



ISPD Asian Chapter Newsletter

International Society for Peritoneal Dialysis (ISPD)

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Asian PD Perspective

Peritoneal Dialysis In China



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History and current status of PD in China

In China, peritoneal dialysis (PD) was first used in the mid 1960s and CAPD in 1979. The penetration of PD picked up in the mid-1980s and then declined and has been maintained at about 10% of the dialysis population during the past few years. To date, about 7000 patients are on PD, which represents an overall penetration rate of 9.5%. The net growth rate over the last year was 26%. The majority of PD patients are on CAPD and less than 1% of the patients are on APD.

The numbers, however, represent only a small fraction (possibly less than 10%) of patients who require dialysis; this is mainly due to financial restrictions. Furthermore, the patient dropout rate in China is quite high (30%) and the quality of dialysis is far from optimal. This is mainly due to the very late start of dialysis (and therefore high early-death rate) and withdrawal of dialysis because of poor long-term financial support.

Overview of the PD program in the First Hospital of Peking University

The PD program in the First Hospital of Peking University is, so far, the biggest in China. The number of patients in our PD program increased from 64 to 260 during the past 2 years. In parallel with the growth, the quality of peritoneal dialysis improved dramatically. For example, the incidence of volume overload decreased from more than 80% to 20% and hypertension decreased from more than 70% to less than 20%. The incidence of hyperphosphatemia decreased from 60% to 20% and the average hemoglobin level increased from 80 g/L to 113 g/L. The incidence of peritonitis decreased from 1 episode per 28 patient months to 1 episode per 54 patient months. We also significantly improved our patients' quality of life and rehabilitation status. The achievements of our program have contributed significantly to the recent dramatic net growth of PD in China.

The success of the PD program can be attributed to the following reasons:

1. Implementation of quality improvement projects. We adopt the concept of continuous quality improvement into the clinical management of fluid overload, phosphate control, anemia control, dietary control, peritonitis control, cost control, etc.
2. The implementation of the 5E (encouragement, education, exercise, employment and evaluation) rehabilitation program. Besides continuous improvement in medical treatment, the program adopts a holistic approach to the management of PD patients.
3. PD awareness campaign. We believed that the low PD penetration rate in China was, to a large extent, due to the low PD awareness both among patients and healthcare professionals. Many of them still regarded PD as second-line therapy. Therefore, 2 years ago, we started to provide regular predial-

ysis patient education courses and CME courses for health-care providers. These, along with the quality improvement of the PD program, have attracted more and more patients, and have encouraged Chinese nephrologists and nurses to provide PD therapy to their patients.



PD round at First Hospital, Peking University

The future of PD in China

With the improvement of PD quality, its growth in China in the coming years is inevitable. However, fast growth may not necessarily be seen in the near future due to the high cost of PD solutions (partially due to a limited number of suppliers) and to the current fee-for-service model that makes HD more profitable as compared with PD.

On the other hand, similar to other countries and regions, the incidence of end-stage renal disease (ESRD) in China is increasing dramatically due to the aging population and high incidence of diabetes. There have also been significant changes in the reimbursement system for dialysis therapy in China. The current insurance system is expected to benefit more patients who require dialysis although the Chinese Government is implementing managed care to control the total costs. We also expect that more companies will be involved in supplying PD solutions and the cost for PD treatment will eventually drop. It is thus most likely that PD will become an important option or even the first option for ESRD patients in China.

While the standard dialysis regimen involved four exchanges a day, more patients (especially new patients) are now getting three exchanges or fewer a day. We have demonstrated that lower dialysis dose is sufficient for most Chinese PD patients due to their smaller size and lower dietary protein intake. In our program, protein intake of 0.8-1 g/kg/day has enabled patients to maintain their nutritional status while cutting down the dialysis cost. The average weekly Kt/Vurea in our program is 1.8. The lower (but adequate) dietary protein intake and therefore reduced dialysis dose may become a standard treatment regimen in China.

Editorial

PD Costing Survey

Dr. Fu-Keung Li

Peritoneal dialysis has been adopted in many Asian countries as a first-line treatment for patients with ESRD. Yet, there is still significant variation in the penetration rate of PD in different Asian countries and, in fact, among different dialysis units. While patient preference may play a key role in treatment choice, cost

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considerations may sway the final decisions of the nephrologists. To better understand the issue and to explore the impact of PD fluid (PDF) costing on the utilization of PD in Asia, we conducted a survey on the costs of PDF in Asian countries. Although the information may not be as comprehensive as we expected, we hope this could provide the first step towards better sharing of information among Asian nephrologists involved in PD management.

Comment

In Asia, the geographical proximity of neighboring countries does not guarantee comparable healthcare economics. The vastly different costs of PDF in the surveyed countries, though preliminary, might have played a determining role in the popularity of PD in those areas. Of course, more studies are required to address the topic in greater depth. In the future, we wish to collect more data in the region, which, hopefully, could facilitate effective utilization of PD in Asia.

Acknowledgements

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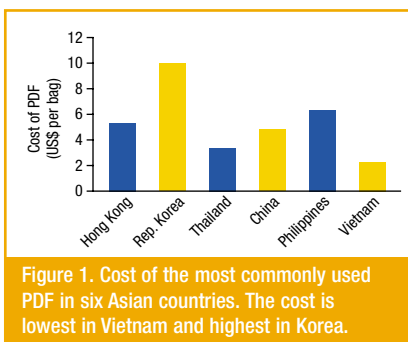


Figure 1. Cost of the most commonly used PDF in six Asian countries. The cost is lowest in Vietnam and highest in Korea.

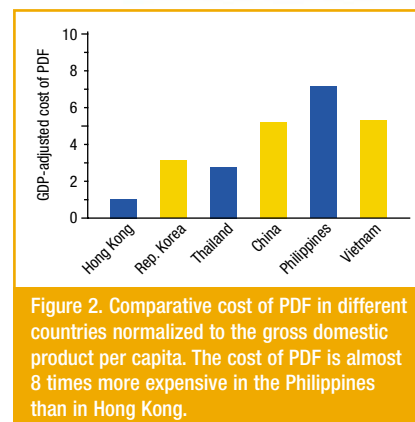


Figure 2. Comparative cost of PDF in different countries normalized to the gross domestic product per capita. The cost of PDF is almost 8 times more expensive in the Philippines than in Hong Kong.

News from ISPD (www.ISPD.org)

The New ISPD Council

The new ISPD council members elected on 30 August 2004 in Amsterdam:

- President: Raymond Krediet (The Netherlands)
- President-Elect: Wai-Kei Lo (Hong Kong, China)
- Council members (Asia): Georgi Abraham (India)
- (N. America): Joanne Bargman
- (S. America): Roberto Pecoits-Filho (Brazil)
- (Europe): Nick Topley

Your other Asian Representative in the council is Masaaki Nakayama (Japan)

The Next ISPD Congress

The 11th Congress of the ISPD will be held from 24-28 August 2006 in Hong Kong. This is the third ISPD Congress held in Asia (previous congresses held in Japan and Korea).

Open Bidding for Hosting the Third Asian Chapter Meeting, 2007

The 3rd Asian Chapter Meeting is now open for bidding. Guidelines for bidding are available at the ISPD Web site, or from Dr. WK Lo at wkloc@hkucc.hku.hk.

Institutional Membership

Specially designed for **developing countries**, the "Institutional Membership" allows 10 members from the same institute to join at the cost of a single member, and all can enjoy ISPD member benefits, including cheaper ISPD meeting registration rates. **Join now! We need you as our members.**

Asian Chapter Scholarship

A scholarship is now available to provide financial support for training in a PD center of excellence within Asia or Australia.

The first recipient is Dr. Wee-Hin GAN, University of Malaya, Malaysia.

Deadline for next application: 31 December 2004. Details are available at the ISPD Web site.

Don't miss the chance!

ISPD-Second Asian Chapter Meeting

The ISPD-Second Asian Chapter Meeting, 'Redefining and Expanding PD Horizons in Asia', will be held in Hyderabad, India on 21-23 January 2005. Weather during that period is a pleasant 16°-28°C. Founded in 1591 AD, Hyderabad is India's fourth-largest city with a population of 7 million. Located almost at the geographic centre of India, with excellent restaurants and hotels, and easy national and international access, Hyderabad is the ideal hub for the tourist to explore India. The meeting venue is the state-of-the-art Hitec center.

For further details, please visit the meeting Web site www.2ndacm-ispd.org.

Abstract Deadline: 20 October 2004.

Upcoming PD Meetings

ISPD-Second Asian Chapter Meeting

21-23 January 2005, Hyderabad, India

Web site: www.2ndacm.ispd.org

Abstract submission deadline: 20 October 2004

(Note: Abstract submission deadline has been postponed to 20 October 2004)

The 25th Annual Dialysis Conference

28 February – 2 March, 2005, Tampa, Florida, USA

Web site: www.muhealth.org/~dialysis

Early registration deadline: 10 December 2004

The First North American Meeting-ISPD

29 April – 1 May 2005

Web Site: www.ispd.org/NA/

Abstract submission deadline: 15 December 2004

Third World Congress of Nephrology

26-30 June 2005, Singapore

Web site: www.WCN2005.org

Abstract submission deadline: 15 January 2005

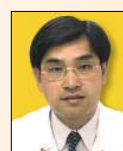
From the Editorial Office

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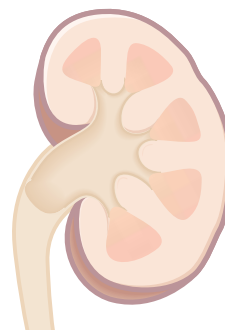
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Research Update in PD



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PD versus HD: what do the patients think?

There is conflicting evidence on the effects of dialysis modality on survival. Patient experience becomes an important consideration in choosing between HD and PD. A group of investigators from Johns Hopkins Hospital, USA, did a cross-sectional survey of 656 new dialysis patients from 37 centers. Based on a questionnaire including 3 overall ratings and 20 items rating specific aspects of dialysis care, patients receiving PD were much more likely than those receiving HD to give excellent ratings of overall dialysis care, and significantly more likely to give excellent ratings for each specific aspect of care rated. The 3 items with the greatest differences were in the domain of information provided. The difference remained significant after adjustment for potential confounding factors.

Comments: The strength of evidence provided by a cross-sectional survey should always be interpreted with caution. Nevertheless, the result appears robust, given the large sample size and high questionnaire completion rate (almost 90%). Above all, there is no convincing data on "hard outcomes" in this area.

* Rubin HR, Fink NE, Plantings LC, et al. Patient ratings of dialysis care with peritoneal dialysis vs hemodialysis. *JAMA* 2004;291:697-703.

Icodextrin-induced peritonitis: more clinical experience

Cases of aseptic peritonitis related to the use of icodextrin solution have attracted much attention. In a case-control study, a group from France compared the clinical and biologic features of 5 patients with icodextrin-induced peritonitis with those of 7 patients with bacterial peritonitis. In this study, the diagnosis of icodextrin-induced peritonitis was confirmed in all cases by a positive re-challenge test. Notably, recurrence was not observed on re-exposure to peptidoglycan-free icodextrin. Peritoneal injury, as represented by weight gain, peritoneal permeability, CA 125 concentration and serum C-reactive protein, appeared to be less severe during icodextrin-induced peritonitis than during bacterial peritonitis.

Comments: This study provides convincing evidence for the role of peptidoglycan, which appears as a contaminant in some batches of icodextrin solution, in the pathogenesis of icodextrin-induced peritonitis. Given that the severity of peritoneal injury is mild, it remains unknown whether long-term exposure to a low level of peptidoglycan has any clinical sequelae.

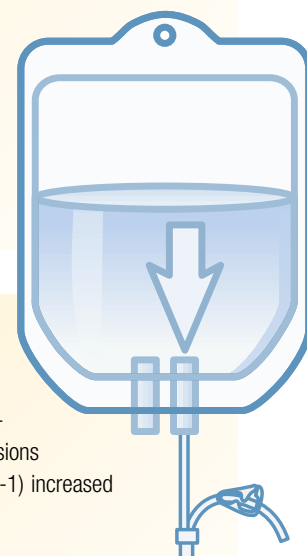
* Toure F, Lavaud S, Mohajer M, et al. Icodextrin-induced peritonitis: study of five cases and comparison with bacterial peritonitis. *Kidney Int* 2004;65:654-660.

Encapsulated peritoneal sclerosis: insights from an animal model

Encapsulated peritoneal sclerosis (EPS) is characterized by thick sclerotic tissue involving vascular alterations in PD patients. A group from Japan evaluated serial morphologic changes and expressions of angiogenic factors in a rat model of EPS. The investigators found that the vessel area, diameter, and length gradually increased for 3 weeks, and then decreased. The mRNA expressions of vascular endothelial growth factor (VEGF) and angiopoietin-2 (Ang-2) increased for 5 weeks, while that of angiopoietin-1 (Ang-1) increased for 3 weeks and then decreased. Co-administration of neutralizing anti-VEGF antibody reduced the severity of experimental EPS.

Comments: Anti-VEGF antibody for human use is now finding its place in the treatment of cancer. It would be interesting to assess its efficacy in the treatment of human EPS. One may also note that the authors induced EPS by chlorhexidine and ethanol, agents commonly used for catheter exit site dressing in some centers.

* Io H, Hamada C, Ro Y, et al. Morphologic changes of peritoneum and expression of VEGF in encapsulated peritoneal sclerosis rat models. *Kidney Int* 2004; 65:1927-1936.



From the PD Industry

Global Biocompatibility of New PD Solutions

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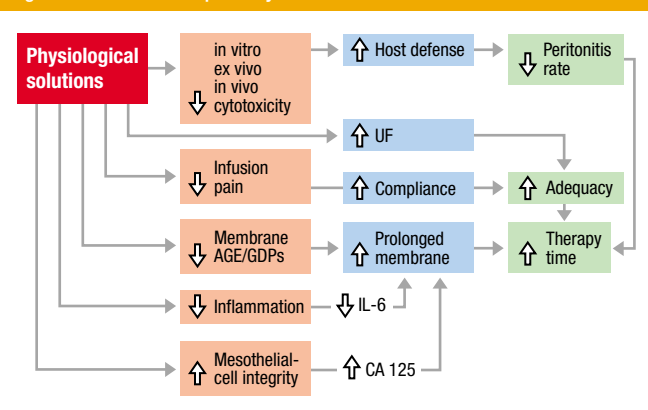
Since the first introduction of continuous ambulatory peritoneal dialysis during the late 1970s, there have been continuous improvements in the quality of peritoneal dialysis (PD) treatment. Survival of patients on PD is now at least as good as that on hemodialysis, especially during the first 2 years of treatment, and results are gradually improving. However, peritoneal membrane failure develops during long-term PD, which is characterized by the occurrence of ultrafiltration failure and by morphologic alterations in the peritoneal tissue, resulting in fluid overload, higher risk of cardiovascular death and consequently lower technique survival and higher mortality in PD patients. Recurrent peritonitis, diabetes, systemic inflammation and uremia per se may contribute to this, and the bioincompatibility of conventional dialysis solution can add to these problems. Conventional PD solutions have unphysiologic characteristics, including low pH, high concentrations of lactate and glucose, hyperosmolality, and a spectrum of glucose degradation products (GDPs) formed during heat sterilization. These, separately or in combination, influence various aspects of peritoneal cell function. Although less is known about the systemic effects of conventional PD solutions, it is established that they contribute to metabolic and nutritional disturbances. Glucose uptake from conventional PD solutions leads to metabolic and nutritional alterations such as hyperglycemia, hyperinsulinemia, anorexia, obesity, and hyperlipidemia. Lactate, especially in high concentrations, has negative systemic side effects, such as anorexia and lactic acidosis. It is also possible that local inflammation induced by bioincompatible solutions leads to increased systemic inflammation. Thus, biocompatibility refers to the effects of a solution on the patient as a whole, systemically as well as locally (intraperitoneally), which is the basis for the concept of global biocompatibility.

GLOBAL BIOCOMPATIBILITY: The ability of a PD solution to permit adequate long-term dialysis without clinically significant disturbances to the structure, function and homeostasis of all cells and tissues

At present, a variety of new, potentially more biocompatible PD fluids are available for clinical use in several countries. An obvious replacement for a low pH, high-lactate buffered PD fluid is a bicarbonate/lactate (B/L) buffered solution, with a physiologic pH, reduced GDPs and lactate. The advantages of this B/L solution include less infusion pain, better correction of acidosis, improved immune function and preserved peritoneal structure and function (Figure 1).

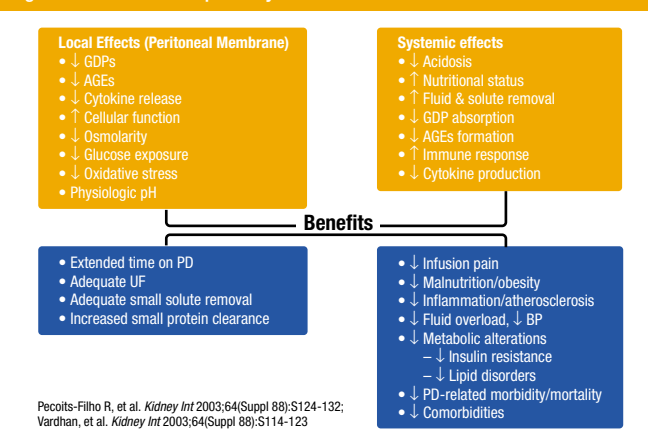
Two glucose-free solutions, icodextrin-based solution and 1.1% amino acid solution, result in a significant reduction of local and systemic problems related to glucose overload. These solutions are particularly helpful in patients suffering from fluid overload and/or ultrafiltration failure and malnutrition. Therefore, the combined use of these new solutions (B/L, amino acid-based, and icodextrin-based solutions) is likely to play an important role in enhancing the global biocompatibility of PD as a therapy. This advanced solution portfolio provides important systemic and local benefits, which should help slow the progression of comorbidities by minimizing glucose load, optimizing fluid balance, delivering 25% of daily protein needs,

Figure 1. Global biocompatibility with bicarbonate/lactate-based solution.



improving dyslipidemia, reducing hypertension, improving blood-glucose control, improving immune defense and preserving residual renal function. On the other hand, these solutions could reduce the negative impact of high lactate, high glucose, high GDPs and low pH on peritoneal membrane. The reduction of systemic inflammatory activity (by more biocompatible dialysis solution) may ameliorate cardiovascular disease in dialysis patients and thereby significantly diminish the high cardiovascular morbidity and mortality of PD patients. Although it remains to be verified whether more biocompatible fluids will ultimately have a measurable impact on patient morbidity and mortality, there is already sufficient evidence of a positive impact on several secondary clinical endpoints related to patient morbidity and mortality. Therefore, it is likely that these solutions will become the global standard for PD treatment in the near future (Figure 2).

Figure 2. Global biocompatibility – clinical benefits



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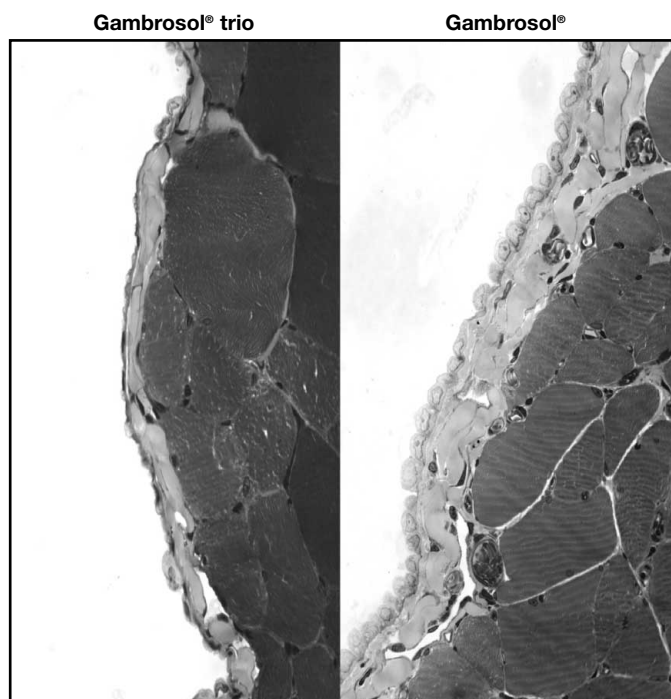
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From the PD Industry

Long-term Exposure to Glucose Degradation Products (GDPs) Affects the Integrity of the Peritoneal Membrane in an Experimental Model

Long-term PD is characterized by a progressive loss of ultrafiltration (UF) capacity, which may lead to UF failure [1]. Fibrosis, peritoneal neovascularisation, reduplication and thickening of the basement membranes, and formation of advanced glycation end-products (AGEs), are some of the most relevant structural changes observed after long-term PD [2, 3]. The exposure of the peritoneal membrane to conventional dialysis solutions may play an important role in this respect. It has been suggested that GDPs, formed during heat sterilization of PD fluids, are one of the most important components of PD fluid that mainly contribute to the long-term deterioration of the peritoneal membrane. The toxic effects of GDPs have been reported in vitro and in vivo. According to various studies, the principal target of GDP toxicity is the peritoneal mesothelium, which forms an interface between the dialysate and the internal milieu [4, 5].

Mesothelial cells of the diaphragmatic peritoneum in the rat after long-term exposure to different PD fluids.



Recently, the effects of the long-term exposure of the peritoneum to GDP on peritoneal morphology and transport characteristics were investigated in a non-uremic PD rat model [6]. The micrographs show that exposure to a conventional PD fluid containing a high amount of GDPs (Gambrosol®) induced a significant transformation of the cell shape from flat to high, cuboidal cells, indicating mesothelial cell damage. No relevant changes were, however, observed in the mesothelial cells after exposure to a new more biocompatible PD fluid containing very low amounts of GDPs (Gambrosol® trio).

The observed mesothelial cell transformation has previously been demonstrated in both an animal study and in PD effluent from CAPD patients treated with conventional PD fluid [7,8]. In comparison, clinical studies have shown increased production of CA 125, a marker of mesothelial cell mass, in the effluent of CAPD patients treated with low GDP-containing PD fluid [9,10]. The results of the present study are in accordance with previous investigations demonstrating that GDPs interfere with the remesothelialization process occurring after injury of HPMC cells [4]. The results clearly indicate that low GDP-containing PD fluids may better preserve the peritoneal membrane integrity and retard its derangement in PD patients.

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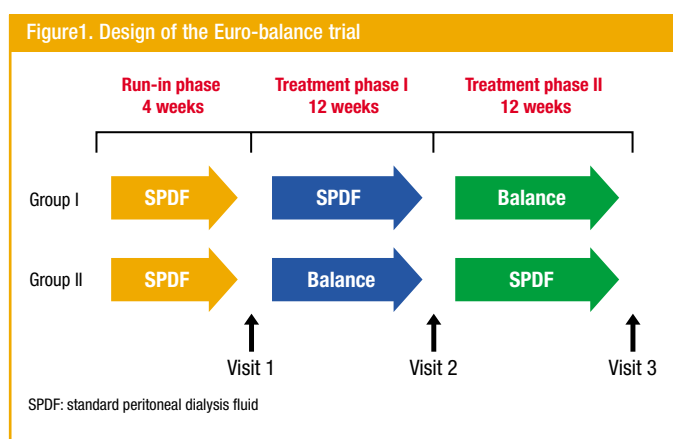
From the PD Industry

New Research in PD: The Euro-balance Trial

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In recent years there have been significant developments in the composition of peritoneal dialysis (PD) solutions. Recently, the Euro-balance Group has published a study of a new, neutral-pH PD fluid, which is low in glucose degradation products (GDP) [1]. This twin-arm crossover study (Figure 1) compared the impact of the new fluid (balance®, Fresenius Medical Care, Bad Homburg, Germany) with a conventional fluid (Stay-safe®, Fresenius Medical Care) on peritoneal homeostasis in PD patients.



In consistence with previous studies, CA 125 was chosen as a marker of mesothelial cell function and peritoneal membrane integrity. All patients exposed to balance® solution showed a three- to four-fold rise in CA 125. While some suggest that CA 125 levels reflect mesothelial cell mass [2, 3] and cannot be induced or suppressed, the evidence using low-GDP fluids appears to contradict this. In the presence of biocompatible fluids, levels of CA 125 can rapidly increase, yet be suppressed again when standard solutions are reintroduced. Therefore, changes in CA 125 levels are likely to reflect changes in synthesis by the resident mesothelial cell population.

“PICP levels rose significantly in patients on balance® and fell when they were switched back to standard fluid”

The integrity of the peritoneal membrane depends on the continuing turnover of its collagenous sub-mesothelial compact zone. Pro-collagen peptide PICP was measured as a marker of this turnover. PICP levels rose significantly in patients on balance® and fell when they were switched back to standard fluid.

Interestingly, urine volume was higher when patients were on balance® (statistically significant in group II patients). Urine and peritoneal urea

clearances were combined and expressed as Kt/V: in Group I, there was a nonsignificant rise in Kt/V when balance® was introduced; in contrast, in Group II, there was a significant fall in Kt/V when the patients were switched back to conventional fluid.

Somewhat surprisingly, dialysate-plasma creatinine ratios were higher in both groups when patients were on balance®, and ultrafiltration in both groups was lower. The decrease in ultrafiltration in patients using balance® was matched by the relative increase in urine volume. Although signs suggestive of overhydration were not seen, further studies are warranted to address the mechanism of these observed effects. Kt/V and creatinine clearance in anuric patients showed no differences in either group.

In addition, levels of hyaluronic acid (HA) were measured as a marker of inflammatory processes in the peritoneal cavity [4]. Patients on balance® had significantly lower HA levels than those on conventional fluid, suggesting that more biocompatible fluids have a less pathophysiological effect on mesothelial cells.

“More biocompatible fluids have a less pathophysiological effect on mesothelial cells”

We also noted that the magnitude of change in the various parameters was almost always greater in the group that switched from balance® to conventional fluid. This suggests that standard solution had an impact on residual renal function, whereas balance® did not.

This study demonstrated changes in the markers of peritoneal biology with a more biocompatible PD fluid, which may contribute to preserving membrane integrity and function during long-term PD therapy. In the future, longer studies will provide further insights into the effects of biocompatible fluids on clinical outcomes such as peritonitis rate, comorbidity, hospitalization and quality of life.

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