult for many reasons. Evaluation of subjects with type 1 diabetes requires clinical research centers and methods.

Results: The C-peptide:insulin relationship was analyzed with a linear mixed effect model where the fixed effects were the time points, and methods. The relationship was analyzed with a linear mixed effect model using data from 60 healthy volunteers and subjects with COPD, and 1 study evaluated subjects with type 2 diabetes who inhaled GLP-1 as well as hepatic insulin extraction. The relationship was observed only with endogenous insulin, either prior to or during an insulin clamp procedure using a rapid acting insulin analogue, which can be distinguished from native human insulin in formulations is difficult for many reasons. Evaluation of subjects with type 1 diabetes requires clinical research centers and methods.

Conclusions: The relationship between C-peptide and insulin has been explored to determine the calibration of insulin levels. However, in vivo studies may also be used to determine the C-peptide:insulin relationship. The interindividual variability of the C-peptide:insulin relationship (\(\beta\)-cell function) is the C-peptide:insulin relationship in the context of severity and stage of disease, and the evaluation of hepatic insulin extraction and methods.

METHODS AND MATERIALS (cover)

Table 1. Parameter Estimates of the Insulin C-peptide Relationship

<table>
<thead>
<tr>
<th>Parameter Estimates</th>
<th>Time 1</th>
<th>Time 2</th>
<th>Time 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>3.80 (0.286)</td>
<td>0.69 (0.57)</td>
<td>1.43 (0.41)</td>
</tr>
<tr>
<td>Slope</td>
<td>16.4% (0.121)</td>
<td>15.6% (0.121)</td>
<td>14.8% (0.121)</td>
</tr>
</tbody>
</table>

C-peptide: Insulin

RESULTS (cover)

Study 1: 12 healthy volunteers

The results of this method are shown for Table 2.

Study 2: 20 subjects with COPD and 20 Subjects without COPD

The results of this method are shown for Figure 6 which displays all of the C-peptide:insulin relationship.

Study 3: 20 subjects with type 2 diabetes

The results of this method are shown for Figure 6 which displays all of the C-peptide:insulin relationship.

Study 4: 11 healthy volunteers given insulin and C-peptide

The results of this method are shown for Figure 6 which displays all of the C-peptide:insulin relationship.

CONCLUSIONS

The relationship between C-peptide and insulin has been explored to determine the calibration of insulin levels. However, in vivo studies may also be used to determine the C-peptide:insulin relationship. The interindividual variability of the C-peptide:insulin relationship (\(\beta\)-cell function) is the C-peptide:insulin relationship in the context of severity and stage of disease, and the evaluation of hepatic insulin extraction and methods.

References


Figure 6: C-peptide:Insulin relationship in humans. Insulin vs C-peptide plotted by subject demonstrating the inter-individual variation for slope and intercept. The results of this method are shown for Figure 6 which displays all of the C-peptide:insulin relationship.