ABSTRACT
Peritonitis is a common complication in patients undergoing continuous ambulatory peritoneal dialysis (CAPD) and automated peritoneal dialysis (APD). In this retrospective study, peritonitis rates and patient survival of 180 patients on CAPD and 128 patients on APD were compared in the period from January 2005 to December 2014 at Al-Nafisi Center in Kuwait. All patients had prophylactic topical mupirocin at catheter exit site. Patients on CAPD had twin bag system with Y transfer set. The peritonitis rates were 1 in 29 months in CAPD and 1 in 38 months in APD ($p < 0.05$). Percentage of peritonitis free patients over 10-year period in CAPD and APD were 49 and 60%, respectively ($p < 0.05$). Time to develop peritonitis was 10.25 ± 3.1 months in CAPD compared to 16.1 ± 4 months in APD ($p < 0.001$). Relapse and recurrence rates were similar in both groups. Median patient survival in CAPD and APD groups with peritonitis was 13.1 ± 1 and 14 ± 1.4 months respectively ($p = 0.3$) whereas in peritonitis free patients it was 15 ± 1.4 months in CAPD and 23 ± 3.1 months in APD ($p = 0.025$). APD had lower incidence rate of peritonitis than CAPD. Patient survival was better in APD than CAPD in peritonitis free patients but was similar in patients who had peritonitis.

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Introduction
Peritonitis is a common complication in patients who are on continuous ambulatory peritoneal dialysis (CAPD) and automated peritoneal dialysis (APD). It accounts for technique failure and shift of patients to the more expensive modality of hemodialysis (HD) in up to 42% of the cases as well as it accounts for hospital admissions with the financial burden on health system.$^{1,2}$ Furthermore these patients have higher mortality than those on long term HD in the first 12 months of transfer to HD.$^3$ The use of double-bag system and Y set in addition to application of mupirocin ointment at catheter exit site reduced incidence of peritonitis in CAPD patients in the last decade.$^{4,5}$ The introduction of APD in recent years was associated with improvement in quality of life as more time is given to work, family and social activities compared to patients who are on CAPD.$^6$ Many studies in the literature have compared peritonitis incidence in patients on APD and CAPD with some studies show less peritonitis rate in those who are on APD than on CAPD; while others show no difference.$^7-10$ These studies included small number of patients and some involved many centers with different care and protocols. Some of the studies included patients before the implementation of the above measures that reduced peritonitis incidence in CAPD patients; which made the comparison between the two modalities difficult.$^9,11$ Moreover, the causal microbes of peritonitis reported in APD and CAPD were inconsistent which clearly influenced the choice of primary therapy with antibiotics.$^{12,13}$ The long-term outcome of peritonitis in both techniques was reported to be similar in some studies while others showed superiority of APD in terms of technique and patient survival.$^{14,15}$

There are limited data about the incidence rate and long term outcome of peritonitis in CAPD and APD patients in Kuwait. The comparison between the two modalities is of special importance to nephrologists and health care providers as APD becomes a preferable choice for patients starting dialysis due to the convenience of its use and less interference with patient’s life style. The objective of this study was to compare the incidence rates and patient survival of CAPD following the application of preventive measures to that of APD in a large renal center in Kuwait over a 10-year period.
Materials and methods

This was a retrospective study that included 341 patients who were 18 years of age and above on maintenance PD at Al-Nafisi Renal Center in Kuwait in the period from January 2005 to December 2014. Data collection was done by reviewing the medical records of patients and included age, sex, weight, systolic and diastolic blood pressure, albumin level, hemoglobin level, PD duration and causative organism from PD fluid culture. Target points of study were episodes of peritonitis and outcome of peritonitis in APD and CAPD patients. Exclusion criteria in 33 patients included PD duration of <3 months, primary failure of PD catheter and lack of proper follow up. Patients were categorized according to modality of dialysis into: APD: 128 patients and CAPD: 180 patients. APD was performed with the use of Serena machines (Gambro, Sweden) for eight cycles daily (16 L exchange). CAPD was done using Y-set and double-bag disconnect system with 2L exchange four times a day. A daily application of mupirocin ointment at the catheter exit site was used as a prophylaxis for *Staphylococcus aureus* infection in all patients.

Peritonitis was defined as presence of cloudy effluent fluid associated with white cell count of 100 or more in the effluent fluid; with or without abdominal pain. The occurrence of peritonitis with the same organism within 4 weeks from completing therapy of a prior episode was defined as relapse. Recurrence of peritonitis was defined as occurrence of peritonitis after 4 weeks with the same or with different organism. An exit-site infection was defined by presence of purulent drainage, with or without erythema of the skin at the catheter-epidermal interface. Patient survival was defined as loss of PD catheter due to death of patient of all cause with shift to hemodialysis or transplantation being censored. The care of PD patients in the center was provided by a dedicated team of doctors and nurses who do not look after HD patients. The choice of modality of PD in our center was according to the patient preference and was not enforced by the treating physician. Peritoneal fluid samples for cell count and culture were done monthly.

Initial empiric therapy for peritonitis was intraperitoneal vancomycin in combination with amikacin if urine output is <100 mL/day and with ceftazidime if urine output is >100 mL/day. Peritoneal catheter was removed if there was no response to treatment after 72 h or immediately in case of fungal peritonitis.

Analysis of the data was performed using SPSS statistical package version 20 (SPSS, Chicago, IL). Data were expressed as mean ± standard deviation. Kaplan–Meier survival curves were used to plot patient survival for APD and CAPD groups. Means for continuous variables were compared using t-test. The differences between categorical variables were compared using chi-squared test. *p*-Values of <0.05 was considered significant.

**Results**

Patients in APD and CAPD groups were of similar age (62.4 ± 12.2 vs 61.8 ± 13.6 years respectively, *p* = 0.07), dialysis mean duration (21.3 ± 4.7 vs 19.6 ± 3.6 months, respectively, *p* = 0.40) and diabetic status (70 vs 60% respectively, *p* = 0.19). Similarly, there was no difference between APD and CAPD patients in weight, S-albumin, blood pressure and hemoglobin levels. There were, however, more females in APD group than in CAPD group (60 vs 46% respectively, *p* = 0.04) (Table 1).

**Peritonitis rates**

The total follow-up was 3540 patient-months in CAPD and 2729 patient-months in APD with no significant difference. The percentage of peritonitis free patients over 10 years were 49% in CAPD and 60% in APD (*p* < 0.05). APD patients had less peritonitis rates than CAPD patients (1 in 38 vs 1 in 29 months, respectively, *p* < 0.05) or (0.26 vs 0.37 episode/year, respectively, *p* < 0.05) (Table 2). This trend was maintained on yearly basis from 2005 till 2014 as shown in Figure 1 with hazard ratio of peritonitis of 0.76 in APD compared to CAPD.

**Table 1. Clinical characteristics of patients on CAPD and APD.**

| Parameter                        | CAPD (n = 180) | APD (n = 128) | *p*-Value |
|----------------------------------|----------------|---------------|-----------|
| Age (years)                      | 61.8 ± 13.6    | 62.4 ± 12.2   | 0.07      |
| Sex (female/male)                | 82/98 (46%)    | 76/52 (60%)   | 0.04*     |
| PD treatment (patient.months)    | 3540           | 2729          | 0.09      |
| PD duration (months)             | 19.6 ± 3.6     | 21.3 ± 4.7    | 0.4       |
| Diabetes mellitus (%)            | 109 (60%)      | 90 (70%)      | 0.19      |
| HbA1c (%)                        | 6.33 ± 0.6     | 7.3 ± 1.1     | 0.12      |
| Weight (kg)                      | 67.5 ± 14      | 64.9 ± 13     | 0.2       |
| S-Albumin (g/dl)                 | 2.9 ± 0.4      | 2.8 ± 0.3     | 0.34      |
| Systolic pressure (mmHg)         | 142 ± 12       | 138 ± 13      | 0.32      |
| Diastolic pressure (mmHg)        | 86 ± 10        | 83 ± 9        | 0.43      |
| Hemoglobin (g/dl)                | 11.1 ± 0.6     | 10.9 ± 0.5    | 0.32      |
| Creatinine clearance (L/week)    | 68.2 ± 6       | 70.3 ± 5      | 0.71      |
| Kt/V                             | 2.1 ± 3.1      | 2.2 ± 2.7     | 0.43      |

*<p*-value < 0.05 is significant.

**Table 2. Peritonitis rates of patients on CAPD and APD.**

| Parameter                                | CAPD (n = 180) | APD (n = 128) | *p*-Value |
|------------------------------------------|----------------|---------------|-----------|
| Months of treatment                      | 3540           | 2729          | NS        |
| Peritonitis free patients (%)/10 year    | 49%            | 60%           | <0.05     |
| Peritonitis rate (episode in months)     | 1 in 29        | 1 in 38       | <0.05     |
| Peritonitis rate (episode/year)          | 0.27           | 0.26          | <0.05     |
| Time from onset (months)                 | 10.25 ± 3.1    | 16.1 ± 4      | <0.001    |
| Relapse (%)                              | 3%             | 2%            | NS        |
| Recurrence (%)                           | 9%             | 11%           | NS        |
| Interval between episodes (months)       | 5.4 ± 2.1      | 6.5 ± 3.6     | NS        |
| Exit site infection (episode/year)       | 0.09           | 0.08          | NS        |

Note: NS: non-significant.
(CI: 0.64–1.00, \( p < 0.05 \)). Time to develop peritonitis was shorter in CAPD patients compared to those receiving APD (10.25 ± 3.1 vs 16.1 ± 4 months, respectively, \( p < 0.001 \)). Peritonitis free interval between episodes was similar in both groups (5.4 ± 2.1 in CAPD vs 6.5 ± 3.6 months in APD, \( p = 0.32 \)). The percentage of patients with episodes of recurrent peritonitis was similar in both groups without significant difference (9% in CAPD patients vs 11% respectively, \( p = 0.43 \)). There was no difference in relapses of peritonitis in CAPD and APD patients (3 vs 5% respectively, \( p = 0.29 \)). Exit-site infection was similar in both CAPD and APD groups (0.09 and 0.08 episode/year, respectively, \( p = 0.39 \)).

**Microbial pattern of peritonitis**

There was no difference in microbial pattern of cultured organisms in CAPD and APD patients (\( p = 0.33 \)) (Figure 2). The commonest organism causing peritonitis in both groups was *Staphylococcus epidermidis* (coagulase negative Staphylococcus) accounting for 29% of cases in CAPD and 34% of APD but without statistical difference (\( p = 0.12 \)). Gram-negative organisms were the second major cause in both CAPD and APD patients accounting for 19 and 18% of cases, respectively (\( p = 0.24 \)). *Staphylococcus aureus* was the causal organism in 13% of CAPD patients and 10% of APD patients (\( p = 0.3 \)). Poly-microbial peritonitis accounted for 8% of the cases in both groups. Culture negative peritonitis was similar in both groups (10% in CAPD vs 9% in APD, \( p = 0.24 \)).

**Patient survival**

The median survival for patients who had peritonitis in APD group was similar to that of CAPD (14 ± 1.4 vs 13.1 ± 1 months, respectively, \( p = 0.3 \)). Patient survival at 24 months was 38% in APD and 35% in CAPD (\( p = 0.42 \)) (Figure 3). However, patients in APD who were peritonitis free had better median survival than peritonitis free CAPD patients (23 ± 3.1 vs 15 ± 1.4 months, respectively, \( p = 0.025 \)) with 24 months survival of 60% in APD patients compared to 37% in CAPD patients (\( p < 0.05 \)).

In those who had peritonitis, the immediate outcome in both modalities was similar (cure: 63 vs 65%, death: 9 vs 6% and shift to HD 28 vs 29%, respectively, \( p = 0.12 \) and was not affected by the type of causal organisms (Table 3). *Pseudomonas* peritonitis was associated with removal of catheter in 55% of CAPD and 67% of APD cases (\( p = 0.08 \)) and candida peritonitis was associated with the worse outcome with removal of PD catheter and shift to HD in 91% of CAPD and 86% of APD cases.

**Discussion**

In our study, the peritonitis rate of APD patients in a single center in Kuwait over 10 years period was lower
than CAPD patients. The rates of one episode in 38 months in APD and one episode in 29 months in CAPD are within the range of the acceptable peritonitis rates for dialysis centers, of no more than one episode every 18 months (0.67/year at risk), according to recommendations of the International Society of Peritoneal Dialysis (ISPD). There are substantial variations among incidence rates of peritonitis in the two PD modalities when multicenter studies or registry data are compared to those of single center studies. Multicenter studies and registry data analyzes tend to show similar peritonitis rates between the two modalities. Single center studies with a relatively large population that have a standard protocol of management within the center; however, often show lower peritonitis rates in APD compared to CAPD. The observed differences may be partly related to patient selection or different approaches of patient care. Furthermore, in order to compare peritonitis rates in APD and CAPD patients; it is essential for the two groups as in our study to have similar demographic characteristics because factors like age, diabetes, hypertension, obesity and duration of dialysis are associated with higher incidence of peritonitis. One of the limitations that we had was that the percentage of females in APD group was higher than males whereas this was not an issue in CAPD group. Female sex, particularly in diabetic patients, was associated with higher incidence of peritonitis in patients undergoing maintenance PD.

Staphylococcus epidermidis was the commonest causal microorganism of peritonitis in our population followed by gram negative organisms. This order of microbial pattern was also reported by studies conducted in the last decade and probably represent the microbial pattern after implementation of techniques of double-bag system with Y disconnect and use of mupirocin to decrease incidence of S. aureus infection. Studies prior to implementation of these measures showed that there was a difference in microbial pattern of APD and CAPD with the latter group having predominantly gram-positive organisms. Van Esch et al. reported a single center experience in Netherlands over 32 years where there was a time related trend of change in the order of causal microorganism from gram positive organisms of both S. aureus and S. epidermidis before 1990 to S. epidermidis

Table 3. Outcome of peritonitis in CAPD and APD according to microbial pattern.

|                      | CAPD (n = 93) | APD (n = 52) | p-Value |
|----------------------|--------------|--------------|---------|
|                      | Cure | Death | HD | Cure | Death | HD |
| Staphylococcus epidermidis | 20 (75%) | 1 (3%) | 6 (22%) | 15 (83%) | 0 (0%) | 3 (17%) | 0.12 |
| Gram negative        | 10 (72%) | 1 (7%) | 3 (21%) | 5 (62%) | 1 (13%) | 1 (13%) | 0.21 |
| Pseudomonas species  | 4 (36%) | 1 (9%) | 6 (55%) | 2 (33%) | 0 (0%) | 4 (67%) | 0.08 |
| Staphylococcus aureus| 10 (84%) | 1 (8%) | 1 (8%) | 4 (100%) | 0 (0%) | 0 (0%) | 0.08 |
| Polymicrobial         | 5 (63%) | 2 (25%) | 1 (12%) | 4 (66%) | 1 (16%) | 1 (16%) | 0.27 |
| Candida albicans      | 0 (0%) | 1 (9%) | 10 (91%) | 0 (0%) | 1 (16%) | 5 (86%) | 0.32 |
| No growth             | 8 (80%) | 0 (0%) | 2 (20%) | 4 (80%) | 0% | 1 (20%) | 0.41 |
| Total                 | 59 (63%) | 8 (9%) | 26 (28%) | 34 (65%) | 3 (6%) | 15 (29%) | 0.12 |

Figure 3. Survival in CAPD and APD patients with peritonitis (A) and without peritonitis (B).
and gram negative organisms in the period from 2000 onwards. The clinical importance of similarity in microbial pattern of peritonitis APD and CAPD groups is that not only the choice of antibiotics for both modalities will probably be the same but also the causal microorganism did not influence the immediate outcome or patient survival.

Although APD had lower peritonitis rate than CAPD in the present study, patient survival was similar. These findings are supported by recent studies that showed no advantage of APD over CAPD in terms of mortality in patients with peritonitis.\(^{15,28}\) In patients who did not experience peritonitis, however, APD had better patient survival than CAPD. Therefore, large population or meta-analysis studies are needed to compare the outcome of APD and CAPD in peritonitis free patients.

The higher rate of shift to hemodialysis was related to the practice in our center of removing PD catheter in case of fungal peritonitis or if no response to appropriate antibiotics within 72 h. Technique survival and mortality was related to the type of microorganism and regardless of PD modality. Fungal peritonitis has been associated with high technique failure and mortality despite use of intravenous amphotericin B and oral flucytosine and early catheter removal has been associated with improved patient survival.\(^{29,30}\) Likewise pseudomonas species are often associated with relapsing peritonitis with lower cure rate and higher mortality.\(^{31}\)

The limitation of this study is that it is a single-center study. The strength of the study is that it has a relatively large number of patients and it was carried out over 10 years and that the two groups of PD modalities were comparable without factors that may influence the results. There was also proper documentation of patient data in this single center by a dedicated team with detailed documentation of each peritonitis episodes. Moreover, it represents the peritonitis rate after application of preventive measures which make the comparison between APD and CAPD representative of the current practice.

In conclusion, in this present study of a single center experience over 10-year period, APD had lower incidence of peritonitis than CAPD but with similar patient survival. However, in those who were peritonitis free, APD had better survival than CAPD. The causal microbial spectrum was similar in both modalities of PD.

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Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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