Overview of Biocompatibility and Clinical Issues on New Peritoneal Dialysis Solutions

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Continuous ambulatory peritoneal dialysis (CAPD) has become a widely accepted renal replacement modality for patients with end stage renal disease. Although CAPD is effective in controlling uremia and fluid balance, it is characterized by a high incidence of technique failure (50-72% after 4 years of treatment). The main reason for discontinuation of CAPD is loss of ultrafiltration due to acquired changes of peritoneal membrane function. These alterations in membrane function are related to the frequency of peritonitis episodes and exposure to hypertonic glucose based PD solutions, which have several unphysiologic characteristics, such as low pH, high glucose levels with associated hyperosmolarity and presence of glucose degradation products (GDPs). Beside local effects, CAPD dialysis fluids may also have systemic effects, since glucose is rapidly absorbed across the peritoneal membrane into the systemic circulation leading to metabolic changes, such as dyslipidemia, obesitas and protein malnutrition. In addition, it has been suggested that GDPs from intraperitoneally administered PD solutions are absorbed into the systemic circulation and may contribute to the formation of advanced glycation end products (AGEs) systemically.

These disadvantages of the conventional dialysis solutions prompted the search for more physiologic PD solutions. Icodextrin has the advantage of containing glucose polymers instead of glucose as osmotic agent, is iso-osmolair and contains low concentrations of GDPs. However, it can only be administered once daily, first, because its ultrafiltration (UF) profile is only profitable during the long dwell and, second, because of the systemic accumulation of glucose polymers and maltose. Amino acid-based PD solutions, originally designed to compensate for protein losses in the dialysate, do not contain glucose either, but can only be used once or twice a day, because its use can result in a rise in serum urea and a mild degree of acidosis. In addition, the amino-acid-based PD solution has a low ultrafiltration capacity that limits its use. Finally, glucose based bicarbonate/lactate buffered solutions have a neutral pH and contain less GDPs. In many animal studies has clearly been demonstrated that both the amino-acid-based PD solution as well as the bicarbonate/lactate buffered solutions with neutral pH induce substantial less damage to the peritoneal membrane compared to the standard PD solutions. In addition, several clinical studies with these bicarbonate/lactate buffered solutions with neutral pH have now been performed demonstrating clinical and (possible) biochemical advantages over the standard PD solutions. We have performed a study in which patients were treated with a regimen as low as possible in glucose and GDPs (one exchange of icodextrin, one with amino acids and supplementary exchanges of bicarbonate/lactate buffered glucose solution) and compared with a standard PD dialysis regimen, in a cross-over design, with focus on efficacy, safety and tolerability of such a regimen.

In this presentation results of animal studies with the newer PD solutions as well as clinical data on studies with these solutions will be presented with emphasis on the study on the combination of these newer solutions.