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DIALYSIS. PERITONEAL DIALYSIS - 1

FP554 OSMOTIC WATER TRANSPORT INDUCED BY ICODEXTRIN OCCURS INDEPENDENTLY OF WATER CHANNELS AND RESEMBLES COLLOID OSMOSIS

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Introduction and Aims: The principle of osmosis has been applied for more than 50 years to generate ultrafiltration (UF) across the peritoneum of peritoneal dialysis (PD) patients. Aquaporin-1 (AQP1) water channels mediate free-water transport and half the UF during PD with hypertonic glucose. In recent years, icodextrin has emerged as a useful alternative to glucose to achieve UF during long dwells and improve water balance in PD patients. However, the mechanisms underlying icodextrin-induced osmosis have not been investigated.

Methods: In this study, we evaluated the molecular and physical mechanisms of icodextrin-induced water transport. The effects of icodextrin on peritoneal solute and water transport were compared to glucose- and aminoacids-based dialysis solutions in a well-established mouse model of PD and in transgenic Aqp1 mice. Hydrodynamic radius of icodextrin was assessed by dynamic light scattering. The impact of icodextrin subfractions and bimodal osmosis on water transport was investigated in vivo, after selective removal of large polymers or with combinations of icodextrin and glucose, respectively.

Results: Contrarily to PD solutions containing glucose or aminoacids, glucose polymer icodextrin induces a sustained water transport across the peritoneal membrane independently of water channels, as indicated by the same net UF in Aqp1 knockout and wild-type mice. The presence of large polymers allows icodextrin (mean hydrodynamic radius, RH, 5.0 nm, range 1-23 nm) to generate an osmotic water transport even when the solution is hypotonic, by a mechanism that resembles colloidal osmosis. Removal of large (> 30 kDa) icodextrin polymers completely abolishes osmosis, but has no effect on dialysate osmolality. Combining icodextrin with glucose in the same solution synergistically enhances UF, as a result of complementary mechanisms of osmotic water transport: glucose induces a fast, AQP1-mediated, transcapillary UF during the first part of the dwell, while large icodextrin molecules maintain a colloid osmotic gradient and prevent backfiltration when the crystalloid gradient has dissipated because of solute absorption.

Conclusions: Altogether, these data contribute to the understanding of the mechanisms of icodextrin-induced water transport during PD, which occurs independently of water channels and resembles colloidal osmosis.