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Modeling of glucose-insulin system in patients on dialysis

One of the most common causes of end-stage renal disease (ESRD) worldwide is diabetes mellitus. According to the US Renal Data System in 2005 above 44% of new ESRD patients were diabetics. The process of regulation of glucose concentration in blood is complicated and can be substantially affected by uremia and dialysis, which both may have an impact on secretion and clearance of glucose and insulin, and on insulin resistance leading to hypo- or hyperglycemia. Low levels of blood glucose may cause shock and death, while too high levels are toxic. Thus, it is essential that glucose levels must be tightly regulated and an analysis of the effects of dialysis (peritoneal dialysis with glucose-based solution and hemodialysis) on plasma glucose and insulin concentration is of great importance. A mathematical model describing glucose-insulin regulation was based on the models proposed by Stolwijk and Hardy (1974) and Tolic et al (2000). Two different sources of glucose were taken into account: hepatic glucose production and an external source (e.g. food digestion, intravenous glucose infusion or transport between dialysis fluid in the peritoneal cavity and blood). There are three types of glucose utilization: 1) glucose leaves blood to enter most cells through facilitated diffusion (insulin independent glucose utilization), 2) in certain types of cells (e.g. muscle and adipose tissue) insulin helps to stimulate the facilitated diffusion process (insulin dependent glucose utilization), 3) glucose can be also excreted by the kidneys. As regards insulin, two sources are taken into account: pancreatic insulin production controlled by the glucose concentration and external source of insulin (e.g. injection). Insulin is degradated through a reaction involving the insulinase at a rate proportional to insulin concentration in blood. All these assumptions are used in the mass balance equation describing the blood concentration changes of glucose and insulin during dialysis (peritoneal dialysis and hemodialysis). The clinical parameters of the glucose-insulin system, insulin sensitivity index and glucose effectiveness at basal and zero insulin (GEZI) were also estimated using clinical data from: 1) six hour

peritoneal dialysis dwells with glucose 3.86% solution performed in 13 stable, fasting, non-diabetic patients, and 2) hemodialysis with a bolus of 33% glucose infused into blood in 8 stable, non-diabetic maintenance hemodialysis patients during their regular dialysis treatment. Computer simulations based on the model were performed for each patient and each dialysis session to estimate the model parameters. The mean values and standard deviations of the parameters were calculated and compared for both studies. There were statistically significant differences between hemodialysis and peritoneal dialysis patients especially in the parameters describing insulin regulation such as the insulin catabolism rate and the maximal level of insulin generation. Clinical and modeling results demonstrated high interpatient variability in glucose and insulin concentration profiles during a peritoneal dwell and during hemodialysis, and in the parameter values of the glucose-insulin system. The proposed model was able to adequately reproduce the clinical data on glucose and insulin transport and plasma levels and to distinguish patients with and without abnormalities in glucose regulation.