Optimizing dialysate bicarbonate concentration during hemodialysis by mathematical modeling
Description for the general public

The normal human body contains two kidneys that filter blood to remove excess fluids and waste products; they also control the concentrations of ions within the body and maintain blood acidity at the value optimal for most body functions. When the kidneys no longer function appropriately, the individual must either undergo a kidney transplant or perform regular dialysis treatments in order to stay alive. The most common type of dialysis treatment is hemodialysis, usually performed in a dialysis center or hospital. Such treatments are typically 4-hours long, three times per week and consist of pumping blood outside the body through a device containing 10,000 fluid- and toxin-permeable, hollow-fiber membranes (called a hemodialyzer) where the blood is cleansed. Toxins are removed by diffusion from the blood by pumping a toxin-free, clean fluid containing largely ions (called dialysate) on the other side of the hollow-fiber membranes.

Hemodialysis treatments do not replicate all of the functions of normal kidneys and are only performed 12 hours per week instead of continuously like normal kidneys. Indeed, the lifespan of patients with kidney failure who require treatment by routine hemodialysis is only slightly better than patients with lung cancer and much worse than the general population. Improved treatment methodologies and therapy prescriptions will likely allow the improved survival of and better quality of life for hemodialysis patients.

One significant limitation with current hemodialysis prescriptions is the inability of this therapy to maintain blood hydrogen ion (acid) and bicarbonate (base) concentrations in the body within the normal range, resulting in the inhibition of essential biochemical systems. For the patient, the loss of kidney function means an increase in blood acidity, called acidosis. To help correct this imbalance in the acid-base chemistry, the dialysate contains bicarbonate anions in high concentration so they are administered to the patient during hemodialysis. Bicarbonate is the most important body buffer solute that binds hydrogen ions (the main source of acidity) and thus reduces acidosis. However, its supplementation during dialysis induces another complication. Between hemodialysis treatments, acid accumulates and bicarbonate concentrations decrease within body fluids. During treatments, bicarbonate administration is rapid and can cause high concentrations of bicarbonate in the blood. Such fluctuations in acid-base are deleterious to body chemistry.

The proposed project will design and evaluate new treatment methodologies and prescriptions for optimization of bicarbonate administration to neutralize acid accumulation in the body of hemodialysis patients. Specifically, it is hypothesized that profiling (decreasing continuously or stepwise) the dialysate bicarbonate concentration and therefore its rate of administration to the body during the treatment will improve acid-base balance. The approach to be employed in this project is to develop a mathematical model to simulate (using a computer) various alternatives for optimization of the dialysate bicarbonate concentration; such a methodology is economic and limits clinical trials in patient populations. The model will describe the most important factors that control body acid-base equilibrium: the buffer system with bicarbonate plus a few other bases in small concentration; the distribution of the bases and acids inside the body, as for example their different concentrations found inside versus outside cells; the ventilation system that is an auxiliary short-term controller of acid base equilibrium; and dialysis itself together with flows of buffers induced by it. Once the optimal treatment prescription for neutralization of acid accumulation has been determined via computer simulations, it will be compared with current standard treatment prescriptions for scientific validation. This project will thereby lead to improvements in hemodialysis treatment methodologies.