Acute Kidney Injury in Critically Ill Patients: A Prospective Randomized Study of Tidal Peritoneal Dialysis Versus Continuous Renal Replacement Therapy

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Abstract: Few studies have discussed the role of peritoneal dialysis (PD) in managing acute kidney injury (AKI) in critically ill patients. The present study compares the outcome of AKI in intensive care unit (ICU) patients randomized to treatment with tidal PD (TPD) or continuous venovenous hemodiafiltration (CVVHDF). One hundred and twenty-five ICU patients with AKI were randomly allotted to CVVHDF, (Group A, \( N = 62 \)) or TPD, (group B, \( N = 63 \)). Cause and severity of renal injury were assessed at the time of initiating dialysis. The primary outcome was hospital mortality at 28 days, and secondary outcomes were time to recovery of renal function, duration of stay in the ICU, metabolic and fluid control, and improvement of sensorial and hemodynamic parameters. No statistically significant differences were observed between groups in regard to patients’ characteristics. The survival at 28 days was significantly better in the patients treated with TPD when compared to CVVHDF (69.8% vs. 46.8%, \( P < 0.01 \)). Infectious complications were significantly less (\( P < 0.01 \)) in the TPD group (9.5%) when compared to the CVVHDF group (17.7%). Recovery of kidney function (60.3% vs. 35.5%), median time to resolution of AKI and the median duration of ICU stay of 9 days (7–11) vs. 19 days (13–20) were all in favor of TPD (\( P < 0.01 \)). This study suggests that there are better outcomes with TPD compared to CRRT in the treatment of critically ill patients with AKI.

Key Words: Acute kidney injury, Acute tubular necrosis, Continuous venovenous hemodiafiltration, Renal replacement therapy, Sepsis, Tidal peritoneal dialysis.

Acute kidney injury (AKI) is a common complication in patients treated in the intensive care unit (ICU) and is associated with considerable morbidity and mortality. Renal replacement therapy (RRT) is frequently needed when supportive therapy and the level of endogenous renal function is not sufficient to meet the patients’ metabolic demands. Since the end of the 1990s, continuous venovenous therapies have gained prominence and become the method of choice for treatment of AKI in the ICU setting (1).

Hyman et al. (2) have reported a transition of dialysis methods prescribed for AKI from 1994–1995 to 1996–2000. During the first period, continuous venovenous therapies accounted for only 9% of all RRT, while intermittent hemodialysis (IHD) and peritoneal dialysis (PD) were prescribed in 83% and 8% of cases, respectively. During the second period, approximately 26% of all treatments for AKI were with CRRT, while PD remained an infrequent choice of treatment. Even though PD is now rarely used to manage patients with AKI (2), and has been replaced by continuous venovenous therapies, it should not be discarded as a therapeutic option (3,4). PD has recently been suggested to provide outcome data as good as daily HD in the management of ICU patients with AKI (3,5), and
Guidelines for the use of PD to treat patients with AKI clearly stated that PD provides an acceptable treatment option for patients with AKI (4). Further, PD offers several advantages over HD by being a simple, safe, gentle, and efficient RRT method. It is able to correct AKI-induced metabolic, electrolytic, acid-base disorders and volume overload in an ICU setting (3,4,6). Aggressive PD modalities, such as high-volume PD and continuous flow PD, can provide RRT doses and efficiency comparable to extracorporeal blood purification methods (7). PD is particularly suitable for patients with hemodynamic instability, and in conditions where systemic anticoagulation should be avoided (8). PD, however, may have some potential limitations such as the need of a viable peritoneal cavity, the risk of peritoneal infection and protein losses and the possible lower efficiency in certain conditions (9–11). There is little recent literature on the use of PD to treat AKI patients, and what exists often does not address fundamental parameters such as adequate quantification of dialysis and patient catabolism. No randomized controlled trial has been done comparing PD to CRRT and, moreover, no study in AKI using tidal peritoneal dialysis (TPD) with the new biocompatible PD solutions has been published. Given these limitations, there is a pressing need to evaluate the adequacy of TPD and biocompatible solutions in AKI in ICU and to compare its outcome with that of continuous venovenous therapy using accepted standards.

PATIENTS AND METHODS

A randomized study of patients with AKI and multi-organ involvement admitted to the ICU and requiring RRT was performed according to Helsinki’s Declaration and the Principles of the Declaration of Istanbul at King Fahd University Hospital, Al-Khobar, Saudi Arabia. The study was conducted from November 2013 to December 2016 with prior approval from the King Fahd University Human Ethical committee. All ICU specialists had longstanding experience with continuous venovenous hemodiafiltration (CVVHDF), whereas the nephrologists had experience with PD. All patients were above 18 years of age. Written and informed consents were obtained from all patients (or legal guardians if patient was unable to consent) to participate in the study and to report individual patient data. AKI was defined as a rise in serum creatinine of 0.3 mg/dL or more from baseline or an hourly urine output of less than 0.5 mL/kg, as per the Acute Kidney Injury Network (AKIN) classification (12). Indications for RRT were any one or a combination of blood urea 80 mg/dL or higher, serum creatinine 3 mg/dL or higher, serum potassium 5.5 mEq/L or higher, metabolic acidosis with arterial pH 7.2 or lower, and hourly urine output of less than 0.5 mL/kg for more than 12 h despite correction of volume depletion. Patients were randomized to receive either pump-assisted CVVHDF (Group A) or continuous TPD (Group B). Exclusion criteria were ESRD (defined as eGFR <15 mL/min per 1.73 m² for ≥3 months), pregnancy, life-threatening pulmonary edema, ongoing peritonitis, recent abdominal surgeries, or AKI of obstructive origin. Vascular access for CVVHDF was a double-lumen 12 Fr hemodialysis catheter introduced into either the internal jugular or the femoral vein. Speed of the blood pump was adjusted between 180 mL and 200 mL/min (PrismaFlex system, Gambro, Hospal, Lyon, France). The dialysate used was Hemosol (Gambro), a bicarbonate-buffered dialysate with a composition of 140 mmol of sodium, 0 mmol potassium, 1.75 mmol calcium, 0.5 mmol magnesium, 109.5 mmol chloride, 25 mmol hydrogen carbonate and 3 mmol lactate per liter. The prescribed dialysis dosage (defined by effluent rate) was 30 mL/kg/h to take into account CRRT “downtime” for clotting and procedures, and fluid removal rate varied based on assessment of volume status. Replacement fluid (Hemosol) was given as 30% pre-filter and 70% postfilter. The replacement fluid rate was adjusted based on the fluid removal rate to keep the prescribed does of 30 mL/kg per h. Unfractionated heparin was given pre-pump, and the dose was adjusted to keep clotting time around 2.5 times normal values. In patients with a bleeding tendency, the circuit was rinsed with heparinized saline and saline flushes 150 mL were given pre-filter every 15 min. Our protocol indicated that treatment should be given continuously with a change of membrane every 48 h. In patients randomized to TPD, a flexible double cuff Tenckhoff catheter (Flex-Neck Classic Peritoneal Dialysis Catheter, Merit Medical Systems, Inc. South Jordan, UT, USA) was used. All PD catheters were inserted by trained nephrologists using Al-Hwiesh technique (13) (Fig. 1). Tidal peritoneal dialysis of 25 L/day, using Physioneal 1.36–2.27% and occasionally 3.8% as clinically indicated, each fill 2.0 L and tidal volume of 70%. Each PD session lasted 24 h, and sessions were repeated daily. Both groups were assessed for organ involved (kidney, liver, heart, lungs) at the time of dialysis initiation in addition to blood urea nitrogen (BUN), serum creatinine, serum electrolytes, and arterial blood gases every 12 h and on termination of dialysis (Table 1). In each group, cause of AKI and severity of illness was assessed using the APACHE (Acute Physiology and Chronic Health Evaluation)
II score (14) and Glasgow coma scale (15); these were assessed by the intensivist. Time taken to initiate dialysis after the initial consultation, time to prepare dialysis access and initiate dialysis, duration of dialysis, and total and net ultrafiltration were analyzed (Table 1 and Table 2). The primary outcome was hospital mortality at 28 days. Uremia was considered to be corrected when BUN declined to less than 40 mg/dL or to less than 50% of its initial value. Acidosis was considered improved when pH reached or exceeded 7.25, or when serum bicarbonate concentration of less than 8.0 mg/dL (corrected for carbon dioxide) was reached or exceeded 15 mEq/L, or both. Hyperkalemia was defined as serum potassium of 5.5 mEq/L or more; it was considered to be corrected when potassium concentration of less than 90 mg/dL or to less than 50% of its initial value. The hollow-blunt introducer (Al-Hwiesh technique) into the pelvis was recorded from inclusion in the study until the hollow-blunt introducer (Al-Hwiesh technique) into the pelvis cavity.

**FIG. 1.** Peritoneal dialysis (PD) catheter introduced through the hollow-blunt introducer (Al-Hwiesh technique) into the pelvic cavity.

| TABLE 1. Patients’ demographic and clinical parameters | Group A | Group B | P-value |
|--------------------------------------------------------|---------|---------|---------|
| Age, years (mean ± SD)                                  | 44.60 ± 12.38 | 45.41 ± 14.12 | 0.3073 |
| Gender (female/male)                                    | 17/45   | 16/47   | 0.2882 |
| Diabetes mellitus, N (%)                                | 14 (21.6) | 16 (25.4) | 0.1680 |
| Cause of AKI, N (%)                                     |         |         |         |
| ATN                                                    | 29 (46.8) | 27 (42.9) | 0.1015 |
| DIC                                                    | 10 (16.1) | 12 (19.0) | 0.1411 |
| Contrast-induced                                       | 8 (12.9)  | 7 (11.1)  | 0.2214 |
| Hepatorenal syndrome                                   | 5 (8.1)   | 8 (12.7)   | 0.0873 |
| Cardiorenal syndrome                                   | 5 (8.1)   | 4 (6.3)    | 0.1326 |
| RPGN                                                   | 3 (4.8)   | 0 (0)      |         |
| Methanol toxicity                                      | 2 (3.2)   | 5 (7.9)    | 0.0284 |
| Systolic BP median (IQR)                               | 90 (84–92)| 88 (81–92) | 0.2542 |
| Diastolic BP median (IQR)                              | 57 (56–62)| 60 (57–60) | 0.2160 |
| Baseline eGFR (mL/min per 1.73 m²)                      |         |         |         |
| Median (IQR)                                           | 13 (10–13)| 11 (11–15)| 0.3631 |
| Days from ICU admission to CRRT                         | 6 (5–7)   | 5 (5–8)   | 0.2928 |
| Time to RRT (hours)                                    | 9 (7.5–10.25)| 9 (8–9.5) | 0.2405 |
| APACHE II score                                        | 21.38 ± 3.65| 22.12 ± 3.13| 0.1820 |
| Mean ± SD                                              | 5.63 ± 3.4| 6.08 ± 2.7|         |
| Mean ± SD                                              | 5.63 ± 3.4| 6.08 ± 2.7|         |
| Initial BUN, mg/dL, Median (IQR)                        | 66 (61–68)| 64 (62–70)| 0.2395 |
| Initial serum creatinine, mg/dL, median (IQR)           | 5.1 (4.6–5.2)| 4.9 (4.6–5.5)| 0.2501 |
| Number of inotropic supports                           | 8 (12.9)  | 7 (11.1)  |         |
| AKI, acute kidney injury; ATN, acute tubular necrosis; BP, blood pressure; BUN, blood urea nitrogen; DIC, disseminated intravascular coagulopathy; RPGN, rapidly progressive glomerulonephritis; RRT, renal replacement therapy; SD, standard deviation.

RRT withdrawal. Hypotension was defined as a systolic arterial blood pressure of 90 mm Hg or less. Hypocalcemia was defined as serum calcium concentration of less than 8.0 mg/dL (corrected for albumin), hypomagnesemia as serum magnesium of less than 1.5 mg/dL, hypophosphatemia as serum phosphate concentration of less than 2.0 mg/dL, hypoglycemia as blood glucose concentrations of less than 90 mg/dL and thrombocytopenia as a platelet count of less than 100 000/μL. A decision to stop dialysis was generally taken when adequate correction of uremia, fluid overload, hyperkalemia,
and acidosis were deemed to have been achieved, or when urine output had improved, or both. Endpoints included cessation of dialysis after improvement and a minimum period of 3 days of not requiring dialysis was necessary for the patients to be classified as successfully withdrawn from dialysis, transfer to conventional dialysis (IHD or PD on chronic basis), cessation of dialysis because of complications, and death.

Statistical analysis

Randomization method was a block randomization by pairs of envelopes: one with TPD and the other CVVHDF. Continuous variables are expressed as median and interquartile range (IQR; 25th (Q1) to 75th (Q3) percentiles) or mean ± SD and categorical variables are expressed as percentage. Non-parametric Spearman’s rank test was used for continuous variables correlation and Mann–Whitney test used for comparison of two groups. P-values were not adjusted for multiple testing and therefore should be considered descriptive. Assuming a 20% difference in primary outcome between the two groups, for 80% power and 95% confidence, it was calculated that a sample size of 188 patients would be required to observe a statistically significant difference. Because we were able to include only 125 patients in a 3-year period at a single center, a significant difference in outcome was not anticipated. Variables with significant univariate associations were candidates for multivariate analysis. Kaplan–Meier curve was used to assess survival in each group. The statistical analysis was performed using SPSS for Windows version 20 (IBM Inc., New York, NY, USA).

RESULTS

The study involved a total of 194 patients with AKI in the ICU setting. Sixty-nine patients were excluded from the study, the remaining 125 patients were then randomized for treatment with either CVVHDF (Group A, N = 62) or TPD (Group B, N = 63) (Fig. 2). Patient’s demographic and clinical characteristics are shown in Table 1. There was no statistically significant difference in age, gender, the median (IQR) systolic and diastolic blood pressure, median (IQR) baseline eGFR and the initial median (IQR) BUN and serum creatinine between the two groups. The median (IQR) time from ICU admission, the median (IQR) time from consultation to start RRT, and the median time to prepare dialysis access and initiate dialysis were similar in both groups. The differences in the mean APACHE II score at initiation of CRRT and the mean Glasgow coma scale were insignificant between the two groups. The CRRT dose prescribed for our patients was 30 mL/kg per h as described in the methods but the mean dose delivered was only 23.55 ± 4.21 mL/kg per h. The primary end-point; the 28 day survival, was significantly better in the patients treated with TPD than in those treated with CRRT (Fig. 3). Recovery of kidney function was better and seen faster in patients of Group B. The median (IQR) time from ICU admission, the median (IQR) duration of ICU stay were also significantly shorter in the patients receiving TPD compared to CRRT (Table 2). Several variables were evaluated at the end of each 24 h of dialysis in each group (Table 3). At the end of day 7, metabolic control, as reflected by BUN and serum creatinine was better in the TPD group when compared with patients treated with CVVHDF. Better response of metabolic acidosis was observed in the former and correction of hyperkalemia was faster and more significant in those patients. Net ultrafiltration was significantly better in the first 4 days in patients treated with CVVHDF as compared to those treated with TPD but at the end of 7 days the difference was not significant (Table 3). Infectious complications related to the RRT were seen more often in the CVVHDF than in the TPD patients. Table 4 shows the adverse events according to treatment group and the causes of death are

| Outcome                                      | Group A N = 62 | Group B N = 63 | P-value |
|----------------------------------------------|----------------|----------------|---------|
| Infectious complications related to dialysis, N (%) | 11 (17.7)      | 6 (9.5)        | 0.0084  |
| Time to prepare dialysis access and initiate dialysis, (min), median (IQR) | 35 (30–37)     | 38 (32–40)     | 0.2010  |
| Recovery of kidney function, N (%)            | 22 (35.5)      | 38 (60.3)      | 0.0056  |
| Resolution of AKI (days), median (IQR)        | 8 (7–10)       | 5 (4–6)        | 0.0044  |
| ICU stay (days), median (IQR)                 | 19 (13–20)     | 9 (7–11)       | 0.0031  |
| Need of chronic dialysis, N (%)               | 7 (11.3)       | 6 (9.5)        | 0.3112  |
| Mortality, N (%)                              | 33 (53.2)      | 19 (30.2)      | 0.0028  |

AKI, acute kidney injury; ICU, intensive care unit; IQR, interquartile range.
Illustrated in Table 5. Six factors met the criteria for inclusion in the multivariate analysis: age (odds ratio [OR] = 1.41, 95% confidence interval [95% CI] = 1.11–1.6, \( P = 0.03 \)), CRRT modality (CVVHDF vs. TPD) (OR = 0.79, 95% CI = 0.66–0.93, \( P = 0.001 \)), sepsis (OR = 1.23, 95% CI = 1.15–1.62, \( P = 0.001 \)), vasoactive drug use (OR = 1.58, 95% CI = 1.24–1.81, \( P = 0.01 \)), mechanical ventilation (OR = 0.89, 95% CI = 0.83–1.1, \( P = 0.01 \)), and UF after 7 days (OR = 2.24, 95% CI = 1.98–2.66, \( P = 0.01 \)). Only sepsis (OR = 1.34, 95% CI = 1.16–1.64, \( P = 0.001 \)) and CRRT modality (OR = 0.79, 95% CI = 0.68 to 0.88, \( P = 0.001 \)) were associated significantly with death.
DISCUSSION

The management of AKI in ICU setting requires, in addition to conservative treatment, a decision concerning when to start RRT. Once RRT is needed, the treating physician should choose between its different modalities, i.e. intermittent hemodialysis, CVVHD, CVVHDF or PD. Such a decision is not always easy, taking into consideration the hemodynamic instability of the ICU patients and the feasibility of implementing the different modalities. For the last two decades, PD has been considered a second class treatment for ICU patients who develop AKI and it has been rarely used in the developed world (2). This might be because of lack of PD experience, and/or knowledge by intensivists and nephrologists working in ICU settings, the limitations attributed to PD, and/or a lack

| TABLE 3. Different parameters at the end of each 24 h during the first week of treatment |
|---------------------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                                | Day 1          | Day 2          | Day 3          | Day 4          | Day 5          | Day 6          | Day 7          | P              |
| CVVHDF                         | N = 62         | N = 62         | N = 62         | N = 62         | N = 69         | N = 66         | N = 60         | N = 63         | N = 63         | N = 63         |
| BUN (mg/dL)                    | Median (IQR)   | Median (IQR)   | Median (IQR)   | Median (IQR)   | Median (IQR)   | Median (IQR)   | Median (IQR)   | Median (IQR)   | Median (IQR)   |
| CVVHDF                         | 66 (61–68)     | 60 (55–64)     | 61 (47–64)     | 64 (45–58)     | 40 (39–50)     | 40 (38–51)     | 44 (40–52)     | 0.025          |
| TPD                            | 64 (62–70)     | 53 (51–58)     | 40 (38–46)     | 33 (30–36)     | 30 (27–32)     | 31 (28–33)     | 28 (27–30)     |
| Cr (mg/dL)                     | Median (IQR)   | Median (IQR)   | Median (IQR)   | Median (IQR)   | Median (IQR)   | Median (IQR)   |
| CVVHDF                         | 5.1 (4.6–5.2)  | 4.8 (4.6–5.0)  | 4.5 (4.0–4.7)  | 4.4 (4.1–4.8)  | 4.0 (3.8–4.4)  | 4.0 (3.6–4.2)  | 3.8 (3.6–3.9)  | 0.031          |
| TPD                            | 4.9 (4.6–5.5)  | 3.6 (3.3–3.8)  | 3.0 (2.7–3.2)  | 2.5 (2.4–3.0)  | 2.5 (2.2–2.6)  | 2.2 (2.0–2.5)  | 2.2 (2.0–2.4)  |
| HCO3 (mEq/L)                   | Median (IQR)   | Median (IQR)   | Median (IQR)   | Median (IQR)   | Median (IQR)   | Median (IQR)   |
| CVVHDF                         | 19.3           | 19.1           | 18.5           | 19.0           | 18.6           | 17.5           | 17.0           | 0.038          |
| TPD                            | 18.7–19.5      | 18.8–19.2      | 18.3–18.8      | 18.5–19.0      | 18.2–18.8      | 17.2–17.8      | 16.4–17.5      |
| K (mEq/L)                      | Median (IQR)   | Median (IQR)   | Median (IQR)   | Median (IQR)   |
| CVVHDF                         | 5.8 (5.4–6.2)  | 5.5 (5.4–6.1)  | 5.1 (4.8–5.4)  | 4.9 (4.7–5.6)  | 4.8 (4.8–5.6)  | 4.9 (4.5–5.2)  | 4.7 (4.5–5.3)  | 0.036          |
| TPD                            | 5.9 (4.8–6.3)  | 5.1 (4.6–5.3)  | 4.5 (3.9–4.7)  | 4.0 (3.8–4.7)  | 3.8 (3.5–4.0)  | 3.6 (3.3–3.7)  | 3.7 (3.4–3.9)  |
| UF (mL/d)                      | Median (IQR)   | Median (IQR)   | Median (IQR)   | Median (IQR)   |
| CVVHDF                         | 1650           | 1580           | 1730           | 1240           | 1265           | 1185           | 1160           | 0.267          |
| TPD                            | 1555–1760      | 1500–1830      | 1720–1775      | 1125–1260      | 1045–1360      | 950–1200       | 840–1165       |
| IQR                            | 840            | 750            | 850            | 940            | 990            | 1135           | 1130           |
|                          | 600–850        | 680–770        | 680–930        | 750–1100       | 900–1230       | 900–1250       | 960–1180       |

BUN, blood urea nitrogen; Cr, serum creatinine; CVVHDF, continuous venovenous hemodiafiltration; HCO3, serum bicarbonate; IQR, interquartile range; K, serum potassium; TPD, tidal peritoneal dialysis; UF, net ultrafiltration.

| TABLE 4. Adverse events according to treatment group |
|----------------------------------------------|----------------|----------------|
| CVVHDF | TPD | P-value |
| Hypotension | 27 (43.5) | 10 (15.9) | 0.0016 |
| Infections | 11 (17.7) | 6 (9.5) | 0.0036 |
| Catheter change | 14 (22.6) | 5 (7.9) | 0.0007 |
| Bleeding events | 17 (27.4) | 4 (6.3) | 0.0008 |
| Arrhythmias | 13 (21.0) | 5 (7.9) | 0.0023 |
| Hypoglycemia | 5 (8.1) | 3 (4.8) | 0.0488 |
| Hypomagnesemia | 6 (9.7) | 7 (11.1) | 0.3212 |
| Hypocalcemia | 6 (9.7) | 6 (9.5) | 0.0006 |
| Hypophosphatemia | 5 (8.1) | 7 (11.1) | 0.1121 |
| Thrombocytopenia | 10 (16.1) | 3 (4.8) | 0.0046 |

All hypotensive episodes were recorded from initiation until end of RRT. Hypotension means at least one hypotensive episode during RRT. †Catheter change due to infection or malfunction. ‡Bleeding events required when transfusion is required. §Arrhythmias means supraventricular or ventricular. ††Thrombocytopenia related to the procedure.

| TABLE 5. Causes of death in the two groups |
|------------------------------------------|----------------|----------------|
| Cause of death | Group A | Group B | P |
| Sepsis | 13 (20.9) | 8 (12.7) | 0.0232 |
| ARDS | 5 (8.1) | 2 (3.2) | 0.0361 |
| DIC | 5 (8.1) | 1 (1.6) | 0.0066 |
| Hepatic failure | 7 (11.3) | 6 (9.5) | 0.2344 |
| Acute infective endocarditis | 1 (1.6) | 0 (0) | 0.5454 |
| Methanol toxicity | 2 (3.2) | 2 (3.2) | 0.0021 |

ARDS, acute respiratory distress syndrome; DIC, disseminated intravascular coagulopathy.

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of appropriate resources. In December 2015, as part of the First African Dialysis Conference organized in Dakar, Senegal, physicians from West African countries who have participated in the Saving Young Lives Program reviewed their experiences establishing peritoneal dialysis (PD) programs to treat patients with acute kidney injury (AKI). What was most notable about that experience was the clear demonstration that PD is a safe and efficient modality for patients with AKI in ICU setting (16). Our PD unit at King Fahd University Hospital is one of the most experienced in the Middle East with PD therapy. Importantly, we have developed a new technique in PD catheter insertion that made the rapid institution of PD much simpler than before (13). In our study, Physioneal was chosen as a potentially more physiologic dialysate as it limits the potential undesirable side effects of the lactate-buffered solution (17). It was suggested, therefore, that a combination of a physiologic bicarbonate concentration (25 mmol/L) and a lower lactate concentration (15 mmol/L) (B/L 25/15 solution, registered as Physioneal) might have the dual benefit of adequately correcting acidosis and improving the biocompatibility profile of the solution, and thus be preferred over a pure lactate-based or bicarbonate-based solution (15). The pCO2 of this B/L 25/15 formulation is at the physiologic level and is therefore considered safe (18–20). This study was initially designed to compare the use of TPD as a form of CRRT with CVVHDF for the treatment of AKI in the ICU, focusing on the impact of the two therapies on mortality and recovery of renal function in this group of hemodynamically unstable patients. The study by Ponce et al. in 2012 (3) renewed the interest in using PD for patients with AKI. Encouraging results were observed in that study for biochemical profile and pH levels. There was significant reduction in BUN and creatinine levels, with stabilization of BUN values (<50 mg/dL) and creatinine (<4 mg/dL) after four daily sessions of large volume PD. Another important study by the same author showed that PD is able to adequately treat critically ill AKI patients without significant complications (21). The same group also performed a randomized trial in 120 AKI patients comparing high volume PD (60 patients) with daily intermittent hemodialysis (60 patients) in terms of efficacy and outcomes (8). In that study, mortality did not differ significantly between the groups (58% for high volume PD vs. 53% for daily hemodialysis). The rate of renal recovery was similar for both modalities, but high-volume PD was associated with a shorter time to recovery (7.2 ± 2.6 vs. 10.6 ± 4.7 days). The interest in PD to manage AKI patients has been increased and PD is now frequently used in developing countries because of its lower cost and minimal infrastructural requirements. Studies from these countries have shown that with careful thought and planning, critically ill patients can be successfully treated using PD. (22) Some of the classic limitations of PD use in AKI, such as infectious and mechanical complications and poor metabolic control, have been decreased with the use of cyclers, flexible catheters, and a high volume of dialysate (23). The relatively good outcomes that have been reported by acute PD programs in low resource settings in the treatment of AKI also contributed to the recent ISPD recommendation that acute PD can be utilized safely and efficiently to treat AKI (4). In 2012–2013, Chionh and his group (11) searched MEDLINE, CINAHL, and Central Register of Controlled Trials. Eligible studies selected were observational cohort or randomized adult population studies on peritoneal dialysis in the setting of AKI. Chionh’s metaanalysis found no evidence to suggest significant differences in mortality between peritoneal dialysis and extracorporeal blood purification in AKI. However, only 11 studies were found comparing PD and continuous or intermittent RRT. And, of the 11 studies, only four were randomized trials and the best of them (8) was criticized for flaws in randomization and inclusion criteria. The authors, thus, strongly pointed to the need for good-quality evidence and additional studies in this important area. To our knowledge, none of the published papers (8,24–28) compared TPD (using Physioneal solutions) with CVVHDF in AKI-ICU patients. Compared with the previous randomized trial of Ponce et al. (29) that did not show differences in terms of survival or recovery of renal functions between HD and high-volume PD, our results demonstrated a remarkable difference in favor of TPD over CVVHDF (survival rates of 69.8% vs. 46.8%, P < 0.01). While Katirtzoglou et al. (30) reported BUN levels below 100 mg/dL which were considered satisfactory at that time for patients with AKI treated with continuous PD, Gabriel and colleagues (7) achieved BUN values around 50 mg/dL and creatinine at <4 mg/dL, with high volume peritoneal dialysis used for treatment of AKI in the ICU setting. Chitalia et al. (31) demonstrated that CPD was able to maintain BUN levels at about 65 mg/dL in mild and moderate hypercatabolic AKI patients from India. Our results are encouraging, as we observed better metabolic outcomes with TPD. There was a significant difference in the levels of solute markers between TPD and CVVHDF after 3–4 sessions of dialysis, with stabilization of BUN values below
33 mg/dL, and serum creatinine below 2.5 mg/dL. In addition, serum bicarbonate increased to above 20 mEq/L and serum potassium declined to less than 4 mEq/L (Table 3) after 3–4 sessions of TPD. As in Ponce’s study (7), we observed a shorter time to recovery of kidney function in patients treated with TPD compared to extracorporeal blood therapy [5 days (IQR 4-6) days versus 8 days (IQR 7-10)] for TPD and CVVHDF, respectively (P < 0.01). In our study, the infectious complications were less common with TPD when compared with CVVHDF. Central venous catheter manipulations by different operators and handling by different nurse staff throughout CVVHDF, in addition to the presumptive value of PD in inflammatory cytokines removal might be responsible. The study conducted by Dittrich et al. (32) illustrated the importance of PD in removing the proinflammatory cytokines, particularly, interleukins that could directly relate to the phenomena of capillary leak syndrome, infections and organ dysfunction. Recently, it has been found that substances that may induce and/or potentiate inflammatory responses are effectively removed mainly by PD but not by dialyzer membranes such as those used in CVVHDF (33,34); these substances include certain advanced glycation end-products, complement proteins, adrenomedullin and others (35). Removal of proinflammatory cytokines by PD may not be the only explanation for the significantly higher incidence of sepsis in our patients’ population with CVVHDF treatment compared with the TPD group. Repeated central vein catheterization by different operators with all its drawbacks, handling of the catheter site by different nurse-staff teams and in some cases the need to change the whole set more than one time because of clotting and other problems may also be responsible. Central vein catheterizations (CVC) afford the luxury of immediate access to the circulation without the requirement for cannulation; however, these devices are plagued by their propensity for infection, thrombosis, inadequate blood flow, damage to large central veins, overall cost and increased mortality risk which make their use problematic. CVC-related bacteremia averages between 3.4 and 5.5 incidences per 1000 catheter days with the resultant potential for the development of complications including sepsis, endocarditis and death (36). Although it has been suggested that diaphragmatic movement may be compromised in patients on ventilators, and vasoconstriction of peritoneal capillaries may limit solute transport in critically ill hypertensive patients (37), we did not encounter a negative impact of these theoretical assumptions during the management of our patients. Our study, however, has its limitations: (i) our patients are less sick as per APACHE scores as to what is reported in the literature. (ii) They are also of a younger age with different causes of AKI and possibly less comorbidities. (iii) Patients with abdominal surgery were excluded to avoid difficulties and complications during PD procedure. (iv) In addition, the study is limited by its small numbers and being a single center design. (v) The main limitation, however, is that our patients’ population may not truly reflect the kind of patients usually seen in an ICU setting and that our threshold to start dialysis was earlier.

**CONCLUSION**

The present study suggests that tidal peritoneal dialysis is an effective form of renal replacement therapy that can be safely used in acute kidney injury patients in the intensive care unit setting. Mortality and infection rates were lower, recovery of kidney function was faster, the duration of renal replacement therapy was shorter, and the length of intensive care unit staying was less with tidal peritoneal dialysis than with continuous venovenous hemodiafiltration. Tidal peritoneal dialysis is a simple technique that may be considered for more widespread use to manage patients with acute kidney injury in the intensive care unit setting.

**Conflict of Interest:** The authors declare no conflict of interest.

**REFERENCES**

1. Bellomo R, Mansfield D, Rumble S, Shapiro J, Patrkin G, Boyee N. A comparison of conventional dialytic therapy and acute continuous hemodiafiltration in the management of acute renal failure. *Ren Fail* 1993;15:595–602.
2. Hyman A, Mendelsohn DC. Current Canadian approaches to dialysis for acute renal failure in the ICU. *Am J Nephrol* 2002;22:29–34.
3. Ponce D, Brebel MN, de Goes CR, Almedia CT, Balbi AL. High volume peritoneal dialysis in acute kidney injury: indications and limitations. *Clin J Am Soc Nephrol* 2012;7:887–94.
4. Cullis B, Abdelraheem M, Abrahams G et al. Peritoneal dialysis in AKI. *Perit Dial Int* 2014;34:494–517.
5. Cho S, Lee YJ, Kim SR. Acute peritoneal dialysis in patients with acute kidney injury. *Perit Dial Int* 2017;37:529–34.
6. Sharma SK, Manandhar D, Singh J, Chauhan HS, Koirala B, Guatam M. Acute peritoneal dialysis in Eastern Nepal. *Perit Dial Int* 2003;23 (Suppl 2):S196–9.
7. Gabriel DP, Nascimento GVR, Caramori JT, Martim LC, Baretti P, Balbi AL. High volume peritoneal dialysis for acute renal failure. *Perit Dial Int* 2007;27:277–82.
8. Gabriel DP, Caramori JT, Martim LC, Baretti P, Balbi AL. High volume peritoneal dialysis vs. daily hemodialysis: a randomized, controlled trial in patients with acute kidney injury. *Kidney Int* 2008;73 (Suppl 108):S87–93.
9. Blumenkrantz MJ, Gahi GM, Kopple JD et al. Protein losses during peritoneal dialysis. Kidney Int 1981;19:593–602.
10. Chionh CY, Ronco C, Finkelstein FO, Soni SS, Cruz DM. Acute peritoneal dialysis: what is the adequate dose for acute kidney injury? Nephrol Dial Transplant 2010;25:3155–60.
11. Chionh CY, Soni SS, Finkelstein FO, Ronco C, Cruz DN. Use of peritoneal dialysis in AKI: a systematic review. Clin J Am Soc Nephrol 2013;8:1649–60.
12. Mehta RL, Kellum JA, Shah SV et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007;11:R31.
13. Al-Hwiesh AK. Peritoneal dialysis catheter insertion by a nephrologist: a new, simple and safe technique. Perit Dial Int 2014;34:204–11.
14. Kanus WA, Draper EA, Wagner DP, Zimmerman IE. APACHE II: a severity of diseases classification system. Crit Care Med 1985;13:818–29.
15. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974;13:81–4.
16. Abdou N, Antwi S, Koffi LA et al. Peritoneal dialysis to treat patients with acute kidney injury. The saving young lives experience in West Africa: Proceedings of the Saving Young Lives session at the First International Conference of Dialysis in West Africa, Dakar, Senegal, December 2015. Perit Dial Int 2017;37:155–8.
17. Pecoits-Filho R, Tranaeus A, Lindholm B. Clinical trial experience in West Africa: Proceedings of the Saving Young Lives session at the First International Conference of Dialysis in West Africa, Dakar, Senegal, December 2015. Perit Dial Int 2017;37:155–8.
18. Ponce D, Berbel MN, Abrao JMG, Goes CR, Balbi AL. A randomized clinical trial of high volume peritoneal dialysis versus extended daily hemodialysis for acute kidney injury patients. Int Urol Nephrol 2013;45:869–78.
19. Chionh CY, Soni SS, Finkelstein FO, Ronco C, Cruz DN. Acute peritoneal dialysis: what is the adequate dose for acute kidney injury? Kidney Int 2001;60:1154–63.
20. Himmelfarb J. Continuous dialysis is not superior to intermittent dialysis in acute kidney injury of critically ill patient. Nat Clin Pract Nephrol 2007;3:120–1.
21. Uehlinger DE, Jakob SM, Ferrari P et al. Comparison of continuous and intermittent renal replacement therapy for acute renal failure. Nephrol Dial Transplant 2005;20:1630–7.
22. Augustine JJ, Sandy D, Seifert TH, Paganini EP. A randomized controlled trial comparing intermittent with continuous dialysis in patients with ARF. Am J Kidney Dis 2004;44:1000–7.
23. Vinsonneau C, Camus C, Combes A et al. Continuous venovenous hemodiafiltration versus intermittent hemodialysis for acute renal failure in patients with multiple organ dysfunction syndrome: a multicenter randomized trial. Lancet 2006;368:379–85.
24. Ponce D, Berbel MN, Abrao JMG, Goes CR, Balbi AL. A randomized clinical trial of high volume peritoneal dialysis versus extended daily hemodialysis for acute kidney injury patients. Int Urol Nephrol 2013;45:869–78.
25. Katrizaoglou A, Kontesis P. Continuous equilibration peritoneal dialysis (CEPD) in hypercatabolic acute renal failure. Perit Dial Bull 1983;3:178–80.
26. Chitalia V, Almeida AF, Rai H, Bapat M, Vipul KC, Khanna R. Is peritoneal dialysis adequate for hypercatabolic acute renal failure in developing countries? Kidney Int 2002;61:747–57.
27. Dittrich S, Aktuerk D, Seitz S et al. Effects of ultrafiltration and peritoneal dialysis on proinflammatory cytokines during cardiopulmonary bypass surgery in newborns and infants. Eur J Cardiothorac Surg 2004;25:935–40.
28. Combe C, Pourtein M, De Precigout V et al. Granulocyte activation and adhesion molecules during hemodialysis with cuprophane and a high-flux biocompatible membrane. Blood Purif 2001;19:370–8.
29. Varela MP, Kimmel PL, Phillips TM, Mishkin GJ, Lew SQ, Bosch JP. Bioocompatibility of hemodialysis membranes: interrelations between plasma complement and cytokine levels. Blood Purif 2001;19:370–9.
30. Ronco C, Dell’Aquila R, Rodighiero MP, eds. Peritoneal Dialysis: A Clinical Update. Contrib Nephrol. Basel: Karger, 2006.
31. Nasser GM, Ayus JC. Infectious complications of the hemodialysis access. Kidney Int 2001;60:1–13.
32. Flessner MA. Peritoneal transport physiology: insights from basic research. J Am Soc Nephrol 1991;2:122–35.