8. PHARMACOLOGIC MANIPULATION OF PERITONEAL TRANSPORT

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1. INTRODUCTION

As peritoneal dialysis has become an increasingly popular alternative to maintenance hemodialysis for therapy of patients with chronic renal failure [1, 2], the effect of pharmacologic and physiologic manipulations on transport parameters have been explored seeking enhanced understanding of transport barriers and clinically useful methods to augment transport.

2. RATIONALE FOR AUGMENTING TRANSPORT RATES

Because of the relatively poor mass transport of small solutes compared to hemodialysis, peritoneal dialysis is more time consuming when the therapeutic endpoint is to achieve a given degree of control of the plasma concentration of low molecular weight solutes like urea. The more often that fluid is exchanged, the more likely is the occurrence of peritonitis, the major complication of chronic peritoneal dialysis. Thus, inefficient transport by necessitating more exchanges of dialysis solution can contribute to the danger of peritonitis. Once peritonitis occurs, solute transport may increase, while the rate of ultrafiltration decreases. Thereafter, transport should be returned to baseline rates unless treatment has been inadequate leading to loss of peritoneal surface area or decreased permeability.

For hypercatabolic or hyperkalemic patients the transport inefficiency for small solutes may be quite significant, clinically.

The efficiency of peritoneal mass transport may be particularly reduced in the presence of systemic vascular disease [3]. Although the splanchnic blood vessels may escape a generalized sclerosing or inflammatory process, usually diseases such as diabetes mellitus, malignant hypertension, scleroderma and systemic lupus become so widespread as to affect all the vasculature before causing terminal renal failure.

Continuous ambulatory peritoneal dialysis does not really have the disadvantage of a long duration of treatment because treatment time does not inhibit rehabilitation. Nevertheless this technique requires an adequate level
of efficiency to be clinically satisfactory [4]. With co-existent systemic vascular disease or after multiple episodes of peritonitis, the efficiency of mass transport may be so borderline as to render the procedure inadequate, unless more frequent exchanges are used, with the attendant hazards of multiple tubing disconnections. Moreover, some patients undergoing this treatment have low rates of ultrafiltration across the peritoneum, while under other circumstances increased dialysis, augmented transport may be required whenever there is decreased transport efficiency or an increased catabolic rate.

When peritoneal dialysis is used for the removal of exogenous toxins, it is usually mandatory that the removal rates be maximal. On the other hand, when protein loss is excessive, it can be judicious to decrease the transport rates at least of larger solutes. It becomes obvious therefore, that further understanding of the mechanisms of mass transport and the influence of various pharmacologic and physiologic manipulations on these mechanisms is important fundamental information to provide the capability of accelerating or decreasing transport rates as clinically indicated. Indeed, patients undergoing peritoneal dialysis often require a variety of drugs that have specific vasoactive or membrane effects. Knowledge of the effects of such drugs on transport parameters can influence the appropriate choice of a drug for a particular indication.

3. MECHANISMS OF TRANSPORT

When dialysis solution is placed in the peritoneal cavity, it approaches concentration equilibrium with plasma by diffusion. Additionally, net osmotic and hydrostatic forces promote the movement of water out of plasma. Such ultrafiltration also augments the removal of solutes by convective transport. Solutes also can be added to dialysate from adjacent tissue rather than from plasma [5]. Finally solutes that are absorbed from peritoneal dialysis solution may undergo hepatic metabolism before reaching the systemic circulation [6].

4. DIFFUSION

Diffusion occurs by random kinetic movement of molecules, a process that tends to spread any substance evenly throughout the space available to it. This process is not affected by drugs, directly, but the barriers to diffusion may be influenced pharmacologically. Diffusion rates correlate directly with temperature, however.