Glucose and Insulin Responses Modeling

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Introduction: Objectives

• To model the glucose and insulin response
• To evaluate influence on the extreme condition on body glucose level
  • Reduced or No insulin production
  • Reduced or No Liver function
  • Reduced or No Kidney function
  • Different insulin delivery methods

• Basic model: www.Aida.org
Introduction: Model

- Single glucose pool
  - One compartment model

- Glucose enters via:
  - Gut absorption,
  - Hepatic glucose production,

- Glucose is removed:
  - Insulin independent glucose utilization
  - Insulin dependent glucose utilization,
  - Exertion of glucose by the kidney,

\[ \frac{dG}{dt} = \frac{G_{in}}{V_g} + \frac{NHGB}{V_g} - \frac{G_{out}}{V_g} - \frac{G_{ren}}{V_g} \]
Model: Gut
Model: Gut

- One compartment model with constant glucose supply

\[
\frac{dG(t)_{\text{gut}}}{dt} = G(t)_{\text{empt}} - k_{\text{abs}} G(t)_{\text{gut}}
\]
Model: Utilization
Model: Utilization

- **Insulin-independent**
  - red blood cells (RBCs)
  - the central nervous system (CNS),

- **Insulin dependent**
  - the liver
  - periphery
Model: Liver
Model: Liver

- Hepatic glucose balance
  - liver glucose production (+)
  - liver glucose utilization (-)

- Function of the
  - plasma insulin level
  - arterial glucose concentration
  - finite capacity of the liver
Model: Kidney

- Excretion from the blood to urine
  - renal threshold (RTG)
  - creatinine clearance rate (CCR)
Model: Insulin Input
Model: Insulin Input

- Insulin input models:
  - Healthy patient
    - glucose threshold (gT)
    - insulin production rate (IPR)
  - Injection of insulin
    - one compartment method with delay
  - Insulin pump with constant drip
Results: Normal Subject

- Healthy patient
  - Input: 20g/6h
  - Liver buffer: 100g - CH initial 50g
  - CH from gut: 160.0g
  - CH to peripheral: 138.4g
  - CH to liver: 21.6g
  - excreted: 0.0g
  - delivered insulin: 2374mU
**Results:** Normal Subject

- **Effect of finite liver capacity**
  - Input: 20g/6h
  - Liver buffer: 15g-CH initial 7.5
  - CH from gut: 160.0g
  - CH to peripheral: 150.0g
  - CH to liver: 10.0g
  - Excreted: 0.0g
  - Delivered insulin: 2452mU

- **Note:** Liver get full
Results: Normal Subject

- **Effect of finite liver capacity**
  - Input: 90g/6h
  - Liver buffer: 100g-CH initial 50g
  - CH from gut: 720.0g
  - CH to peripheral: 659.3g
  - CH to liver: 60.6g
  - Excreted: 0.0g
  - Delivered insulin: 7839mU

- **Note:** Liver get full
Results: No Insulin production

- Input: 20g/6h
- Liver buffer: 100g-CH initial 50g
- CH from gut: 160.0g
- CH to peripheral: 6.7g
- CH to liver: 57.6g
- Excreted: 95.4g
- Delivered insulin: 0.0mU

Note: Kidney excretion occur. Liver full.
Results: No Insulin production

- Constant drip 49.4mU/h
  - Input: 20g/6h
  - Liver buffer: 100g-CH initial 50g
  - CH from gut: 160.0g
  - CH to peripheral: 137.9g
  - CH to liver: 22.6g
  - excreted: 0.0g
  - delivered insulin: 2371mU

Note: Look Normal :)
Results: No Insulin production

- Constant drip 149.4mU/h
  - Input: 20g/6h
  - Liver buffer: 100g-CH initial 50g
  - CH from gut: 160.0g
  - CH to peripheral: 214.9g
  - CH to liver: -54.3g
  - Excreted: 0.0g
  - Delivered insulin: 7171mU

Note: ouch!!
Results: No Insulin production

- Injection: 40U/6h 20 min before meal
- Input: 20g/6h
- Liver buffer: 100g-CH initial 50g
- CH from gut: 160.0g
- CH to peripheral: 126.7g
- CH to liver: 32.9g
- excreted: 0.0g
- delivered insulin: 2503mU
Questions

\[ \frac{dI}{dt} = k_1 I_a - k_2 I \]

\[ \frac{dG_{\text{gut}}}{dt} = G_{\text{empt}} - k_{\text{gabs}} G_{\text{gut}} \]

\[ \frac{dG}{dt} = G_{\text{in}} + NHGB \]

\[ G_{\text{out}} = G_{\text{in}} \]

\[ G_{\text{rent}} = \frac{G_{\text{c}} S_F \cdot I + G_I}{G_x K_m + G} \]

\[ I = \begin{cases} I_{\text{PR}} & G > gT \\ 0 & \text{elsewhere} \end{cases} \]

\[ \frac{dI_a}{dt} = \frac{I_{\text{abs}}}{V_i} - k_e I_a \]