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Model of the Glucose-Insulin-Glucagon Dynamics after Subcutaneous Administration of a Glucagon Rescuer Bolus in Healthy Humans

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Abstract

In healthy individuals, insulin and glucagon work in a complex fashion to maintain blood glucose levels within a narrow range. This regulation is distorted in patients with diabetes. The hepatic glucose response due to an exogenous glucagon bolus depends on the current insulin concentration and thus endogenous glucose production (EGP) can no longer be determined. Thus knowledge about the in vivo dynamics of glucagon and insulin in the model of the glucose-insulin-glucagon dynamics in man including secretion of EGP.

1 Background

There is currently no consensus on a model describing the endogenous glucose production (EGP) as a function of glucose. Recent studies suggest a multiplicative effect of insulin and glucagon on EGP [1].

The pharmacokinetics (PK) model is a one-compartment model with fixed basal EGP. I(t) and q(t) are the masses of glucagon (pg) in the accessible and non-accessible compartments, respectively. The concentration of both hormones in plasma. Furthermore, literature suggests an upper limit to EGP.

3 Methods

The pharmacokinetics (PK) model is a one-compartment model with first order absorption.

\[
\frac{dC(t)}{dt} = -\frac{C(t)}{V} + \frac{F(t)}{V}
\]

\[
\frac{dI(t)}{dt} = -\frac{I(t)}{b} + \frac{q(t)}{b}
\]

\[
\frac{dq(t)}{dt} = \frac{q(t)}{a} - \frac{q(t)}{a}
\]

The PK model is the parameter distributions enable simulations of glucagon bolus in healthy male subjects weighing 84.5 ± 7.4 kg (mean ± SD). The PK model is the parameter distributions enable simulations of glucagon bolus in healthy male subjects weighing 84.5 ± 7.4 kg (mean ± SD). The PK model is the parameter distributions enable simulations of glucagon bolus in healthy male subjects weighing 84.5 ± 7.4 kg (mean ± SD). The PK model is the parameter distributions enable simulations of glucagon bolus in healthy male subjects weighing 84.5 ± 7.4 kg (mean ± SD). The PK model is the parameter distributions enable simulations of glucagon bolus in healthy male subjects weighing 84.5 ± 7.4 kg (mean ± SD).

Table 1: Average PK and PD parameter estimates and 95% confidence intervals. *Fixed parameter.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>F(t)</td>
<td>0.0005</td>
<td>-0.0012 to 0.0022</td>
<td>0.30</td>
</tr>
<tr>
<td>b</td>
<td>12</td>
<td>6 to 18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>a</td>
<td>329</td>
<td>10 to 550</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

4 Results

Figure 1: PK model fit of glucose with 95% confidence interval (blue) for each of the ten subjects.

5 Conclusions

The PK model and the parameter distributions enable simulations of glucagon bolus in healthy male subjects weighing 73.4 kg (mean ± SD). The PK model and the parameter distributions enable simulations of glucagon bolus in healthy male subjects weighing 73.4 kg (mean ± SD). The PK model and the parameter distributions enable simulations of glucagon bolus in healthy male subjects weighing 73.4 kg (mean ± SD). The PK model and the parameter distributions enable simulations of glucagon bolus in healthy male subjects weighing 73.4 kg (mean ± SD). The PK model and the parameter distributions enable simulations of glucagon bolus in healthy male subjects weighing 73.4 kg (mean ± SD). The PK model and the parameter distributions enable simulations of glucagon bolus in healthy male subjects weighing 73.4 kg (mean ± SD).

References


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