Peritoneal transport and ultrafiltration

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GUIDELINES

No recommendations possible based on Level I or II evidence

SUGGESTIONS FOR CLINICAL CARE
(Suggestions are based on Level III and IV sources)

- **A patient's membrane transport status should be evaluated by the standard peritoneal equilibration test (PET).**
- **A PET should be performed approximately 4 weeks after initiating peritoneal dialysis, but no earlier.**
- **PETs should be repeated at 2 years and then annually. PETs should be repeated earlier if there is clinical evidence of fluid overload with a significant decrease in ultrafiltration, hypertension or elevated serum urea levels, particularly in those patients who have had episodes of peritonitis.**
- **Icodextrin should not be used in the preceding exchange before a PET as it increases the dialysate:plasma (D/P) creatinine ratio.**
- **There is some evidence that there is a group of patients with high transporter status who have an increased mortality and an increased risk of technique failure even with adequate small solute clearance, however this is not conclusive.**

Background

The PET was introduced by Twardowski in 1989 and is the standard method for evaluating peritoneal transport characteristics in peritoneal dialysis (PD) patients. Based on the dialysate to plasma creatinine ratio of creatinine, patients can be classified as high, high average, low average or low transporters as summarised in Table 1 (Twardowski 1989). The incidence of transport status varies among different populations; the Australian distribution is shown in Table 1. The PET is very helpful for prescribing both APD and CAPD, since knowledge of a patient's peritoneal permeability allows a better estimation of the dwell time that will achieve the greatest efficiency in terms of ultrafiltration and small solute clearance.

The objective of this CARI guideline is to recommend when an initial PET should be done and then at what frequency it should be repeated. The clinical relevance of the patient's membrane transport status is also discussed.

Search strategy

Databases searched: Medline (1966 to November Week 2 2003). MeSH terms and text words for peritoneal equilibrium test (PET), ultrafiltration and peritoneal dialysis were used. The search strategy was not limited by study type.

Date of search: 18 November 2003.

What is the evidence?

No randomised controlled trials (RCTs) are available which address this issue.

After commencing PD, the initial PET is best performed after the first 4 weeks, since peritoneal permeability appears to increase during the first 2–4 weeks. A retrospective cohort study by Rocco et al (1995) demonstrated that D/P creatinine ratios at 4 hours in PETs performed within the first 2 weeks of dialysis commencement significantly increased on subsequent follow-up PETs, performed an average of 7 months later (0.58 ± 0.13 – 0.66 ± 0.09, P < 0.05). In contrast, PETs performed between 4 and 28 weeks after dialysis commencement showed no such change (0.63 ± 0.10 – 0.63 ± 0.13, P = ns).

It is a matter of debate as to how stable PET results remain thereafter. Some investigators have found no clinically significant changes in transport characteristics, particularly in those patients who do not have peritonitis after follow-up periods of up to 18 months (Kusb et al 1990, Davies et al 1998) or 24 months (Wong et al 2000, Hung & Chung 2001), while others have observed an overall tendency of PET values to increase (Lo et al 1994, Procaccini et al 1988, Blake et al 1989, Passlick-Deetjen et al 1990, Struijk et al 1994).

In one series, a group of 22 PD patients that was monitored for 5 years showed that 60% had stable membrane transport with no change in their D/P creatinine whereas 40% had a sustained increase over the 5-year period (Davies et al 2001). Those patients who experienced an increase in their membrane transport had earlier loss of their residual renal function (RRF) and were exposed to significantly more hypertonic glucose during the first 2 years of treatment. Davies et al (1993) noted that 17 (49%) PET values for D/P creatinine exceeded the 95% confidence limits of PET reproducibility (10.5%). In 16 of these 17 PETs, an increase in solute transfer was demonstrated and was associated with a clinically significant fall in ultrafiltration in the majority.

Heimburger et al (1990) found that the prevalence of ultrafiltration failure (which is principally due to increased small solute permeability) steadily increased with increasing duration of dialysis (ranging from 2.6% at 1 year to 30.9% at 6 years). In contrast, another study with a mean follow-up PET at 32.8 ± 23.7 months showed that the mean D/P creatinine decreased over time, with an inverse relationship

between the change in D/P creatinine and the initial D/P creatinine (Hung et al 2000). This was also seen in another study by Grzegorzewska et al (2002). In patients over 60 years of age, there was a significant decline in the D/P creatinine over a mean of 20.1± 12.1 months, but there was no significant change in the younger patients. This was a retrospective study of 39 routinely repeated PETs in 42 patients who had no clinically overt dialysis problems.

Some studies have suggested that peritonitis may cause an increase in membrane transport (Lamb et al 1995, Davies et al 1996). One study showed that a single episode of peritonitis did not permanently affect membrane transport when patients were followed for 24 weeks (Ates et al 2000). As there is controversy in this area, with some patients showing stable membrane transport and others demonstrating either an increase or decrease in their D/P creatinine, it would seem prudent to periodically monitor PETs.

The development of ultrafiltration difficulties should prompt the repeating of a PET to ensure that there has not been a significant change in transport status that might warrant additional investigations (e.g. screening for sclerosing peritonitis) or alternative dialysis regimens (e.g. conversion to APD if the patient has become a high transporter).

There is conflicting evidence that membrane transport status, independent of weekly Kt/V and C_{Cr}, is associated with patient and technique survival. Several studies have shown that high transporters do have increased mortality and reduced technique survival, independent of other risk factors (Wu et al 1996, Fried 1997, Churchill et al 1997, Churchill et al 1998, Davies et al 1998, Kang et al 1998, Wang et al 1998, Cueto-Manzano et al 1999, Cueto-Manzano et al 2000, Hung et al 1999).

Churchill and colleagues (1998), in an analysis of the CANUSA data demonstrated that the relative risk of either technique failure or death was 1.19 (95% CI 1.05–1.34) for each 0.1 increase in D/P creatinine. Two-year survival probabilities of high, high-average, low-average and low transporters were 70.5%, 72.4%, 80.4% and 90.9%, respectively ($p = 0.11$). The 2-year probabilities of both patient and technique survival were 48%, 52%, 61% and 86%, respectively ($p = 0.006$). These results were observed despite the fact that small solute clearances were greater (although not significantly) with higher transport status.

The exact mechanisms for the poor survival of high transporters is uncertain, but may relate to poor ultrafiltration and fluid overload leading to hypertension and left ventricular hypertrophy, dialysate protein losses and poorer nutrition, chronic inflammation or other unknown mechanisms (Heimburger 1996, Blake 1997, Tonbul et al 2003). However, other studies have not shown any correlation between high transport status and reduced patient survival, particularly when patients do not have comorbid diseases, or in studies that have corrected for independent predictors of mortality such as serum albumin, age, diabetes and cardiovascular disease (Passadakis et al 2000, Chung et al 2003, Cueto-Manzano et al 2000, Szeto et al 2001, Park et al 2001). One suggestion that could explain these different results is that there are two groups of high transporters, one with chronic inflammation and comorbidities with low serum albumins, higher chronic reactive protein (CRP), lower RRF and lower protein nitrogen appearance (PNA), which have a poor prognosis,

and a second group, without evidence of inflammation, who do not have a worse prognosis than the lower transporters (Voinescu et al 2002).

There is evidence that high transporters do have poor nutrition as measured by serum albumin, PNA and percentage of lean body mass in comparison with low transporters, in whom a weak correlation between D/P creatinine and baseline serum albumin ($r = -0.249$, $p < 0.001$), PNA ($r = -0.190$, $p < 0.01$) and percentage of lean body mass ($r = -0.194$, $p < 0.01$) has been found (Szeto et al 2001). However, peritoneal transport status was not associated with longitudinal change of the nutritional parameters, with no significant change in the nutritional indices demonstrated at 2 years in new cases and prevalent cases, regardless of transport status (Szeto et al 2001).

There is also evidence that patients with symptomatic fluid retention are 3.7 times more likely to be high than low transporters (Tzamaloukas et al 1995). Thus, although there are no trials regarding the optimal management of such patients, it would seem prudent to more aggressively attend to fluid overload and nutrition in high transporters.

If patients have clinical evidence of persistent fluid overload despite appropriate measures, then consideration should be given to conversion to haemodialysis regardless of measured small solute clearances (Opinion). The main cause of morbidity and mortality in PD patients is cardiovascular disease (Diaz-Buxo 1989) and this may be contributed to by chronic fluid overload. Moreover, there is some evidence that PD patients tend to be chronically volume loaded (Rottembourg 1993). Hypertonic glucose exchanges to promote fluid removal are best avoided in view of experimental evidence that they may hasten membrane damage (Topley 1998).

Several studies have shown that the use of icodextrin-based exchanges may produce ultrafiltration that is equivalent to (Mistry et al 1994) or superior to (Posthuma et al 1997) hypertonic dextrose exchanges. A retrospective analysis suggests that the use of icodextrin may extend PD technique survival in patients with ultrafiltration problems by at least 9 months; 20 patients were still on PD using icodextrin after an average of 20.2 months compared with 19 patients not on icodextrin who transferred to haemodialysis after 11.9 months (Wilkie et al 1997).

A recent preliminary report of an RCT of 60 incident PD patients shows that long-term frusemide therapy (250 mg once/day) produces a statistically and clinically significant increase in urine volume over a 6-month period (+185 ± 117 versus control -151 ± 100 mL/24 hours, $P = 0.036$), but has no effect on preservation of RRF (Medcalf et al 1998).

There is evidence that if a PET is to be performed, icodextrin should not be used in the preceding exchange as it increases the D/P creatinine ratio (Lilaj et al 2001).

Summary of the evidence

There are no RCTs on this topic.

The PET as introduced by Twardowski (1989) is the recognised standard method for evaluating peritoneal transport characteristics in PD patients. Current and evolving

evidence suggests that the PET provides a rational basis for assessing the membrane transport characteristics and is thus a clinical guide to managing ultrafiltration and solute clearance. The PET may also provide adjunctive information about prognosis and nutrition.

What do the other guidelines say?

Kidney Disease Outcomes Quality Initiative (2000): Guideline 3. CPG for PD Adequacy. There is evidence that the PET performed within the first week after initiation of peritoneal dialysis may yield higher transport results than a PET performed a few weeks later. This difference is statistically significant, but may not be clinically relevant. It may be more convenient to perform the first PET at the end of training, rather than at the end of the first month, and the Work Group thinks this is acceptable. However, the results after a month of peritoneal dialysis may more accurately reflect peritoneal transport properties for the subsequent period.

British Renal Association: A PET should be performed after 4–8 weeks on dialysis, and when clinically indicated, e.g. when biochemical indices raise suspicion of changes in peritoneal transport characteristics, and annually as a routine.

Canadian Society of Nephrology: Guideline 5.3.1. Perform a PET within 6 weeks of initiating peritoneal dialysis, and repeat it when or if unexplained changes in peritoneal ultrafiltration or equilibration occur. (Opinion)

5.3.2. Pay particular attention to hydration, serum albumin, and nutritional status in patients who are high transporters on peritoneal equilibration testing. (Opinion)

5.3.3. Emphasise clinical detection and treatment of volume overload and hypertension in all patients on peritoneal dialysis. (Opinion)

European Best Practice Guidelines: No recommendation.

International Guidelines:

International Society of Peritoneal Dialysis: No recommendation.

Implementation and audit

Reporting of peritoneal transport parameters to ANZDATA on an annual basis should be encouraged. ANZDATA should report outcomes according to peritoneal transport status.

Suggestions for future research

No recommendation.

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Appendix

Table 1 Peritoneal membrane characteristics according to PET result

Membrane type	4–hr D/P creatinine	Australian non-diabetics (ANZDATA 2003)	Australian diabetics (ANZDATA 2003)
High	0.81–1.03	9%	10%
High Average	0.65–0.80	56%	51%
Low Average	0.50–0.64	32%	37%
Low	0.34–0.49	3%	2%