

SIGNIFICANCE STATEMENT

Osmosis sustains the efficiency of peritoneal dialysis to restore fluid balance in patients with ESRD. The water channel aquaporin-1 (AQP1) plays a critical role in glucose-driven (crystalloid) osmosis across the peritoneal membrane, but it is not known whether it contributes to ultrafiltration induced by colloid osmotic agents such as icodextrin. On the basis of studies in *Aqp1* mice, biophysical experiments, and computer simulations, these data re-examine mechanisms of crystalloid versus colloid osmosis and demonstrate that colloidal fractions of icodextrin induce an osmotic flow that is independent of AQP1. They also show the role of large icodextrin fractions to generate colloid osmosis and provide a rationale for using combinations of osmotic agents to improve fluid volume control in patients treated with peritoneal dialysis.