INSULIN CLEARANCE DURING HYPER-INSULINEMIA EUGLYCEMIA THERAPY

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Abstract

Patients with post-operative cardiogenic shock can be treated with very high insulin doses (HIET). A model-based HIET protocol should allow safe and effective treatment. This study shows that modeled plasma insulin clearance should be decreased during the first 10 hours of HIET then largely increased. This insulin clearance increase could result from both elimination via the urine and storage in the interstitial space. These findings should lead to new clinical protocols, as HIET should not be applied for more than 10 hours.

Keyword(s): clinical engineering – modeling of physiological systems

1 Introduction

Insulin has beneficial effects on cardiac function at very high doses. Hyper-Insulinemia Euglycemia Therapy (HIET) uses these insulin effects to treat patients with post-operative cardiogenic shock. During HIET, insulin infusions can reach 1 U/kg/h and exogenous glucose is thus required to avoid hypoglycemia but must also be limited to avoid gluco-toxicity effects. Clinical application of HIET is currently empirical, the hypoglycemic risk is high and controlling high insulin dosing can be very difficult as patient metabolism and insulin sensitivity are variable during the therapy. Our work aims to develop a model-based protocol to optimize HIET interventions (exogenous insulin and dextrose dosing), enabling a safe and effective therapy.

2 Method

The model of the glucose-insulin system is adapted for HIET patients, especially the plasma insulin clearance [1]. Data from 5 patients treated with HIET in Liege University Hospital (Belgium) include insulin data (exogenous insulin input, measured plasma and urine insulin concentrations), glycemic data (blood glucose concentrations) and exogenous dextrose input data (enteral and parenteral nutrition, medication).

3 Results

Comparison of simulated and measured plasma insulin concentrations shows that modeled plasma insulin clearance should be reduced during the first 10 hours of HIET, then increased significantly (Fig.1). To better capture observed patient behavior, we assumed that renal clearance initially saturates and de-saturates after 10 hours. At this point, a supplemental plasma insulin clearance term was introduced into the model. Figure 1 also shows a sudden increase in measured plasma insulin concentration (from 208.7 to 18880 mU/L) when HIET was stopped (t=66h), suggesting storage in some remote compartment. Insulin concentrations in urine were 262.5 mU/L (t=23h10), 444.8 mU/L (t=36h10) and 27.25 mU/L (t=84h10), suggesting that insulin is eliminated via the urine.

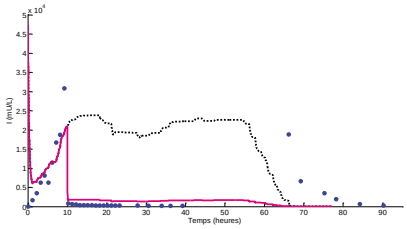

Figure 1 – Measured (blue circles), simulated (black curve) and re-simulated (pink curve) plasma insulin concentration.

4 Conclusion

The adapted model better captures HIET patient behavior. After 10 hours of HIET, insulin clearance increases, normalizing plasma insulin concentration. We have shown that insulin is eliminated via the urine but possibly also stored, most likely in the interstitial space. More data should validate these findings but we can say that HIET becomes ineffective and should be stopped after 10 hours. Thus, HIET clinical protocols should be adapted.

References

[1] Lin J. *et al*. A physiological Intensive Control Insulin-Nutrition-Glucose (ICING) model validated in critically ill patients. *Comput Methods Programs Biomed*, 102(2), 192-205, 2011.