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Peritoneal Fluid Transport: Mechanisms, Pathways, Methods of Assessment

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Fluid removal during peritoneal dialysis is controlled by many mutually dependent factors and therefore its analysis is more complex than that of the removal of small solutes used as markers of dialysis adequacy. Many new tests have been proposed to assess quantitatively different components of fluid transport (transcapillary ultrafiltration, peritoneal absorption, free water, etc.) and to estimate the factors that influence the rate of fluid transport (osmotic conductance). These tests provide detailed information about indices and parameters that describe fluid transport, especially those concerning the problem of the permanent loss of ultrafiltration capacity (ultrafiltration failure). Different theories and respective mathematical models of mechanisms and pathways of fluid transport are presently discussed and applied, and some fluid transport issues are still debated. © 2013 IMSS. Published by Elsevier Inc.

Key Words: Peritoneal absorption, Free water transport, Osmotic conductance, Three pore model, Spatially distributed model.

Introduction

The removal of excess water is one of the primary objectives of peritoneal dialysis (PD) and the reason for the application of hypertonic dialysis fluids in this treatment. The means to obtain the target volume of removed water are less effective than those available in hemodialysis (1,2). Furthermore, there exists a trade-off between the amount of removed water and the absorbed amount of osmotic agent, which may have adverse effects during long-term application (3–7). The characteristics of the peritoneal transport barrier (PTB) decide often about the optimal modality and schedule of peritoneal dialysis (6,8).

The clinical assessment of peritoneal transport of fluid and small solutes can provide the basic information about the transport barrier and is typically based on 24 h collection of spent dialysate and/or peritoneal equilibration test (PET) (8). In this way one can measure the total volume removed per 24 h and/or the volume removed during standardized test of 4 h duration. However, the problems related to fluid transport need more advanced methods of investigations. The removed fluid volume is the net result of two processes: a) ultrafiltration from capillaries to the peritoneal cavity induced by osmotic pressure of dialysis fluid, and b) absorption of dialysis fluid from the peritoneal cavity induced by increased intraperitoneal pressure (9–11). Furthermore, the occurrence of ''sodium dip'' in clinical and experimental studies suggested the existence of ultrasmall pores in PTB that are permeable only for water molecules but not for small solutes such as sodium, urea, creatinine and glucose (12). The function of ultrasmall pores may be associated with the presence of aquaporins in endothelial cell membrane (13,14). The quantitative assessment of the intrinsic aspects of fluid transport needs more sophisticated clinical tools and the present review is devoted to new clinical tests and interpretations of fluid transport mechanisms. Details of the process of fluid transport are important from the clinical point of view because of the high prevalence of complications related to water removal that are the reason for the change of peritoneal dialysis modality and/or schedule or the change from peritoneal dialysis to hemodialysis (6,8).

The large number of different tests of peritoneal transport comes from the importance of transport phenomena for successful dialysis and the sophistication of transport mechanisms that are addressed by the tests. A few good reviews of the available tests were published some time ago (8,15,16), but new approaches have been proposed and tested in recent years (17–19). The well-established

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methods include Standard Peritoneal Permeability Analysis (SPA) and other studies based on the application of volume marker, PD Adequest and Personal Dialysis Capacity test (10,20,21). Recently, several other tests were proposed: mini-PET, double mini-PET, two-in-one protocol, threefold peritoneal test, and sequential peritoneal equilibration test, sPET (17,19,22,23). All these new tests are taken into account in this review that is focused on the assessment of fluid removal, its mechanisms and their quantification.

Methods of Assessment of Fluid Transport Components

Multiple transport mechanisms and pathways are involved in fluid transport during PD. Some fluid transport parameters can be obtained directly from clinical tests, whereas others need mathematical models to be derived from clinical data.

Rate of Peritoneal Absorption

Isotonic and hypotonic fluids infused into the peritoneal cavity are absorbed at a constant rate (24,25). Hypertonic fluids induce ultrafiltration from blood during the initial few hours of peritoneal dwell but are finally absorbed when the osmotic pressure of the fluid is dissipated by diffusion and inflow of water from blood. The fundamental quantitative difference between transcapillary ultrafiltration to the peritoneal cavity and peritoneal fluid absorption from the peritoneal cavity was established in studies with hypertonic dialysis fluids and volume markers used for the assessment of the kinetics of dialysis fluid volume (26,28). The macromolecular markers (radiolabeled human serum albumin, dextran 70, autologous hemoglobin, and others) are continuously absorbed from the peritoneal cavity and a correction for this absorption is necessary for the estimation of dialysis fluid volume by the dilution principle. The rate of marker absorption was assumed constant throughout the peritoneal dwell and, based on the observation that the rate did not depend on the size of the marker, it was attributed to convective absorption of markers together with absorbed dialysis fluid (26–29). The rate of this absorption is typically about 1 mL/min (Table 1); however, in some patients it may be as high as 5 mL/min and may be a reason for ultrafiltration failure (9,30–32). It was found that about 10–30% of the peritoneal absorption is by lymphatic vessels that are open directly to the peritoneal cavity, and the other fraction is absorbed to the tissue that is in contact with dialysis fluid (9,31). The absorbed fluid increases the hydration of the interstitium and hydrostatic pressure of the interstitial fluid and is gradually absorbed from the tissue to the blood by lymphatic vessels inside the tissue and/or directly to the capillaries by Starling forces (33).

The method of volume markers is the only direct experimental approach to measure the rate of peritoneal absorption (26). A simple indirect method for the estimation of peritoneal absorption demands only a few measurements (three or more, for example, by temporal drainage of dialysis fluid, weighing the drained fluid, and its infusion back to the peritoneal cavity) of dialysis fluid volume, V_D, during a peritoneal dwell (34,35). Calculation of peritoneal absorption is then based on the application of mathematical formula proposed by Pyle:

$$V_D(t) = V_0 + Q_{U,max}(1 - \exp(-kt)) - PA \cdot t$$

where $Q_{U,max}$ is the (estimated) maximal value of ultrafiltration from blood to the peritoneal cavity, and k describes the rate of the decrease of ultrafiltration with dwell time t (35,36).

Other methods for the estimation of peritoneal absorption are based on the assumption that the net change of dialysis fluid volume, netUF, is the difference of two terms: 1) transcapillary ultrafiltration rate that is proportional to osmotic pressure difference $\pi_D - \pi_B$ between dialysis fluid (D) and blood (B) (or glucose concentration difference if applied to glucose-based dialysis fluids), and 2) peritoneal absorption rate that is assumed constant. Thus,

$$netUF = OC(\pi_D - \pi_B) - PA$$

where the parameter OC is called osmotic conductance (see below). Application of this equation (which is a linear regression with two coefficients: OC and PA) to data on dialysis fluid volume and osmotic pressure yields both coefficients OC and PA (36,37). A similar equation is included into the threefold peritoneal test, which is based on three 24 h dialysate collections with different

Table 1. Rate of peritoneal absorption (PA), mean ± SD or median (range), estimated using different tests for different patient populations and dialysis fluids

Patient population/dialysis fluid	PA mL/min	Method of assessment
Non-UFF patients	1.9 ± 0.5	Volume marker (81)
UFF with HDR	2.2 ± 0.4	
UFF with LAR	4.9 ± 0.1[a]	
General population	0.95 (0.4–3.9)	SPA (10)
General population	1.6 ± 0.6	Linear regression (36)
Non-UFF patients	1.0 (0.0–2.4)	SPA (32)
UFF	1.6 (0.5–6.3)[a]	
General population	0.8 ± 0.2	Pyle function (35)
Neutral fluid	2.3 ± 1.1	Volume marker (82)
Acidic	1.8 ± 0.9	
Osmotic agent: glucose	1.6 ± 0.9	Volume marker (83)
Amino acids	1.6 ± 0.5	
General population	0.9 ± 1.0	Threefold test (19)
General population	1.0 ± 0.7	sPET (18)

Non-UFF, patients with normal net ultrafiltration; UFF, patients with ultrafiltration failure; UFF with HAR, patients with UFF due to high absorption rate; UFF with HDR patients with UFF due to high diffusion rate.
[a]$p < 0.5$ vs. non-UFF patients.

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