AJKD

Special Article

Solute and Water Transport in Peritoneal Dialysis: A Case-Based Primer

Ramesh Khanna, MD

Peritoneal dialysis (PD) is an effective therapy for patients with end-stage kidney disease. Dialysis solutions containing physiologic concentrations of electrolytes and base, as well as glucose often at supraphysiologic concentrations, are infused into the peritoneal cavity for solute and water exchange, and the patient's own peritoneal membrane is used for dialysis. The peritoneal membrane is dominated by small pores, which allow transport of water and small-molecular-size solutes, including electrolytes, by way of both diffusion and convection. Through small pores, diffusion allows the movement of solutes from the high-concentration compartment to a lower-concentration region. Also, through small pores, water and solutes move together by convection in response to an osmotic force. The glucose in the dialysis solution generates osmotic force to drive convection. In addition to small pores, the peritoneal membrane contains a specialized water channel, aquaporin 1, which is also present in capillaries of the peritoneal membrane. These specialized water channels, which are upregulated by glucose, allow water transport without solute (free water) in response to the osmotic force induced by glucose in the PD solution. During a PD exchange, net loss or gain of electrolytes and base is determined by both their gradient between capillary blood and dialysis solution and the net ultrafiltration volume. Developing a PD prescription, including the amount of glucose used, and changing the prescription in response to dietary changes and/or loss of residual kidney function requires a sound understanding of the peritoneal physiology. The case studies presented here help solidify the basic elements of PD prescription and how the PD prescription should be altered in response to changing clinical situations.
Am J Kidney Dis. ■(■):■-■. © *2016 by the National Kidney Foundation, Inc.*

INDEX WORDS: Peritoneal dialysis (PD); peritoneal physiology; peritoneal membrane; peritoneum; pores; diffusive transport; convective transport; solute transfer; water channel; aquaporin 1; PD exchange; ultrafiltration; electrolyes; icodextrin; dwell time; end-stage renal disease; review.

Ramesh Khanna, MD, was the J. Michael Lazarus Distinguished Award recipient at the 2016 National Kidney Foundation Spring Clinical Meetings, together with Karl Nolph, MD, who was awarded this distinction posthumously. This award was established to honor Dr Lazarus for his major contributions to the clinical science and care of dialysis patients and to recognize individuals whose research has yielded novel insights related to renal replacement therapy.

INTRODUCTION

Overview

Peritoneal dialysis (PD) is an effective treatment for patients with chronic kidney failure. PD uses a patient's own peritoneal membrane, across which fluids and solutes such as creatinine, urea, electrolytes, glucose, and many other unmeasured uremic toxins are exchanged between the capillary blood and PD solution. The PD solution is infused into the peritoneal cavity through a permanently implanted silicone rubber tube, the PD catheter. After dwelling in the cavity for a predetermined period, the PD solution is drained out and fresh PD solution is reinstilled. Such exchanges are performed regularly throughout the day, either with manual exchanges as in continuous ambulatory PD (CAPD) or with the help of a machine as in automated PD (also referred to as continuous cycling PD [CCPD]). Experience with PD therapy over the past 3 to 4 decades has shown that 5-year patient survival is comparable to in-center hemodialysis. Importantly, PD costs much less than hemodialysis in most parts of the world and can readily be performed at home without the need for complicated machines. Critically, successful PD requires a hygienic environment and attention to detail to minimize the risk for peritonitis.

Peritoneum

The fraction of the peritoneal membrane actively involved in the PD exchange is largely unknown. Nevertheless, it is apparent that the surface area of peritoneum involved in the transport process is not a fixed quantity. Therefore, it is more meaningful to measure it functionally. Consequently, physiologists have suggested estimating the proportion of functional

From the Division of Nephrology, Department of Medicine, University of Missouri-Columbia, Columbia, MO.

Received May 24, 2016. Accepted in revised form November 27, 2016.

Address correspondence to Ramesh Khanna, MD, Division of Nephrology, Department of Medicine, University of Missouri-Columbia, Columbia, MO 65212. E-mail: khannar@health.missouri.edu

0272-6386
http://dx.doi.org/10.1053/j.ajkd.2016.11.007

pore area in relation to the effective diffusion path length of the membrane. This calculation takes into account capillary surface area and the distance between capillary and dialysis solution/mesothelial contact.[1-5] The capillary wall (to a great extent), the interstitium, the mesothelial cell layer (to a lesser extent), and the unstirred dialysate fluid layer at the mesothelium (to a minor extent) all offer resistance to the free transport of water and solutes during dialysis.

Pores in the Peritoneal Membrane

The peritoneal membrane contains predominantly small pores of 40 to 50 Å and rare large pores of 150 Å. Specialized water channels, ultrasmall pores or aquaporin 1, are present in the mesothelial cells and the capillaries.[6-9] In the presence of glucose, these channels are upregulated.[10] Aquaporin 1 channels allow transport of solute-free water in response to a crystalloid-induced osmotic pressure. In clinical practice, such water movement is termed free water transport. Small pores and aquaporin 1 play major roles in solute and water transport. Because of their paucity, large pores do not contribute significantly to solute and water transport. Macromolecules such as albumin and larger proteins are transported through large pores at a very low rate and do not reach equilibrium between capillary blood and dialysis solution even after a 24-hour PD solution dwell, although their concentration in the PD solution is extremely low. Nevertheless, such small losses of protein and albumin result in lower serum protein and albumin levels in PD patients.

Diffusive and Convective Transport

Solute and water are transported through the peritoneal membrane by diffusion and convection. Small pores allow the transport of small-molecular-size solutes, including electrolytes, by way of both diffusion and convection. During the diffusion process, the solute concentration gradient between 2 compartments (capillary blood and PD solution in the peritoneal cavity) that are separated by the semipermeable peritoneal membrane allows solute to move from a higher to a lower concentration compartment. The rate of transfer by diffusion of a solute is determined by the diffusive permeability (ratio of free diffusion coefficient and the distance of diffusion) of the peritoneum to that particular solute and the surface area available for transport.

Convective solute transport occurs in conjunction with water transport from one compartment to the other. In PD, the glucose in the dialysis solution in the peritoneal cavity generates crystalloid osmotic pressure, which, along with transmembrane hydrostatic pressure, promotes convective water and solute transport from the capillary blood to the dialysis solution. The effectiveness of glucose in promoting water and solute transport during convection is determined by the resistance offered by the peritoneal membrane to glucose transport from the peritoneal cavity to the capillaries. In physiology, this resistance is expressed as the osmotic reflection coefficient. For the peritoneal membrane, the reflection coefficients reported for small solutes vary greatly, depending on the measurement method,[11] and differ for different solutes and pores. By definition, the reflection coefficient is 1.0 for a solute with complete resistance, such that the solute cannot cross the membrane, and 0 when the membrane offers no resistance to solute movement. The osmotic reflection coefficient for small osmotic solutes including glucose is very low, reportedly between 0.02 and 0.05 when calculated by assessing the transperitoneal ultrafiltration rate in response to the solute concentration rate.[11] However, other studies have noted reflection coefficients that are significantly greater, between 0.2 and 0.6, based on assessing the transperitoneal solute transport rate during a hypertonic exchange.[12,13]

During a peritoneal dialysis exchange, the reflection coefficient for glucose is the mean of its reflection coefficient for all pores, including small and large pores and aquaporin 1 channels. The sieving coefficient is determined by the ratio of the solute concentration in the filtrate divided by its concentration in plasma in the absence of diffusion. The value, 1.0 minus the sieving coefficient, is an approximate estimate of the reflection coefficient for a given solute; this is called the rejection coefficient.

Solute Transfer

Dialysis solution contains physiologic concentrations of electrolytes, including sodium, calcium, magnesium, and bicarbonate. Consequently, diffusion plays an inconsequential role in the removal of these electrolytes from the body during peritoneal dialysis. These electrolytes may enter the body by diffusion from the dialysate into the body based on their concentration gradient. Accordingly, ultrafiltration is the dominant way of removing electrolytes from the body.

During a PD exchange, both small pores and aquaporin 1 contribute somewhat equally to water transport.[3,14,15] Because water transport through aquaporin 1 is solute free, sodium concentration decreases in the dialysate during the first 2 to 3 hours of a PD exchange because the high volume of free water, generated through aquaporin 1 in the early phase of an exchange in response to glucose-induced osmotic pressure, dilutes the sodium in the dialysis solution. Due to free water loss from the blood compartment, serum sodium concentration increases. This phenomenon, in which