

Use of Peritoneal Dialysis and Mesothelium in Non Primary Renal Conditions

Lazaro Gotloib,¹ Roberto Fudin²

The management of a handful of non renal clinical conditions includes peritoneal dialysis (PD) as a therapeutic tool. Peritoneal lavage after abdominal surgery is still performed in infectious peritonitis and cases of necrotizing hemorrhagic pancreatitis. Use of PD in active psoriasis resulted in approximately 40 papers reporting mostly isolated cases and showing both therapeutic success and failure. That ambiguous picture persisted during controlled studies, and interest in treating psoriasis with PD faded over the last 20 years. As an emergency tool, PD has been also used in the treatment of metabolic crisis resulting from inborn errors of metabolism such as deficiency of any of the five enzymes of the urea cycle and other inherited disorders of organic and amino-acid metabolism such as maple syrup urine disease, citrullinemia, and propionic acidemia. Recent studies have shown that continuous hemofiltration therapies have more effective clearances than PD does. Similar observations were reported for the use of PD in drug poisoning. Peritoneal dialysis is still a valuable tool as a complementary measure in the treatment of hypothermia. Recently, prospective work in patients affected by end-stage congestive heart failure has shown that maintenance PD significantly lowers morbidity and mortality and substantially improves functional capabilities and quality of life in these otherwise terminally ill patients.

Key words

Surgical peritonitis, pancreatitis, hypothermia, congestive heart failure

Introduction

The topic of non renal indications for peritoneal dialysis (PD) has been covered in the past by a handful of excellent reviews (1–3). The present analysis offers a historical overview mentioning onetime proposed

applications, several indications still currently used, and some new possibilities that, in the opinion of the authors, deserve to be further explored.

Discussion

Peritoneal lavage as complement to abdominal surgery

Intra- and postoperative peritoneal lavage is probably as old as modern abdominal surgery. It has been performed at least since the early years of the 20th century in situations of generalized peritonitis. Initially, saline was the commonly used perfusion solution, lately replaced by glucose-enriched PD solutions. The usefulness of this therapeutic tool is being challenged by more recent publications, raising a controversy concerning the effectiveness of continuous peritoneal lavage over no lavage at all (4).

Peritoneal dialysis was also postulated to be a reliable therapeutic asset in acute necrotizing hemorrhagic pancreatitis. Two different applications were proposed: plain dialysis performed at the beginning of the disease to overcome the early phase of pancreatitis, or “sump” dialysis after necrosectomy, with the purpose of washing out necrotic tissue resulting from new tissue injury (5). However, controversy is still ongoing regarding the most appropriate timing for surgery: early, late, or sequential; through a zipper, or by means of repeated interventions (6). Thus far, past and recent information support the contention that peritoneal lavage remains a valuable complementary tool in the therapeutic package offered to such critically ill patients.

Psoriasis

The first report about clearing of psoriasis during hemodialysis (7) eventually stimulated interest in an evaluation of the benefits of PD performed on patients affected by that disease, in spite of the fact that development of psoriasis had also been recorded in chronic uremia being treated with hemodialysis.

From: ¹Laboratory of Experimental Nephrology and ²Division of Nephrology, Ha'Emek Medical Center, Afula, Israel.

Retrospectively, analysis of results obtained with PD appeared better than those achieved with hemodialysis. Approximately 40 papers were published, conveying information obtained mostly from isolated cases and showing both therapeutic success and failure. This ambiguous picture persisted in controlled studies performed in larger groups of patients (8). Up to that point, it seemed evident that, in an unpredictable but not large proportion of patients, PD could be helpful, leading to clearing of the psoriatic plaques. In this sense, it was postulated that the peritoneal membrane could clear from the blood some hypothetical "psoriatic factor" of middle molecular size involved in the development of the skin lesions, being more effective than hemodialysis in this property (9). Another pathophysiologic approach was elaborated by Glinski and colleagues (10), on the basis that the proteinase content of polymorphonuclear cells (PMNs) recovered from patients with active psoriasis appeared significantly higher than was detected in cells from subjects with inactive psoriasis or from normal controls. Accordingly, epidermal infiltration by these activated PMNs could be the origin of the tissue lesions characteristic of psoriasis. Consequently, it has been suggested that removal of these proteinase-rich PMNs from the peritoneal cavity with the dialysis effluent may account for the beneficial effect of PD in the clearing of psoriatic lesions, given that similar observations were made with sequential leukapheresis.

In any case, interest in treating psoriasis with PD has faded during the last 20 years. Uncertainty of clinical success in addition to the potential risks of the method may well be the source of this development (2).

Poisoning

Therapy of acute poisoning cannot always be based just on specific antidotes. In addition to the need for life-support measures, treatment includes interventions to reduce gastrointestinal absorption, to remove the harmful ingested substances from the body, and to appropriately manage the eventual end-organ failure resulting from the intoxication. Here, PD has been used as a measure complementary to blood purification in not a few critical situations.

A detailed discussion of the use of PD in the treatment of acute intoxication is beyond the scope of this short review. However, it would be illustrative to mention some of the more common clinical situations

in which PD has been successfully used: propoxyphene, barbiturate, methanol, ethylene glycol, and hydantoin poisoning. True, the clearance capability of PD is relatively modest compared with that of hemodialysis, hemofiltration, or charcoal hemoperfusion (11); however, it should be noted that PD is still being used in infants and in circumstances in which technical problems such as access to the circulation cannot be crowned with success or in which severe hypotension precludes the use of more effective methods of blood purification.

Hypothermia

Peritoneal dialysis performed with warmed dialysate still represents a valuable asset in the treatment of moderate (30°C – 34°C) or severe (<30°C) hypothermia (1–3,12). The procedure is performed with dialysate warmed to 42°C – 43°C, for a rate of core rewarming at around 1°C – 2°C per hour. Of course therapy also includes measures such as hemodynamic and, at times, respiratory support, and careful electrocardiographic monitoring because both moderate and severe hypothermia can cause bradycardia, atrial fibrillation, and ventricular arrhythmia, as well as hypotension and a fall in cardiac output. As body temperature drops below 30°C, the risk of ventricular fibrillation dramatically increases (12).

Metabolic diseases

Inborn errors of metabolism is an other area in which PD has been extensively used. Deficiency of any of the five enzymes in the urea cycle becomes evident in the newborn period as catastrophic illness, or later in child- or adulthood with an indolent course punctuated by hyperammonemic episodes that in turn lead to encephalopathy and associated symptoms. If untreated, these symptoms are lethal or produce severe brain damage and even death.

The treatment of newborns with disorders of the urea cycle has evolved over the years into a complex multidisciplinary effort. Peritoneal dialysis has been used mostly as an emergency tool for correction of hyperammonemia, coupled with additional measures such as dietary restrictions, sodium benzoate, sodium phenyl butyrate, and arginine that can exploit alternative pathways for the elimination of nitrogen (13). This approach offers more effective results than those obtained with the classically performed exchange transfusion. However, more recent work has

demonstrated that a more successful blood detoxification is rapidly reached by means of hemodialysis or continuous hemofiltration techniques (14). It should be pointed out that liver transplantation appears to be the more effective therapy to achieve a definitive solution to these metabolic anomalies.

Methods of blood purification are also being used in the emergency treatment of metabolic crises resulting from other inherited disorders of organic and amino acid metabolism such as maple syrup urine disease, citrullinemia, and propionic acidemia. More recent clinical work has shown that continuous hemofiltration therapies provide more effective clearances than those obtained with PD (15).

Congestive heart failure refractory to optimal pharmacologic therapy

The persistently increasing presence of congestive heart failure (CHF) affects 1% – 2% of the adult population, reaching a 6% – 10% prevalence in people 65 years of age and older. It has been predicted that, in the coming 40 years, this proportion of patients will substantially increase, reaching, at least for the United States, approximately 77.2 million patients as compared with the 34.8 million identified 3 years ago (16).

At a certain point in most of those patients, cardiac reserve comes to an end, resulting in the clinical manifestations of New York Heart Association (NYHA) class III – IV disease, and finally, pump failure becomes refractory to optimal pharmacologic therapy. Under these circumstances, heart transplantation, cardiomyoplasty, or another surgical procedure represents the only possibility to keep the patient alive. However, not everyone with end-stage CHF is suitable for heart transplantation. Under these circumstances, the 1-year survival is lower than 25%.

The possibility of using PD as a rescue and maintenance therapy in severely decompensated cardiac patients is not new. After Scheneierson published the first known case of severe overhydration in a cardiac patient treated with intermittent “peritoneal irrigation” in 1949 (17), approximately 300 additional patients were reported in the literature, mostly as isolated case reports. The efficiency of this therapeutic approach was further substantiated by two additional studies performed in groups of 15 patients that showed substantial clinical improvement (18,19).

A more recent prospective study using hemofiltration as an emergency rescue measure to reach dry weight,

with automated PD for long-term maintenance therapy, was performed in 20 patients (mean age: 65.7 ± 7.6 years) with severe heart failure (NYHA class IV; mean ejection fraction: $31.2\% \pm 4.7\%$) and a high Charlson comorbidity index (7.8 ± 1.8) that disqualified them as candidates for eventual heart transplantation (20). (It should be noticed that a Charlson score higher than 5 implies an 85% mortality rate after the first year of follow-up.) After 1 year of follow-up, all patients showed substantial functional improvement as indicated by a regression from NYHA class IV to class I and significantly better left ventricular function. The first-year mortality was 10%, substantially lower than the mortality expected from the baseline Charlson scores. The overall mortality during 396 months of follow-up in the 20 patients was 30%. The total number of hospitalization days attributable to CHF during the 1 year before the start of APD was 157; the corresponding figures for the entire period of dialytic therapy was just 13 days ($p < 0.001$).

It has been proposed that fluid overload may be more a consequence than a cause for the progression of CHF. Indeed, cytokines and humoral factors are involved in the development and progression of CHF. Atrial natriuretic peptide, tumor necrosis factor α , and interleukins 1 and 6 have been shown to induce apoptosis of cardiac myocytes and to have negative inotropic effects; they appear to be a fundamental step in the chain of events that launch or aggravate heart failure (21,22).

So far, the encouraging results with PD call for additional clinical and basic research to confirm the observations and to reach a deeper insight into the pathophysiology of CHF.

Next wanted steps

The huge amount of scientific information accumulated in some 30 years of basic research on the peritoneum as a whole, and on the mesothelium in particular, created fertile ground for further exciting research and development. Mesothelial cell transplantation, pioneered by Di Paolo and colleagues (23), is waiting to be tried in situations of early glucose hyperpermeability and inadequate ultrafiltration, and in prevention and eventual therapy of postsurgical peritoneal adhesions. In addition, the possibility of using mesothelial cells as adult stem cells for tissue engineering deserves to be explored (24).

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Corresponding author:

Lazaro Gotloib, MD, Laboratory of Experimental Nephrology, Ha'Emek Medical Center, Afula 18101 Israel.

E-mail:

gotloib@012.net.il