A Correlative Study Of Adequacy Parameters Using Kt/V And Dialysis Prescription And Survival In Continuous Ambulatory Peritoneal Dialysis

Thiagajaran T, Georgi Abraham, Milli Mathew, Padma G, Ramalakshmi R, Chowdhary BSBN, Soundararajan P, Sunil Shroff
Sri Ramachandra University, Chennai, India.

Abstract: Seventy six patients with CKD on CAPD, 50% diabetics were studied from a single centre over a two years period for adequacy, PET, nutritional status and technique survival. Mean age of the patients were 56.18±14.31 years, 65.8% were using six liters per day, 34.2% were using ≥8 Liters/day. The mean survival was 24.06 months. The major cause of technique failure was peritonitis. The one year and two year technique survival for those who were dialyzing with 6 liters and 8 liters, where 64% and 84% respectively, the two year survival was 53% and 52% respectively.

Key Words: CAPD, Adequacy, Survival, Nutrition, PET

Introduction:

There is greater utilization of chronic peritoneal dialysis(CPD) in the form of CAPD and APD in the Indian sub-continent as renal replacement therapy. The concept of adequate dialysis, which will improve the quality of life and the survival of the patients, should not be conceived simply as increasing the volume and frequency of exchanges there by incurring additional cost and inconvenience to the patient. Adequacy involves assessment of solute removal, ultrafiltration, achievement of euvoolemia, preserving residual renal function, maintaining nutritional status, and cardiovascular risk assessment and risk reduction, controlling blood pressure, phosphorus and acid-base balance, correction of anemia and absence of uremic symptoms.

The international society of peritoneal dialysis (ISPD) has given guidelines on target for solute and fluid removal in adult patients on CPD (1). Renal clearance and peritoneal clearance have different effects on patient survival (2, 3). Prospective randomized trial do not provide evidence to support a beneficial effect of increasing dialysis to total Kt/V urea above 2 or weekly creatinine clearance(WCCr) above 60 liters per week per 1.73 m². Interventional studies have demonstrated that a total Kt/V below 1.7 is associated with poorer primary or secondary outcome (4,5). Ultrafiltration below 750 ml/day was associated with poorer survival in anuric patients on CPD(6). A peritoneal equilibrium test (PET) provides knowledge of the transport characteristics of the patients peritoneal membrane to optimize the prescription profile of the patient(1). Those patients with residual renal function(RRF) which enable them to achieve the minimal target level of the small solute clearance, the RRF should be monitored regularly every one to two months if practicable, otherwise no less than every four to six months. If there is decrease in urine volume suggesting a decline in RRF, it should be measured sooner. A round the clock PD regimen is preferred than the intermittent schedule (1).

We undertook a study (2002 -2004) to measure the adequacy on CAPD, using urea clearance (Kt/V) and WCCr, which also looked at survival and correlation of morbidity and mortality with adequacy parameters.

Materials and methods:

We performed a single center prospective observational study for a period 24 months, on 76 newly started CAPD patients. The ratio between male and female was 57:19 with mean age of 56.18±14.31 years. Dialysis adequacy (Kt/V and WCCr), residual glomerular filtration rate (GFR), creatinine clearance, normalized protein catabolic rate(nPCR) and plasma albumin were analyzed. All end stage renal failure patients who are on CAPD was included in this study. In the table 1 base line demography and exchange volume of dialysis is given. Base line membrane characteristic assessed by standard PET is given in table 2.
Table 1: Base Line Demography and Exchange Volume

<table>
<thead>
<tr>
<th>Variables</th>
<th>PD patients</th>
</tr>
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<tbody>
<tr>
<td>Total Patients</td>
<td>76</td>
</tr>
<tr>
<td>Male female ratio</td>
<td>57:19</td>
</tr>
<tr>
<td>Mean Age (years)</td>
<td>56.18±14.31</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>38</td>
</tr>
<tr>
<td>Mean Survival</td>
<td>24.06 months</td>
</tr>
<tr>
<td>Total exchange volume</td>
<td>6 liters-50 patients (65.8%)</td>
</tr>
<tr>
<td></td>
<td>≥8 liters-26 patients (34.2%)</td>
</tr>
</tbody>
</table>

Table 2: PET Result of the Cohort

<table>
<thead>
<tr>
<th>Transport Classification</th>
<th>Peritoneal transport rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>30%</td>
</tr>
<tr>
<td>High Average</td>
<td>42%</td>
</tr>
<tr>
<td>Low Average</td>
<td>27%</td>
</tr>
<tr>
<td>Low</td>
<td>1%</td>
</tr>
</tbody>
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Results

The results of combined Kt/V (Renal + Peritoneal), Weekly Creatinine clearance, serum albumin, and normalized protein catabolic rate are given in Table 3.

Table 3: Adequacy and nutritional parameter

<table>
<thead>
<tr>
<th></th>
<th>Kt/V</th>
<th>WCC</th>
<th>Albumin</th>
<th>nPCR (p=NS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6L</td>
<td>1.67</td>
<td>49.8</td>
<td>3.32</td>
<td>0.73</td>
</tr>
<tr>
<td>≥8L</td>
<td>2.1</td>
<td>65.6</td>
<td>3.38</td>
<td>0.70</td>
</tr>
</tbody>
</table>

The graph shows cumulative survival technique over 30 months (figure 1). The one year and two year technique survival for those who were dialyzing with 6 liters and 8 liters, where 64% and 84% respectively, the two year survival was 53% and 52% respectively. The major cause of technique failure was peritonitis and major cause of drop out (Patient survival) was cardiovascular death. The peritonitis rate is one episode in every 21 patient months. Diabetics constituted 50% of the population under study.

Discussion:

Ever since CAPD was initiated in India 1991 as a renal replacement therapy growing number of patients are utilizing this mode of therapy (7,8). There are limitations and constraints for CAPD predominantly due to cost and reimbursement policy (9). There is a scarcity of data from South Asian region with regard to dialysis adequacy and survival. In our study there was no significant difference in nutritional status as assessed by serum albumin level and nPCR in patients with higher and lower Kt/V. The great majority of our patients belongs to high and high average transport group. This is not surprising as majority of the patients who were on CAPD were diabetics.

As the RRF declined in the high Kt/V group over a period of 24 months the survival almost equalled in both groups predictive of survival in prospective observational studies (2,10-12).

A recent publication from India showed Kt/V of 1.45±0.26, WCCr 55±10.6 L/week in malnourished patients and Kt/V 1.61±0.19 and WCCr 68.8±29.1 L/week in normally nourished patients (p=NS) (13). On Kaplan-Meier analysis this study showed peritonitis-free survival in patients with normal nutrition (42 months) was significantly higher compared to patients with malnutrition (21 months) based on SGA (log rank p=0.003). Serum albumin was 2.8±0.56 gm/dl and 3.5±0.44 gm/dl in malnourished and normal nutritional group respectively (p=0.001) (13). They concluded that peritonitis rate is high in patients with malnutrition and that malnutrition indices, especially SGA, can predict the peritonitis rate in CAPD patients (13).

In the NECOSAD study two year survival of all included
patients is 75%; 2 year survival is 80% for patients starting with PD and 73% for patients starting with hemodialysis (2).

The association between timing of dialysis initiation and differences in patient outcomes is important, that is survival and Health related quality of life (HRQOL). After 3 years of dialysis treatment, the benefit in survival of patients who started dialysis in time as per the K/DOQI PD work group published opinion based guideline for the benefit in the survival time was 2.5 months (14). Even before the start of dialysis treatment HRQOL is severely impaired in dialysis patients (15). In a developing economy where patient have to pay from out of their pocket for the initiation of dialysis, they present to the nephrologist late in the course of illness and hence the low survival as found in our study. However the survival of the patients on chronic peritoneal dialysis has remarkably improved over the last decade(7,8,13).

Mortality risk varies substantially in dialysis patients according to the underlying cause of ESRD, age, level of baseline comorbidity. As in our cohort, PD was associated with a lower risk of death among younger patients and high risk among older patients with diabetes mellitus.

There is lack of beneficial effect of a higher dialysis dose in the two randomized controlled trials as demonstrated by Lo et al in Hong Kong study and Paniagua R et al in the ADIMEX study(16,17). Currently we lack the data on whether increasing the PD dose improve survival. Patients treated with very low dialysis prescription with weekly Kt/V urea (<1.5/week) and low creatinine clearance (40L/Week/1.73m2) had a three times increased risk of death compared to anuric PD patients treated with a higher dose. This suggests that anuric patients on PD require higher dose of dialysis. Predefined fixed levels of small solute clearance should not strictly determine the timing of the initiation of dialysis, but other factors should be taken into account, such as fluid status, inflammation, hypertension, nutritional status, quality of life, and complaints of the patients. As long as a patient is doing well with a renal function lower than that recommended by K/DOQI, signs and symptoms of uremia should be monitored closely. When they are absent, initiation of dialysis treatment can be postponed(2).

In CANUSA study with 680 patients with Kt/V 2.1 and WCCr 70liters/1.73m2, the two year patients survival was 78% and the technique survival was 75%. Which was one of the largest study to evaluate the relationship of adequacy of dialysis, nutritional status, mortality, technique failure and morbidity. This study showed decrease of 0.1ml of Kt/V per week was associated with 5% increase in the relative risk of death. A decrease of 5 litres/1.73m2 of WCCr was associated with 7% increased relative risk of death. The relative risk of technique failure was increased with decrease in serum albumin and decreased creatinine clearance. In this study a one gram fall in serum albumin was associated with a 6% increase in the relative risk of death. One unit in the decline in the subjective global assessment score was associated with a 25% increased risk of death.

In the Hong Kong study 937 patients were assessed. Among them (68.2%) were using 3 x 2-L exchange per day; mean age was 54.6±13 years mean total Kt/V was 1.83±0.42 and total weekly creatinine clearance was 55.6±19.5 L/week/1.73m2. Nineteen percent of the patients were moderately to severely malnourished according to the composite nutritional index. There was no significant correlation between indices of adequacy and serum albumin. The 1- and 2-years patient survival from the time of assessment was 90.9% and 79.8%. There was a trend toward better survival in patients with Kt/V greater than 2.0, but it was not statistically significant.

The ADEMEX (Adequacy of peritoneal dialysis in Mexico) study was a prospective, randomized controlled trial of 965 continuous ambulatory peritoneal dialysis patients in Mexico who were followed for a minimum of two years. This landmark trial was designed to test the hypothesis that increasing the removal of certain toxins could reduce patient mortality. Patients were randomized into two study groups; the control group was prescribed as standard 2L exchange 4 times a day, which is the usual prescription used in Mexico in non-study patients (average peritoneal creatinine clearance 45L/wk). The treatment group was prescribed a modified dose that consisted of increasing the fill volume to 2.5L or 3L or involved increasing the number of exchanges to 5 daily using 2.5L fill volumes, to achieve a prescription target clearance of 60L/wK and Kt/V of 1.62. The treatment group had a Kt/V 2.3 were as the control group had a Kt/V of 1.62. There was no difference between the groups.

In an environment with limited resources cost effectiveness of intervention is an essential consideration. Small volume PD with 6L/day may be an acceptable compromise in some population with smaller body size with residual renal function, given the financial constraint. In Asian countries the PD treatment rates show a definite relationship with the wealth of the nation. Important differences are seen in the survival rates of dialysis population across countries based
on ethnicity. Although good median term survival is seen in our patients despite an apparent lower Kt/V as compared with Western standard, these favorable outcomes should not prevent nephrologist from providing adequate dialysis to patients. In the current guidelines the focus has shifted from optimum to minimum Kt/V of $\geq 1.7$ for those patients with signs and symptoms of under dialysis, a trail of increasing dialysis should be provided even if Kt/V greater than aforementioned(1). For relevant patients RRF should be monitored frequently every 2-4 months or 4-6 months(1).

In conclusion dialysis adequacy means more than Kt/V for urea, ultrafiltration volume and should include other clinical parameters which are equally are more important.

References:


