Metabolic consequences of PD

Börje Haraldsson

The institute of Medicine, Göteborg University, Sahlgrenska University hospital, SE-413 45 Gothenburg, Sweden, Phone +46 31 342 7086, E-mail borje.haraldsson@gu.se

Disclosure: The author has no conflicts of interest, such as consultant agreement or board position, in any company producing or manufacturing PD solutions.

Today, we know that patients treated with peritoneal dialysis have outcomes that are similar to, or slightly better than, those with in-centre hemodialysis (7, 9). Such comparisons are hampered by the lack of randomized controlled trial (3), but it is important to remember that it holds for patients with the first generation of glucose-based PD solutions with high concentrations of toxic glucose degradation products (GDP) (4). In the last years, glucose has been suggested to be toxic *per se* (2). In fact, there is little evidence to support that statement, since studies showing an association between loss of ultrafiltration and high glucose concentrations have a confounding factor in the concomitant change GDP levels (8). Also, *'glucose-free'* PD solutions are assumed to be beneficial for diabetic and/or obese patients (1), but the scientific support remains to be seen. Indeed, the long-term studies that have been done do not show any significant benefits (5). There are however physiological aspects about the metabolism of PD solutions that seem to be neglected.

Regarding energy, we know that one mmol of glucose gives rise to 0.72 kilocalories. Amino acids are glucogenic, ketogenic or both. When not used for protein synthesis, most of them will enter gluconeogenesis and finally the Krebs cycle to produce approximately 0.64 kcal/mmol.

This means that the caloric intake is rather similar to a 15 g/l glucose PD solution. Also, intraperitoneal administration of amino acids (Nutrineal) has not been shown to increase protein synthesis (10, 5). Moreover, icodextrin (Extraneal) is an excellent second-line choice for many patients with loss of ultrafiltration and for patients on a cycler with long day-time dwells, but is not a '*glucose-free'* solution. In an excellent pharmacokinetic study (6), it was shown that icodextrin eventually will be metabolized to glucose and hence calories. Thus, 40 % of the icodextrin is taken up to blood during a 12 hour PD dwell. Of these molecules, 20 % are excreted via urine & dialysate and the remaining icodextrin is metabolized (6). A simple calculation, will give 0.4 x 0.8 x 75 g/L x 2 L = 48 g, which would imply 192 kcal. Thus, icodextrin gives the fluid removal of 40 g/l glucose solutions at the price of a 25 g/l glucose PD solution.

To conclude, glucose solutions with ultra-low GDP levels should be considered the 'golden standard' in PD. This is definitely true for glucose concentrations of 15 – 25 g/l, while there is some concern for the prolonged use of glucose at the 40 g/l level. Thus, based on the physiology of PD solutions, the increased use of 'glucose-free' solutions seems to be unwarranted.

References

1 Dasgupta, MK: Strategies for managing diabetic patients on peritoneal dialysis. *Adv Perit Dial,* 20**:**200-2, 2004.

2 Davies, SJ, Phillips, L, Naish, PF & Russell, GI: Peritoneal glucose exposure and changes in membrane solute transport with time on peritoneal dialysis. *J Am Soc Nephrol,* 12**:**1046-51, 2001.

3 Foley, RN: Comparing the incomparable: hemodialysis versus peritoneal dialysis in observational studies. *Perit Dial Int,* 24**:**217-21, 2004.

4 Kjellstrand, P, Martinson, E, Wieslander, A & Holmquist, B: Development of toxic degradation products during heat sterilization of glucose-containing fluids for peritoneal dialysis: influence of time and temperature. *Perit Dial Int,* 15**:**26-32, 1995.

5 le Poole, CY, Welten, AG, Weijmer, MC, Valentijn, RM, van Ittersum, FJ & ter Wee, PM: Initiating CAPD with a regimen low in glucose and glucose degradation products,

with icodextrin and amino acids (NEPP) is safe and efficacious. *Perit Dial Int*, 25 Suppl 3**:**S64-8, 2005.

6 Moberly, JB, Mujais, S, Gehr, T, Hamburger, R, Sprague, S, Kucharski, A, Reynolds, R, Ogrinc, F, Martis, L & Wolfson, M: Pharmacokinetics of icodextrin in peritoneal dialysis patients. *Kidney Int. Suppl.***:**S23-S33, 2002.

7 Murphy, SW, Foley, RN, Barrett, BJ, Kent, GM, Morgan, J, Barre, P, Campbell, P, Fine, A, Goldstein, MB, Handa, SP, Jindal, KK, Levin, A, Mandin, H, Muirhead, N, Richardson, RM & Parfrey, PS: Comparative mortality of hemodialysis and peritoneal dialysis in Canada. *Kidney Int,* 57**:**1720-6, 2000.

8 Rippe, B, Simonsen, O, Heimburger, O, Christensson, A, Haraldsson, B, Stelin, G, Weiss, L, Nielsen, FD, Bro, S, Friedberg, M & Wieslander, A: Long-term clinical effects of a peritoneal dialysis fluid with less glucose degradation products. *Kidney Int*, 59**:**348-57, 2001.

9 Schaubel, DE, Morrison, HI & Fenton, SS: Comparing mortality rates on CAPD/CCPD and hemodialysis. The Canadian experience: fact or fiction? *Perit Dial Int,* 18**:**478-84, 1998.

10 Tjiong, HL, Fieren, MW, Rietveld, T, Wattimena, JL, Schierbeek, H, Huijmans, JG, Hop, WC, Swart, GR & van den Berg, JW: Albumin and whole-body protein synthesis respond differently to intraperitoneal and oral amino acids. *Kidney Int*, 2007.