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ISPD GUIDELINES/RECOMMENDATIONS

GUIDELINE ON TARGETS FOR SOLUTE AND FLUID REMOVAL IN ADULT PATIENTS ON CHRONIC PERITONEAL DIALYSIS

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The previous decade saw the generation of a series of consensus and evidence-based guidelines for the optimal management of dialysis patients. The majority of these have emanated from national and regional committees. There is not always agreement among these documents; part of this disparity may have to do with the nuances of dialysis practice in different parts of the world.

The International Society for Peritoneal Dialysis (ISPD) has commissioned a working group with representation from Asia, Australia, Europe, and North America to formulate a series of recommendations concerning the delivery of adequate peritoneal dialysis (PD). It is the hope of the authors that the comments and recommendations presented here are relevant and applicable to those worldwide who manage patients on PD, and that they are readable, precise, and concise.

These recommendations have been approved by the Standards and Education Committee of the ISPD.

PART A: SUMMARY LISTING OF FINDINGS FROM EXPERT OPINION AND PEER-REVIEWED PUBLICATIONS ON RELEVANT SUBJECTS UP TO SEPTEMBER 2005

1. Residual renal function (measured by renal clearance or urine volume), but not peritoneal clearance, is predictive of survival in prospective observational studies and can account for most of the association between total clearance and survival (1–4).
2. Renal clearance and peritoneal clearance have different effects on patient survival (4,5). Simple addition of the two into a combined total clearance is therefore not supported scientifically. However, in the absence of better markers of renal and peritoneal clearances, they can, for convenience, be added together.
3. Prospective randomized interventional studies do not provide evidence to support a beneficial effect of increasing dialysis to total Kt/V urea above 2.0, or creatinine clearance above 60 L/week/1.73 m^2, in patients on continuous ambulatory peritoneal dialysis (CAPD) with a total Kt/V urea above 1.70 or creatinine clearance above 50 L/week/1.73 m^2 (6,7).
4. Interventional studies have demonstrated that total Kt/V below 1.70 is associated with poorer primary or secondary outcome:
   (a) more clinical problems and greater need for erythropoietin therapy (7);
   (b) poorer patient and technique survival in a prospective nonrandomized study (8).
5. There is no prospective randomized study exploring the lower limit of target clearance in terms of mortality.
6. A retrospective study showed that survival was poorer for anuric patients with peritoneal Kt/V urea below 1.67, with better outcomes in those with peritoneal Kt/V urea 1.67 – 1.87 (9). In another retrospective study involving a slightly smaller sample of both anuric CAPD and automated peritoneal dialysis (APD) patients, there was a trend of reduced mortality, although not statistically significant, in patients with peritoneal Kt/V urea above 1.85 (10). In the prospective observational study on anuric

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patients in the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD), peritoneal Kt/V below 1.5 and creatinine clearance below 40 L/week/1.73 m^2 were associated with increased mortality (11).

7. Ultrafiltration was predictive of survival in anuric APD patients in the prospective observational European APD Outcome Study (EAPOS) (12): baseline ultrafiltration below 750 mL/day was associated with poorer survival, but the time-averaged ultrafiltration was not when analyzed time dependently. In contrast, ultrafiltration analyzed as a continuous variable was a significant factor for survival in the time-dependent analysis of anuric patients in NECOSAD (11). It appears from these data that no numerical target for ultrafiltration can be formulated.
8. While Kt/V urea and creatinine clearance are generally closely correlated in patients on CAPD, their relationship is more variable in patients on APD, depending on the dialysis regime and peritoneal transport (13).
9. There is a significant discrepancy between small solute clearance and middle molecule clearance. Small solute clearance is determined by the frequency and volume of dialysate dwell, while middle molecule clearance is determined by duration of contact of the peritoneum to dialysate (14).
10. Small solute clearance is only one parameter of renal failure treated by PD. The association of small solute clearance with other functions of the native kidney, such as fluid removal, electrolyte and acid–base homeostasis, metabolic function, and blood pressure control, is weak.
11. There are no long term, randomized, prospective interventional studies showing outcome data for more than 4 years.
12. There is no evidence for a different target Kt/V urea or creatinine clearance between diabetic and non-diabetic patients, or for patients of different sizes.
13. All studies on the effect of Kt/V quoted in this document used the Watson formula (using actual body weight) for the estimation of V. There have been no studies supporting an alternative method for estimation of V in patients on PD.

PART B: RECOMMENDATIONS BASED ON PART A

1. Adequacy of dialysis should be interpreted clinically rather than by targeting only solute and fluid removal. Clinical assessment should include clinical and laboratory results, peritoneal and renal clearances, hydration status, appetite and nutritional status, energy level, hemoglobin concentration, responsiveness to erythropoietin therapy, electrolytes and acid–base balance, calcium phosphate homeostasis, and blood pressure control (*Evidence level C*).
2. In order to emphasize that there is more to adequate dialysis than a focus on small solute kinetics and ultrafiltration targets, the Committee decided to name this guideline, *Guideline on Targets for Solute and Fluid Removal in Adult Patients on Chronic Peritoneal Dialysis* instead of *Guideline on Adequacy of Peritoneal Dialysis*.
3. For small solute removal, the total (renal + peritoneal) Kt/V urea should not be less than 1.7 at any time (*Evidence level A*). That means, in anuric patients, peritoneal Kt/V urea has to be above 1.7. In the presence of residual renal function, the contributions of renal and peritoneal clearances may be added for practical purposes, although, as mentioned previously, renal and peritoneal clearances may not be truly additive (*Opinion*). Solute removal above this level should not be equated with "adequate dialysis." Knowledge of the transport characteristics of the patient's peritoneal membrane by peritoneal equilibration test or other tests may help to optimize the prescription to meet this target.
4. A separate target for creatinine clearance is not required in CAPD. In APD, due to a more variable relationship between urea and creatinine clearance, an additional target of 45 L/week/1.73 m^2 for creatinine clearance is recommended (*Evidence level C*).
5. For patients who rely significantly on residual renal function to achieve the minimal target level of small solute clearance, residual renal function should be monitored regularly and at an appropriate frequency (every 1 – 2 months if practicable, otherwise no less frequently than every 4 – 6 months) so that the PD prescription can be adjusted in a timely manner (*Evidence level C*). If there is a decrease in urine volume or a change in blood chemistries suggesting a decline in residual renal function, it should be measured sooner.
6. A continuous around-the-clock PD regime is preferred to an intermittent schedule whenever possible (*Evidence level B*).
7. Attention should be paid to both urine volume and the amount of ultrafiltration, with the goal of maintaining euvolemia. A small ultrafiltered volume despite the use of dialysis solutions with a high glucose concentration should be regarded as a warning sign for the presence of ultrafiltration failure. This should be investigated further with a peritoneal

equilibration test according to the ISPD recommendations on evaluation and management of ultrafiltration problems (15) (*Evidence level B*).

8. For patients with signs and symptoms suggestive of underdialysis, a trial of increasing dialysis should be provided even if Kt/V urea is well above the minimal target (*Evidence level C*).
9. The benefit of increasing the amount of peritoneal dialysate (either number of exchanges or volume of each exchange), or change to hemodialysis, when these targets cannot be met should be balanced against the potential side effects, effects on the patient's lifestyle, and cost consideration (*Evidence level C*).

APPENDIX: MEANING OF EVIDENCE LEVEL

Level A: Evidence was obtained from meta-analysis of several randomized controlled trials, or from at least one randomized controlled study.

Level B: Evidence was obtained from well-conducted clinical studies but no randomized controlled trials. The evidence may be extensive, but is essentially descriptive.

Level C: Evidence was obtained from expert committee reports or opinions and/or clinical experience of respected authorities.

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