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Review

Peritoneal Dialysis in Acute Kidney Injury

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Abstract

The role of peritoneal dialysis in the treatment of acute kidney injury is still under debate and it is underused in many countries. Most of the studies performed in 1970s and 1980s have reported that patients with ARF treated by PD had mortality and incidence of renal recovery at least equal to similar patients treated by hemodialysis (HD) and possibly better. Over the past decade, continuous renal replacement therapies (CRRT) have achieved better cardiovascular stability, and decreased risk of bleeding by the use of low-dose heparinization. These advantages have reduced the indication for PD in critically ill patients. In the meantime, some comparative studies have not demonstrated that CRRT achieves any reduction in mortality compared to IHD. Disadvantages of CRRT were also apparent: although described as 'gentle' forms of therapy, continuous blood therapies require considerable attention by nurses to assure adequate blood flow, monitor anticoagulation status, adjust ultrafiltration rate and calculate fluid balance; the patient is immobilized during therapy and vascular access catheters often provide insufficient blood flow and have a risk of infection leading to sepsis. By contrast, PD is a continuous dialysis therapy with less risk and less nursing effort than CVVH or CVVHD providing more mobility during therapy. PD should be considered as a valuable method for ARF since it offers several advantages over HD such as technical simplicity, no extracorporeal circuit and no bleeding risk; it offers gradual and continuous solute and liquid removal with good cardiovascular tolerance and less cardiovascular instability thus reducing kidney aggression by ischaemia and hydroelectrolytic imbalance.

CAPD may help to maintain renal perfusion by smaller daily variation in body weight, more constant blood pressure and continuous mild overhydration, persistant high blood osmolality and by continuous removal of proteins from the blood including β2-microglobulin, albumin, plasminogen-activator inhibitor type 1 (PAI-1) and immunoglobulins. These physiologic and chemical benefits may account for the highest recovery of renal function in patients with ARF treated by PD than with HD. In resource-poor countries, the cost, practicability and feasibility of CRRT may be a limiting factor whereas peritoneal dialysis is relatively simple and inexpensive and is more widely used. Finally, even in developed countries a major catastrophe can cause severe damage to the infrastructure. PD is an alternative when reliable power, clean water supply and facilities for water treatment are unavailable. Various techniques of peritoneal dialysis have been developed and these have been adapted for use in ARF.

While waiting for better, multicenter comparative studies, there are many patients with acute kidney injury that may benefit from continuous, gentle, affordable and efficient peritoneal dialysis.

Key words: acute kidney injury, peritoneal dialysis, mortality

Introduction

Despite the initial decline in mortality from 90% to 50% with the introduction of acute dialysis more than 55 years ago, [1] the mortality rate of patients with acute renal failure (ARF) remains very high: it is 40%-50% [2] overall but rises to approximately 70%-80% when ARF occurs in the intensive care unit (ICU) [3].

There are many factors contributing to the extremely high death rate seen in ARF. While most patients die from causes unrelated to their renal failure, age, comorbid condition, and severity of illness in patients with ARF have all increased in the last 20 years. Therefore, recent studies suggest that the relatively constant unadjusted mortality rate paradoxically represents better management of this syndrome [4]. Still, understanding of all factors that might influence survival in ARF is critical.

The most important question in the management of ARF probably relate to modality selection, dialysis dose, adequate start and stop of dialysis and the consequence of therapy on residual renal function.

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Peritoneal dialysis as a method of treatment for patients with acute renal failure

As with all dialysis techniques, peritoneal dialysis (PD) was first used in therapy of acute renal failure [5]. Most of the studies performed in 1970s and 1980s have reported that patients with ARF treated by PD had mortality and incidence of renal recovery at least equal to similar patients treated by hemodialysis (HD) and possibly better [5-9]. The article by Firmat reviewed literature reports including over 1,100 patients and in summation the mortality rate was identical for ARF patients receiving PD and HD [7]. In study of 100 patients with ARF in two community hospitals reported in 1983, there was a higher rate of recovery of renal function (and survival) in those treated by PD *vs*. HD. Similar results were obtained 10 years later by the same authors: 10% higher patient survival was recorded for patients treated by PD.

In the meantime, both, PD and HD have improved. Still, among intermittent treatments of ARF patients, IPD and IHD was considered equal [10]. In addition, continuous PD may give even superior results to those of conventional HD including better control of toxic metabolites and volume abnormalities in critically ill patients [11-13].

For many years the standard of practice in treating ARF was intermittent hemodialysis (IHD), three or more times per week for 3 to 4 hours. Over the past decade, continuous renal replacement therapies (CRRT) have achieved better cardiovascular stability, and decreased risk of bleeding by use of low-dose heparinization. These advantages have reduced the indication for PD in critically ill patients. In the meantime, some comparative studies have not demonstrated that CRRT achieves any reduction in mortality compared to IHD [14-16]. Disadvantages of CRRT were also apparent. Although described as 'gentle' forms of therapy, continuous blood therapies require considerable attention by nurses to assure adequate blood flow, monitor anticoagulation status, adjust ultrafiltration rate and calculate fluid balance of the patients. The patient is immobilized during therapy and vascular access catheters often provide insufficient blood flow and have a risk of infection leading to sepsis. By contrast, PD is a continuous dialysis therapy with less risk and less nursing effort than CVVH or CVVHD providing more mobility during therapy. Even so, there is a trend of using CRRT with a progressive decline in use of PD in patients with ARF. Survey of Canadian adult nephrology centers compared two periods (1999-2000 and 1994-2000) and found that the largest increase was in CRRT (from 9% to 26%), while the use of PD decreased from 8% to 3% [17]. In a study involving 54 nephrology centers distributed over five countries, Uchino *et al*. reported that CVVH were the major methods used in patients with ARF in almost 80% of services, while PD was used in 3.2% of these centers and intermittent HD in 16.8% [18]. In Latin America, particularly in Brasil, PD was used in 23% of patients with ARF and in Europe in 21% [19]. Peritoneal dialysis for ARF still constitutes the mainstay of therapy in many developing countries [20].

Indication and contraindications for acute peritoneal dialysis in acute renal failure

Despite its decreasing use, PD should be considered as a valuable method for ARF since it offers several advantages over HD such as technical simplicity, no extracorporeal circuit and no bleeding risk. Because of its gradual and continuous nature, it leads to solute and liquid removal with good cardiovascular tolerance and less cardiovascular instability thus reducing kidney aggression by ischaemia and hydroelectrolytic imbalance. Therefore, peritoneal dialysis proved to be a valuable renal replacement therapy in many instances but mainly in patients with cardiovascular problems and active bleeding (Table 1).

Several reports suggest that patients with ARF seconddary to atheroembolic renal disease may have a better chance of recovery if PD is used over HD [21]. Also, it has been reported that PD has a beneficial role in recovery of renal function in patients with renal failure due to malignant hypertension [22]. In resource-poor countries, the cost, practicability and feasibility of CRRT may be a limiting factor whereas peritoneal dialysis is relatively simple and inexpensive and is more widely used. Simplicity of PD permits interns and postgraduate students to be trained to manage ARF earlier at primary care centers, thus avoiding the delay caused by referring critically ill patients to nephrologist or ICU. Finally, even in developed countries a major catastrophe can cause severe damage to the infrastructure. PD is an alternative when reliable power, clean water supply and facilities for water treatment are unavailable.

Table 1. Indications and relative contraindications for peritoneal dialysis in patients with acute renal failure

Indications for acute peritoneal dialysis	Relative contraindication for acute peritoneal dialysis
Hemodynamically unstable patients	Recent abdominal or cardiothoracic surgery
Bleeding diathesis or active hemorrhage	Diaphragmatic pleuroperitoneal connections
Problem with vascular access	Fecal or fungal peritonitis
Pediatric ICU	Severe respiratory failure
Atheroembolic renal disease?	Abdominal wall celulitis
ARF due to malignant hypertension?	Severe reflux disease
Unavailability of other continuous therapies	Extremely high catabolic status with hyperK
	Pulmonary edema
Special circumstances (disasters)	Peritoneal adhesions

PD is still a very suitable method of treatment for pediatric ICU, especially in critically ill infants and children with ARF and post-cardiovascular surgery [23-24].
There are several relative contraindications to acute PD (Table 1): recent operation with abdominal drainage, peritonitis (fecal or fungal), known pleuroperitoneal fistula (after cardiothoracic surgery). The presence of abdominal hernia or intra-abdominal adhesions might make PD difficult. PD may be relatively contraindicated in the presence of abdominal wall cellulitis or severe gastroesophageal reflux disease, adynamic ileus and recent aortic graft (< 6 months).

Techniques of peritoneal dialysis and dialysis dose

Various techniques of peritoneal dialysis have been described in the literature and these have been adapted for use in ARF (Table 2).

Table 2. Techniques of peritoneal dialysis for ARF treatment

Technique	Description
Acute Intermittent Peritoneal Dialysis (AIPD)	Most often used in the past. Frequent and short exchanges with volumes 1-2 liters and dialysate flows of 2-6 liters/h. Each session lasts 16-20 h, usually tri session per week. The solute clearance is likely inadequate due to its intermittent nature
Chronic Equilibrated Peritoneal Dialysis (CEPD)	Long dwells of 2-6 h with up to 2 liters of dialysate each (similar to CAPD). The clearance of small molecules may be also inadequate but clearance of middle molecules is possibly higher due to the long dwells
Tidal Peritoneal Dialysis (TPD)	Typically involves an initial infusion of 3 liters of dialysate into the peritoneal cavity. A portion of dialysate, tidal drain volume (usually 1-1.5 liters) is drained and replaced with fresh dialysate (tidal fill volume)The reserve volume always remains in the peritoneal cavity throughout the tidal cycle
High Volume Peritoneal Dialysis (HVPD)	Continuous therapy proposed to increase high small solute clearances. Frequent exchanges, usually with cycler (18-48 exchanges per 24 h, 2 liters per exchange). The total dialysate volume range from 36-70 liters a day
Continuous Flow Peritoneal Dialysis (CFPD)	In-flow and out-flow of dialysate occurs simultaneously through two access routes. By inflow of 300 ml/min it is possible to achieve a high peritoneal urea clearance

Patients with ARF are hypercatabolic and require adequate clearance of toxins to avoid complications. Part of the reason for underuse of PD may be related to the perception that PD is not adequate for treatment of ARF. However, studies in literature report efficient fluid removal and metabolic control in patients on CPD [20,25,26]. These studies have limitations such as small sample size and inadequate parameters for measuring catabolism and dialysis adequacy.
Adequacy of dialysis dose is controversial since many authors believe that there is no satisfactory marker for dialysis adequacy in ARF. Katirtzoglou *et al*, reported blood urea nitrogen levels below 100 mg/dL, which were considered satisfactory at that time for ARF patients on CPD [27]. Mehta and Letteri reported that intermittent peritoneal dialysis was not adequate for treating ARF patients, as it maintained BUN levels higher than 75 mg/dl.[28] Phu *et al*, showed that PD failed to keep optimal control of BUN and creatinine levels compared with CVVH, the later having significantly lower mortality rate [29]. However, this study was frequently commented by others since their peritoneal dialysis technique was not optimal: they produced PD solutions locally by using acetate buffer, they used rigid peritoneal catheter, performed manual PD exchanges with short dwell time leading to inadequate solute clearance and dialysis adequacy.
The adequacy of PD in ARF was evaluated in a prospective, randomized, crossover trial that included 87 hypercatabolic patients [25]. This study showed that tidal PD and continuous equilibrated PD (CEPD), which is similar to but more intensive than CAPD, were adequate methods of maintaining BUN levels at about 65 mg/dl in mild and moderate hypercatabolic ARF patients in developing countries. Tidal PD provided better clearances at the same dialysis volume for a lower inpatient cost and only limitation was greater protein loss. In a prospective study, Gabriel *et al,* treated 30 ARF patients who received 236 dialysis sessions of CPD with encouraging results for metabolic, electrolytic and acid-base control [30]. They showed that high doses and CPD using flexible catheter and cycler was an effective treatment of ARF providing high solute removal, sufficient dialysis dose with higher values than described in previous literature.
An old but good idea is about the use of continuous flow PD (CFPD) [31]. This variant of PD utilizes two access points: one for inflow of dialysate and other for outflow. Since there is no interruption of inflow to outflow, flow rates are determined only by the rate at which the draining catheter can reproducibly drain the abdomen. With CFPD dialysate flow rates of up to 300 ml/min can be maintained through the peritoneum.
Besides removal of uremic toxins, dialysis must also remove fluid and salt from the patient. With a properly functioning PD catheter, exchanges of 2 liters of dialysate with 2.5 or 4.25% glucose concentration provides daily fluid removal at the same or greater rate than other regimens without causing hypotension in most patients.

Peritoneal dialysis and renal outcome in patients with acute renal failure

In many of the studies of PD versus HD for ARF, the reason for improved survival in the PD group was related to an increased rate of renal recovery. It is already known that in patients with ESRD, treatment by CAPD resulted in better preservation of intrinsic renal function than treatment by intermittent HD. This preservation of renal function is important because it maintains endocrine function of the kidneys, diminishes the clearance requirements for dialysis, minimizes ultrafiltration and physiologic stress during dialysis. On the other hand, hemodialysis has several known nephrotoxic effects such as generation of inflammatory mediators by extracorporeal circuit, rapid decrease in osmolality and vascular volume, diminishing renal perfusion. All of the above may influence renal recovery during the course of ARF [32].

By contrast, CAPD may help to maintain renal perfusion by smaller daily variation in body weight, more constant blood pressure and continuous mild overhydration, persistent high blood osmolality and by continuous removal of proteins from the blood including β2 - micoglobulin, albumin, plasminogen-activator inhibitor type 1 (PAI-1) and immunoglobulins [33]. These some physiologic and chemical benefits may account for the highest recovery of renal function in most studies, in patients with ARF treated by PD than HD.

Limitations of peritoneal dialysis in patients with acute renal failure

The major criticism of PD is low clearance of uremic toxins; the clearance of low-molecular weight toxins is lower than for other therapies (CAVH, CVVH and daily HD). It is apparent that PD with a modest dialysate use of 1 liter/h is less efficient than other modalities for urea and creatinine but is similarly efficient in removal of larger molecules such as vitamin B_{12}. It is likely that larger molecular weight toxins are the real cause of uremic illness and PD is quite effective in removing various anionic organic compounds that function as middle molecules. Small molecular clearance may be increased by increasing flow rate of dialysate to 1.5-1.0liters/h or more. Tidal peritoneal dialysis can easily deliver 2 liters/h into and out of peritoneum.

Infectious, mechanical and metabolic complications may be major problems. The incidence of peritonitis in PD therapy of ARF is much different than in CAPD therapy. Previous studies have reported a 12%-25% incidence of peritonitis [13]. If peritonitis is detected during therapy of ARF it usually occurs within 2 or 3 days of starting therapy [6,34]. This indicates that PD may detect contamination of the peritoneum that predates the implementation of PD. There is predominance of Staphylococcus epidermidis and Candida (in debilitated patients undergoing antibiotic therapies) but also mixed infections [35]. Peritonitis during PD therapy does not result in septicemia in ARF patients. This is a much different outcome than catheter-related infections during hemodialysis or continuous therapies which frequently result in septicemia. The increasing use of automated PD via flexible catheter has led to a reduction in peritonitis frequency.

Studies have shown that mechanical complications occur in fewer than 10% of patients due to immediate use just after catheter insertion [30]. Also, there is controversy about abdominal distension leading to reduced diaphragm mobilization and consequently about pulmonary compliance.

Protein losses may play an important role, mainly during peritonitis. It may exacerbate conditions in undernourished, critically ill patients with ARF. It was measured that total weekly protein losses were around 45 g in intermittent and 62 g in CPD; albumin accounted for approximately half of this loss. Despite this depletion, plasma albumin and total protein levels were not decreased [36]. However, large variability among individuals was seen and peritonitis was the only factor influencing these losses. This observation was reported by Gabriel *et al.* [30] who reported no significant difference between median plasma albumin values obtained before and after CPD session (median 2.6 g/dL) despite considerable losses in protein (median 21.7 g/day). The authors concluded that dialysate protein loss, although significant, was not a limiting factor for using CPD. In these situations it is necessary to increase patient's protein ingestion which should be 1.5 g/kg/day.

The fact that PD results in protein loss is generally considered a nutritional problem. However, this loss may contribute to the chemical effectiveness of the PD. In patients with hemolytic uremic syndrome, PD significantly reduces plasminogen-activator inhibitor type 1 (PAI-1) which inhibits fibrinolysis in hemolytic uremic syndrome [37]. Most of the organic anions removed by PD in uremic patients are in fact strongly bound to protein, so protein loss increases their clearance. These protein-bound organic anions act as middle molecules and the presence of protein within the dialysate facilitates the transfer of these compounds into the peritoneum. The peritoneal transfer of proteins can be increased by application of hypertonic solutions; the globulin removal by PD on a daily basis could equal or exceed daily therapeutic plasmapheresis [33].

Hyperglycemia is another metabolic complication resulting from PD with glucose-based solutions. Therefore, it is necessary to closely monitor glucose metabolism even by using insulin via continuous infusion pump [25].

When comparing the overall risk of each type of therapy for ARF, there are marked differences between CVVH, CVVHD, HD and PD. The blood treatment therapies have a significant risk of septicemia, low flow from blood access, hypotension, membrane clothing and bleeding. PD therapy includes risk of PD catheter outflow failure, hyperglycemia and asymptomatic peritonitis.

There are controversies about the influence of PD on respiratory system in critically ill patients. Bazari reported that PD impairs diaphragm mobilization because of increased intra-abdominal pressure [38]. As a result, pulmonary compliance and ventilation are impaired. Venous return is also reduced leading to hypotension and consequently to organ and tissue hypoperfusion which favor acidosis However, Epstein *et al.* [39] showed that although it reduces pulmonary volume, characteristics of vital capacity and expiratory volume remain unaltered. They con-

cluded that PD is rarely associated with ventilatory impairment in patients without pulmonary pathologies.

Conclusions

In conclusion, while waiting for better, multicenter comparative studies, there are many patients with acute kidney injury that may benefit from continuous, gentle affordable and efficient peritoneal dialysis.

Conflict of interest statement. None declared.

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