

## Comparison between continuous ambulatory peritoneal dialysis and automated peritoneal dialysis: An Indian perspective

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### Abstract

**Background:** CAPD & APD are two modalities of chronic PD. Usage of APD has been steadily increasing in western countries. Data regarding APD from India are lacking. This study was undertaken to compare the outcomes of APD & CAPD. **Methods:** Retrospective study of 40 patients on APD matched with 40 CAPD patients from 2011-2015. **Results:** A total of 80 (40-APD, 40-CAPD) incident PD patients were retrospectively analysed. Baseline characteristics were similar in both groups. 42.5% in APD and 55% in CAPD group respectively had one or more episodes of peritonitis (Ns). Peritonitis rate in APD group was 0.27 episode per year as compared to 0.30 episode per year in CAPD group. Exit site infection developed in one APD patient & 2 in CAPD. 16 patients in APD and 20 patient in CAPD developed PD peritonitis. 77% were culture negative & 23% were culture positive. 2 patients developed fungal peritonitis. 61.5% responded to standard therapy & 28.5% had refractory peritonitis (APD-7 vs. CAPD-8). Need for hospitalisation for any cause more in CAPD than APD (CAPD-33 vs. APD-29, ns). Hospitalisation rate was also less in APD than CAPD (0.55 episode per year vs. 0.63 episode per year). Residual urine output at tie of admission & the end of follow up was less in APD than CAPD, although non-significant. Technique failure was not significant between groups (APD-6 vs. CAPD-7). Overall 28.7% had died at the end of follow up. APD had 11 deaths as compared to CAPD who had 12 deaths. Peritonitis related death was commonest cause in either groups. **Conclusion:** APD when compared to CAPD did not differ significantly in terms of peritonitis rate, hospitalisation rate, preserving of residual renal function, technique failure. All-cause mortality did not differ significantly between groups. Our study did not show any clear benefit of APD over CAPD.

**Keywords:** CAPD, APD, peritonitis rate, hospitalisation rate, RRF, technique failure.

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### Introduction

Chronic peritoneal dialysis is used as renal replacement therapy (RRT) among a large number of patients in the developing Asian countries and is gaining popularity in many countries[1]. PD offers certain clear advantages over HD such as simplicity, reduced need for trained technicians and nurses, minimal technical support requirement, lack of electricity dependence, online water purification and home-based therapy with institutional independence which has potential cost savings. CAPD & APD are two forms of PD. CAPD- the conventional PD, involves performing the PD exchanges manually & APD is a broad term that is used to refer to all forms of PD employing a mechanical device to assist the delivery and drainage

of dialysate. Lack of sustained patient motivation over long periods of time, technique failure and recurrent peritonitis led to development of APD[2]. The proportion of PD patients on APD has been steadily increasing in the past decade especially in western countries.

Various registries have compared CAPD & APD as to which modality is better[3]. However data regarding the usage of APD in India and comparison between APD & CAPD from India are lacking. Hence this study was taken up to compare the outcomes of CAPD & APD.

### Materials & methods

This retrospective study was performed at a state government run tertiary care institute of North India. CAPD was started at this institute in 1992 & APD was started in 2007

After screening all PD patients from 2011-2015, we found 75 patients on APD & 325 on CAPD. Amongst 75 APD patients 25 were excluded from the study (Fig-1).

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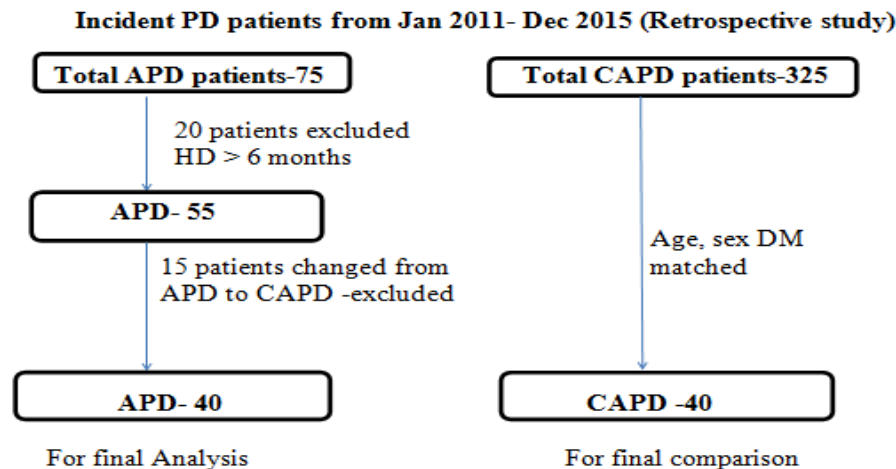


Fig 1: Study Design

40/325 CAPD patients matched for age, sex & Diabetes Mellitus were selected using simple lottery method.

Patients started on APD were at Patient-physician discretion & were not based on any compelling reason.

80 incident PD patients (APD-40, CAPD 40) were included. All patients remained in the same cohort & there was no crossover of the patients between the groups. Medical records were screened from SGPGIMS-PD Registry. Baseline characteristics at the time of initiation of PD including age, sex, Co-morbid conditions, etiology of CKD, Serological status, reason for choosing PD, Laboratory parameters, residual urine output, Ultra filtrate, time to 1<sup>st</sup> episode of peritonitis & hospitalisation, total number of peritonitis & hospitalisation & reason for the same were recorded. Laboratory parameters, residual urine output & Ultra filtrate were recorded at 6 months, 12 months, 24 months & during last follow up period which was December 2016.

#### Primary End points

1. Technique failure
2. Death due to any cause

#### Secondary End points

1. Peritonitis episode/s
2. Hospitalisation Rate/s

Patients of both cohorts were trained by the same PD nurse. APD patients used APD cyclor (Home Choice) of Baxter India Pvt. Ltd, New Delhi. They were prescribed 2 night exchanges of 5.0 l bags of either 1.5% or 2.5% dextrose Dianeal solution as per the clinical condition. CAPD patients were prescribed three exchanges per day of

2.0 l bags of 1.5% or 2.5% dextrose Dianeal solution. A fourth exchange of Dianeal/Extaneal was added only when the patient failed to achieve adequacy and/or edema free State.

#### Statistical Analysis

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean  $\pm$  SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Kaplan-Meier survival analysis used for calculating the median survival. Log rank test was used for the significance between different groups. SPSS version 15.0 software was used for the above analysis.

#### Results

##### Patient characteristics

A total of 80 (APD-40, CAPD-40) incident PD patients were followed up. Mean age, Sex, Diabetes Mellitus, Co-morbid medical conditions, serological status, reason for choosing PD, duration of CKD were all similar & did not achieve any statistical significance as shown in (Table-1). Aetiology for CKD was comparable between the groups & was significant  $p=0.028$ .

Table 1: General characteristics of study population

	APD (N=40)	CAPD(N=40)	P VALUE
Age	53.95 $\pm$ 13.3	52.28 $\pm$ 13.79	0.577
Sex (m:f)	1.85:1	1.85:1	1.00
Diabetes	16(40%)	17(42.5%)	1.00
HTN	18(45%)	20(50%)	
Cad	4(10%)	3(7.5%)	0.384
Hypothyroidism	4(10%)	3(7.5%)	
Duration of ckd	31.1 $\pm$ 26 MONTHS	31 $\pm$ 40 MONTHS	0.987
Mean duration of followup	26.30 $\pm$ 12.9 MONTHS	31.8 $\pm$ 17.5 MONTHS	0.12
<b>ETIOLOGY OF CKD</b>			
DKD	14(35%)	14(35%)	<b>0.028</b>
CKD-u	21(52%)	18(45%)	
Obstructive uropathy	3(7.5%)	2(5%)	
ADPKD	0	3(7.5%)	
CGN	1(2.5%)	2(5%)	

CIN	1(2.5%)	0	
Mm	0	1(2.5%)	
SEROLOGY			
Hepatitis b	1(2.5%)	4(10%)	0.381
Hepatitis c	3(7.5%)	4(10%)	
Hiv	1(2.5%)	0	
REASON FOR CHOOSING PD			
Logistic issues	11(27.5%)	2(5%)	0.06
Medical illness	4(10%)	3(7.5%)	
Positive serology	5(12.5%)	8(20%)	
Access issues	2(5%)	5(12.5%)	
Self decision	18(45%)	22(55%)	

Laboratory parameters like Haemoglobin, serum creatinine, calcium, phosphorous, PTH were analysed at the time of initiation, 6 months, 12 months, 2 years & at last follow up. Serum Sodium, potassium & albumin were analysed at the time of initiation of PD & at the last follow up. The results of all laboratory parameters are given in (Table-2).

**Table 2: Clinical parameters of the study population**

Lab characteristic	APD	CAPD	P VALUE
<b>At initiation</b>			
Hemoglobin	9.3±1.2	8.6±1.7	<b>0.033</b>
Creatinine	6.5±1.4	7.7±2.7	<b>0.015</b>
Calcium	8.3±0.9	8.4±1.0	0.655
Phosphorus	4.9±1.6	5.6±1.7	0.063
Albumin	3.3±0.5	3.5±0.5	0.15
Sodium	134±4.2	136±3.9	0.07
Pottasium	4.1±0.5	4.5±0.5	<b>0.02</b>
iPTH	399±368	526±485	0.19
Urine output	413±197	529±343	0.07
Ultrafiltrate	1211±247	1142±125	0.120
<b>At 6 months</b>			
Hemoglobin	9.9±1.2	9.5±1.4	0.4
Creatinine	6.4±1.3	7.2±2.3	<b>0.05</b>
Calcium	8.7±0.6	8.5±0.7	0.19
Phosphorus	4.7±1.1	5.1±1.2	0.36
iPTH	287±240	415±424	0.112
Urine output	278±182	380±274	<b>0.05</b>
Ultrafiltrate	1159±204	1107±111	0.166
<b>At 1<sup>st</sup> year</b>			
Hemoglobin	10.5±1.3	9.5±1.3	0.13
Creatinine	6.7±1.9	6.7±2.6	0.96
Calcium	8.7±0.7	8.7±0.7	0.46
Phosphorus	4.7±1.0	5.0±1.2	0.37
iPTH	209±238	360±353	0.29
Urine output	212±172	302±248	<b>0.07</b>
Ultrafiltrate	1168±178	1116±171	0.212
<b>At 2<sup>nd</sup> year</b>			
Hemoglobin	10.2±1.3	9.1±1.1	0.06
Creatinine	6.7±1.5	7.4±2.2	0.20
Calcium	8.7±0.8	8.6±0.9	0.70
Phosphorus	5.0±4.2	4.8±1.0	0.67
iPTH	285±243	443±483	0.16
Urine output	150±209	259±256	0.11
Ultrafiltrate	1186±208	1152±154	0.517
<b>At last followup</b>			
Hemoglobin	9.9±1.6	11.4±1.4	0.53
Creatinine	6.4±1.7	6.4±1.9	0.97
Calcium	8.6±0.8	8.4±0.8	0.17
Phosphorus	4.8±1.3	3.3±0.8	0.06
iPTH	259±222	310±314	0.42
Urine output	159±169	206±217	0.286
Ultrafiltrate	1184±1138	1979±138	0.23

Overall Means of Haemoglobin, serum calcium and albumin were higher in APD group than compared to CAPD group. Mean Hb value

at the time of initiation & at 2 years between APD & CAPD group were significant  $p<0.05$ . Similarly Serum Creatinine at the time of

initiation & at 6 months were statistically significant between the groups  $p<0.05$ . Mean serum albumin at last follow up in APD group was higher than CAPD group & was statistically significant  $p<0.05$ . Mean serum Sodium, potassium, phosphorous, PTH were lower in the APD group than CAPD group & were not significant. Ultra filtrate rate in both APD & CAPD groups was comparable without any statistical significance. Mean duration of follow up in APD group was  $26.30 \pm 12.9$  months compared to CAPD  $31.80 \pm 17.5$  months & was non-significant.

#### Peritonitis (Table-3)

In APD group 42.5% (n=17) had one or more episodes of peritonitis as compared to 55 % (n=22) in CAPD group, however statistically non-significant. In the first 6 months of catheter insertion 10 patients developed peritonitis (APD-4 vs. CAPD-6). In the 2<sup>nd</sup> year it was 15 (APD-7 vs. CAPD-8). First episode of peritonitis developed early in APD group than CAPD group ( $15.53 \pm 11.1$  months vs.  $18.64 \pm 15.9$  months) & was not significant.

**Table 3: Peritonitis & outcomes**

Characteristics	APD	CAPD	P VALUE
Peritonitis occurrence	17(42.5%)	22 (55%)	0.370
Mean time for 1 <sup>st</sup> episode	15.53±11.1 months	18.64±15.9 months	0.498
Peritonitis rate	0.27 episodes/year	0.30 episodes/year	0.352
Exit site infection	1 (2.5%)	2 (5%)	0.57
PD peritonitis	16(40%)	20(50%)	0.52
Culture negative	11(27.5%)	18(45%)	0.208
Culture positive	5(12.5%)	4(10%)	
Bacterial	3(7.5%)	4(10%)	
Fungal	2(5%)	0	
Treatment outcomes			
Improved	10(25%)	13(32.5%)	1.00
Refractory	7(17.5%)	8(20%)	

Peritonitis rate in APD group was 0.27 episode per year as compared to 0.30 episode per year in CAPD group & was non-significant. All patients who developed peritonitis required hospitalisation. Overall 3/39 patients had Exit-site infection (1 in APD at 12 months & 2 in CAPD at 4 & 13 months respectively). Pseudomonas aeruginosa was isolated in APD patient & responded to standard treatment. In CAPD patients with exit-site infection Enterococci & Methicillin-resistant coagulase negative Staph. aureus was isolated respectively. The 2<sup>nd</sup> patient developed refractory peritonitis leading to catheter loss. 36/39 patients developed peritonitis (APD-16, CAPD-20). 77% (30/39) were culture negative peritonitis & 23% (9/39) were culture positive. Among culture positive 1 had Gram positive (MSSA) isolate, 3 patients had Gram negative (E. coli, pseudomonas & Radiobacter respectively) isolates. All Culture positive patients had refractory peritonitis leading to catheter loss. 2 patients in APD group developed fungal peritonitis (Candida & Aspergillus respectively) & lead to catheter loss.

61.5% (APD-10, CAPD-14) patients who developed peritonitis responded to Intra-peritoneal antibiotics & 28.5% (APD-7, CAPD-8) developed refractory peritonitis leading to catheter loss. In our study cohort, peritonitis developed as early as first month & as late as 55<sup>th</sup> month.

#### Hospitalisation (Table-4)

Need for hospitalisation for any cause was assessed. 77.5% (APD-29, CAPD-33) required hospitalisation during the study period. Mean duration of time for first hospitalisation in APD group was  $17.3 \pm 13.1$  months & in CAPD group was  $15.03 \pm 14.5$  months. However this was not statistically significant. Hospitalisation rate in APD group was less than CAPD group (0.55 episode per year vs. 0.63 episode per year), although non-significant. The reason & mean time duration for hospitalisation/s amongst the groups are given in (table-) & are non-significant.

**Table 4: Hospitalisation & outcomes**

Characteristics	APD	CAPD	P VALUE
Number of hospitalisation	29(72.5%)	33(82.5%)	0.13
Catheter related	4	1	
Uf failure	0	3	
Peritonitis	15	14	
Medical reasons	9	15	
Uremic reasons	1	0	
Time for 1 <sup>st</sup> hospitalisation(n)	$17 \pm 13$ (n=29)	$15 \pm 14$ (n=33)	0.523
Time for 2 <sup>nd</sup> hospitalisation(n)	$16.7 \pm 9.7$ (n=17)	$21.05 \pm 16$ (n=19)	0.43
Time for 3 <sup>rd</sup> hospitalisation(n)	$19 \pm 11$ (n=6)	$25 \pm 14$ (n=10)	0.40
Hospitalisation rate	0.55 episodes/year	0.63 episodes/year	0.066

#### Residual Renal Function

The residual urine output at the time of initiation of PD was lower in APD group than CAPD group (413ml/day vs. 529ml/day) & was non-significant. After 6 months of follow up there was significant difference between the groups (APD-278ml/day vs. CAPD-380ml/day)  $p=0.05$ . There was a gradual non-significant decline in residual urine output over time in both groups & it was lower in APD group than in CAPD group (table-). Also patients who succumbed during the course of study period had lower residual urine output than who are surviving (table). However it failed to achieve any statistical significance.

#### Technique failure (Table-5)

There was no significant difference between the two groups in terms of technique failure. 6/40 patients in APD group were shifted to HD. Similarly in CAPD group 7/40 patients were shifted to HD, 2 patients underwent renal transplant. The reason/s for technique failure are given in (table-). In the APD group 3 patients had developed refractory peritonitis & the other 3 had mechanical/catheter related problems. Similarly in the CAPD group 5 patients had developed refractory peritonitis & 2 had mechanical/catheter related problems. Median time duration for shift to HD was earlier in APD group than in CAPD group, although non-significant ( $17 \pm 18.2$  months vs.  $21.14 \pm 16.5$  months) [fig-2].

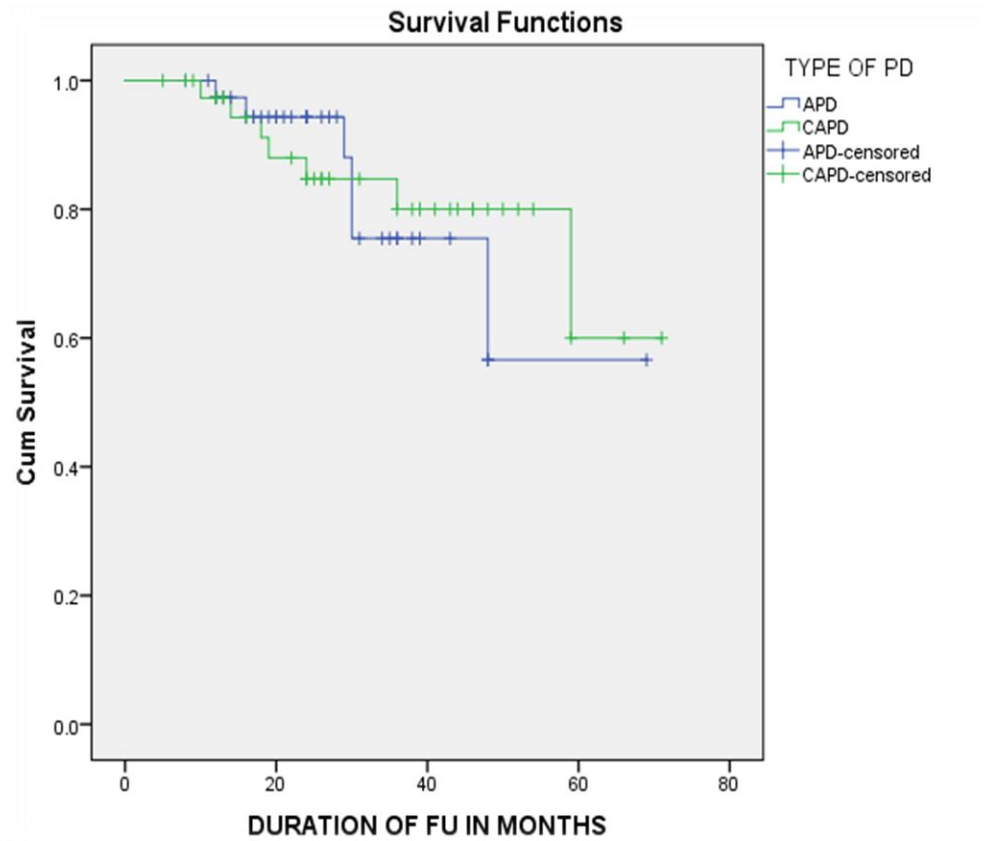


Fig 2: Technique survival

pvalue-0.825

Table 5: Technique failure

Characteristic	APD	CAPD	P VALUE
Shift to HD	6 (15%)	7 (17.5%)	0.075
Transplant	0	2 (5%)	
Cause for Technique failure			
Refractory peritonitis	3 (5%)	5 (12.5%)	
Mechanical cause	1 (5%)	2 (5%)	
Chronic hyponatremia	1 (2.5%)	-	
Suicidal tendency	1 (2.5%)	-	

**Outcome (Table-6)**

Overall 28.7% (23/80) had died, 8.75 % ( 7/80) were lost during follow up & 62.5%(50/80) survived in our study. There was a significant difference in age amongst non-survivors and survivors ( $61.78 \pm 9.7$  years vs.  $48.64 \pm 13.75$  years,  $p < 0.05$ ). There was no significant difference in number of deaths in both the groups (APD-11 vs. CAPD-12). Peritonitis related death was the most common cause (APD-6, CAPD-7), followed by septicaemia other than peritonitis (APD-2, CAPD-5). 2 patients in APD group developed Myocardial infarction & succumbed. One patient in APD group succumbed due to Intra-cranial bleed. Using Kaplan-Meier survival analysis, mean survival in APD group was  $51.4 \pm 4.3$  months and in CAPD group was  $51.9 \pm 4.4$  months respectively. However it was not significant using log rank analysis (fig-3).

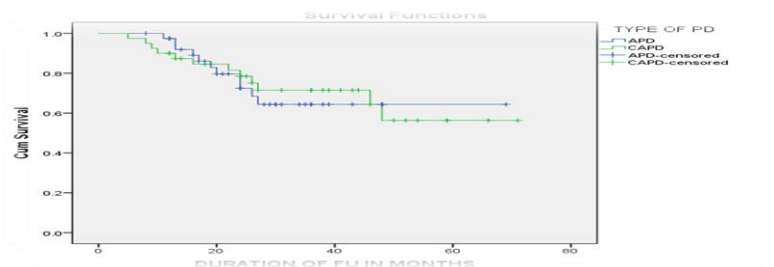


Fig 3: Overall outcome

pvalue- 0.911

1year & 3 year survival rates in APD group were 97.5% & 73% respectively. Similarly 1 & 3year survival rates in CAPD group were 90% & 75% respectively.

**Table 6: Survival outcomes**

Character	APD	CAPD	P VALUE
Survivor	26(65%)	24(60%)	0.875
Lost to followup	3(7.5%)	4(10%)	
Death	11(27.5%)	12(30%)	
Cause of death			
Peritonitis	6(15%)	7 (17%)	0.228
Septicemia	2(5%)	51(12.5%)	
MI	2(5%)		
ICH	1(2.5%)		

## Discussion

The utility of peritoneal dialysis (PD) as a modality of renal replacement therapy in India is less than compared to other forms, mainly Haemodialysis. PD penetration in India is around 18-20%. The majority of PD patients are on CAPD due to its cost-effectiveness, however data regarding the same are lacking from India. APD, another form of PD was being increasingly used as an alternative to CAPD because of its earlier reported benefits as against CAPD. However the high costs involved precludes its routine use & is offered to those who can afford it. This retrospective study was undertaken to compare CAPD & APD modalities and their clinical outcomes. Ours is one of the largest centres for PD in North India. 40 APD patients were compared to well matched CAPD patients from Jan 2011- Dec 2015.

Our study was comparable to other studies in terms of patient's demographics (mean age, sex, and Co-morbid conditions, reason for choosing type of PD)[4]. In our study the aetiology of CKD was significant amongst the two groups & was similar to study done by Mehrotra et.al. In two prior studies the aetiology was non-significant. Mean Haemoglobin values in APD group was higher than in CAPD group, and was statistically significant at the start of study period & continued even at 2 years. This was comparable in studies done by Rao et.al, Mehrotra et.al. In our study iron status, Erythropoietin dose of patients are not recorded & could be a limiting factor. APD patients had better solute clearance as evidenced by lower mean Serum creatinine levels after the start of APD than in CAPD as against study done by Rao et.al. However this effect was lost over period of time and both groups had similar levels at the end of study period. We did not measure weekly creatinine clearance which is a better indicator of solute clearance.

Also patients on APD had better control of CKD-MBD parameters i.e. calcium, phosphorous & PTH than compared to CAPD and was comparable to other studies[5]. In our study, serum albumin levels improved significantly in APD patients than in CAPD patients. More episodes of peritonitis and fluid overload states may explain the low serum albumin levels in CAPD. Study done by Mehrotra et.al also showed the time-averaged albumin levels were lower in CAPD patients[6,7]. In our study we did not find any significant difference between sodium & water removal. Other studies have shown better sodium & water removal in CAPD than APD.

## Peritonitis

In a systematic review comprising of three RCT's done by Rabindranath et.al showed that APD patients had significantly lower rates. Similarly ANZDATA, Mexican study also showed that rates were less in APD than CAPD[8,9]. An Indian study done by Rao et.al also showed lower rates of peritonitis.<sup>3</sup> The USA data base did not show any significant difference. In our study the peritonitis rates were lower in APD group, however it failed to achieve statistical significance. Peritonitis rate in APD group was 0.27 episode per-patient year as compared to 0.30 episode per-patient year in CAPD group & was non-significant. It was similar to ANZDATA study. The peritonitis rates during first 6 months & in second year of follow up in APD group was lower than in CAPD group, but failed to achieve any

significance. **Overall Median time for first episode of peritonitis was earlier for APD than CAPD (15.53±11.1 months vs. 18.64±15.9 months).** Culture negative peritonitis was the most common cause in both the groups. Similar results were also seen in the Mexican study[10,11,12]. In our study only 23% (n=9) were culture positive. There was no significant difference between Gram positive & Gram Negative peritonitis in our study amongst the group as against ANZDATA & Mexican study. The present study also shows paradigm shift from culture positive peritonitis as reported from our own center earlier by Prasad et.al to culture negative peritonitis. There was no difference between the incidences of culture negative peritonitis between the groups as against ANZDATA showing lower rates in APD group. Our study had higher rates (28.5%; n= 15) of refractory peritonitis leading to removal of Tenckhoff catheter & was similar in both the groups. In contrast, ANZDATA study had lower rates of Tenckhoff catheter removal; however type of PD modality was not taken into account[13,14,15,16].

## Hospitalisation

Overall hospitalisation rates for any cause were similar in both the groups. Mean duration of time for first hospitalisation in APD group was 17.3 ± 13.1 months & in CAPD group was 15.03 ± 14.5 months & was non-significant. The most common cause of hospitalisation was peritonitis & related problems. This was similar to other studies. Other than peritonitis, catheter related (catheter migration) & Ultra-filtrate failure were countered. Hospitalisation due to other medical reasons was the next common cause. Lower respiratory tract infection was the commonest cause followed by cardiovascular complications. Hospitalisation rate in APD group was less than CAPD group (0.55 episode per-patient year vs. 0.63 episode per-patient year), although non-significant. A systematic review of RCT's done by Rabindranath et.al had similar outcomes in terms of hospitalisation rates.

## Residual Renal Functions

APD patients have a faster decline in urine volume per day due to more intensive ultrafiltration during shorter dwell times as compared to CAPD where there is gradual fluid removal through long dwell time[17]. In our study there was a significant difference in residual urine output between the groups after 6 months of follow up. However this effect was lost subsequently. Overall APD had lower residual urine output than CAPD. This was similar to most studies. However we cannot conclude as to which modality of PD would better preserve residual renal functions.

## Technique Survival

In our study 2 patients in CAPD group underwent renal transplant & after excluding patients who died, we found that there was no significant difference between the two groups in terms of technique survival. 15% & 17.5 % in APD & CAPD groups respectively were shifted to HD. Refractory peritonitis was the main cause for transfer to HD. Similar outcomes were also seen in earlier studies. However, median duration of time required to shift to HD in APD group was



less when compared to CAPD(17± 18.2 months vs. 21.14±16.5 months).

### Mortality

All-cause mortality in our study was 28.7% & there was no significant difference in mortality rates between the two groups (APD- 13.75% vs. CAPD-15%). 56.5% were Peritonitis related mortality. Most of the previous studies did not show any difference between the mortality rates between the two groups.

The present study is adequately powered & robust in nature. Firstly, only incident patients started on PD were included, thereby avoiding the effect of previous dialysis modality. Second, none of the patients were shifted from one modality to other. Both the groups were well matched to avoid confounding factors influencing the outcome & type of modality.

Despite its strength, this study is not without limitations. Firstly, the study being a retrospective observational study & a smaller sample size. Secondly, patients were assigned to APD at physician discretion & such patients may be high transporters causing a selection bias. In ANZDATA, even after adjusting for peritoneal transport rates failed to show any significance, thereby nullifying selection bias in our study. Lastly, weekly creatinine clearance & transport characteristics of the patients were not available.

### Conclusion

In our study APD & CAPD groups did not differ significantly in terms of peritonitis rates, hospitalisation rates, technique survival & mortality. CAPD is cost-effective, largely available and is not inferior compared to APD. We conclude that the choice of therapy should be based on patient's preference and availability of resources.

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