



ISPD Asian Chapter Newsletter

International Society for Peritoneal Dialysis (ISPD)

www.ISPD.org

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The 11th Congress of the ISPD

25-29 August 2006

Hong Kong

www.ispd2006.org



Q: What is the main theme of the Congress?

A: The motto of the Congress is 'Achieving PD Excellence'. Since CAPD was introduced 30 years ago, the therapy has been improved substantially with a marked reduction in peritonitis rate and improved patient survival. Clinicians and scientists are still working hard to further improve the therapy. This Congress will highlight the recent advances in PD therapy development, and point out areas that we still need to work hard on. The program is very stimulating and challenging. There will be several debates on hot, controversial issues like aggressive use of statins, and choice of CAPD/APD. There are five main themes for the symposia:

1. Managing a PD program
2. PD general issues: socioeconomics, trends, etc
3. PD practices
4. PD complications
5. Peritoneal pathophysiology

Q: Will there be educational courses?

A: On 25 August, there are two pre-congress courses; one on basic science research and the other on clinical PD, which caters for both nephrologists and renal nurses. You will have a chance to learn from world experts on different areas of PD. It is a perfect arena for you to learn both important basic science and up-to-date clinical knowledge.

Q: I am a nurse; why can I not find a nursing program in the Congress?

A: Actually, we have integrated the nursing program into the doctors' program in various areas, because we think that doctors and nurses are both important in delivering excellent PD care. They should have mutual understanding of what the other parties are doing. For instance, during the diabetic patient symposia, there will be doctors talking about diabetes and peripheral vascular

disease management, and a nurse will discuss diabetic renal nursing in PD. Similarly, adult and pediatric topics in the same area will also be integrated into one symposium to promote mutual understanding.

Q: I heard that PD is very successful in Hong Kong. Can I make use of this chance to visit some PD centers in Hong Kong?

A: Yes, the Congress has organized a PD unit visit in the morning of 29 August. Most PD units in Hong Kong have more than 200 PD patients, some even up to 400 patients. You can take the opportunity to visit them, and discuss with management and frontline staff to share their experience. You may select your PD unit of choice during registration. For obvious reasons, there is a limited quota for each center; please register as early as possible to secure the visit. Apart from Hong Kong, you can also visit a PD center in Macao, coupled with a 1-day tour of this charming city with its Euro-Chinese feel.

Q: If I do not have adequate funding, are travel grants available?

A: Yes. With the support of Baxter Healthcare Corporation, the Congress will be providing Young Investigator Travel Grants to 40-50 delegates from various countries. The applicant must be younger than 40 years of age and have submitted an abstract. The selection criteria are based on scientific merit as judged by the scientific program committee, independent of Baxter Healthcare. For delegates in Asia, the grant is around US \$1,000 per delegate.

Abstract Submission Deadline: 15 March 2006
Early Bird Registration Deadline: 15 May 2006

To our industry partners:

The editorial office welcomes your assistance in distributing this newsletter in electronic or printed form to the dialysis community. If you are interested in sending scientific messages through the newsletter, please contact the editor at: ccszeto@cuhk.edu.hk

Asian PD Perspective

CAPD in Thailand



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CAPD was established in Thailand in 1974. Initially, the technique was not very popular because of a high rate of peritonitis. Later, after the introduction of the collapsible bag, it became an accepted choice of treatment. However, the use of CAPD remains largely confined to university and government hospitals.

It is estimated that about 50,000 patients currently suffer from ESRD, of which only a quarter are treated. The remaining patients do not receive any treatment at all, largely due to a lack of awareness of the disease and its treatment options, as well as limited access to medical facilities and problems of affordability. Treatment affordability is hampered by low incomes, low reimbursement for chronic illnesses and low penetration of health insurance in Thailand. At present, Health Care Universal Coverage (the '30-Baht scheme') does not cover the cost of renal replacement therapy (RRT) for poor people. However, some patients get full reimbursement from the Civil Servant Medical Benefits Scheme and some receive partial support from the Social Security Scheme.

To date, there are 65 centers providing CAPD treatment to approximately 900 patients, compared with about 230 centers providing HD treatment to about 12,000 patients. Only a few centers provide automated PD because of the relatively higher cost and more complicated technique. The patients on PD are significantly older, and have a higher incidence of diabetes and coronary heart disease compared with HD patients.

The reasons for the lack of popularity of PD in Thailand are multifactorial, including the low incentive for medical personnel to provide PD treatment, insufficient patient and professional education about PD, misconceptions about the risk of peritonitis, patient preference, and the absence of an organized PD program. Surprisingly, only 30% of patients on HD are aware of PD as a modality of RRT, indicating that most patients do not receive clear information about PD from their doctors.

There are three brands of dextrose-based solution available; two are made locally and are therefore easily available in Thailand. For technical reasons, single bags (Safelock®) are still used in about 25% of cases because of simplicity and low cost. Double bags (ANDY disc® and Twin bag®) are more popular despite being slightly more expensive. Presently, no special solutions, such as amino acid- or icodextrin-containing solutions, are being used in routine practice because of their high cost. However, they are used in monitored cases in some clinical trials.

The cost of PD has fallen by about 40% over the past 5 years, and varies within a narrow range depending on the brands used, giving more ESRD patients access to this treatment modality. The cost of CAPD fluids and consumables per patient per year is US \$4,563 to US \$5,474 for single-bag systems and US \$5,474 to US \$7,300 for double-bag systems. Cost reductions have been achieved through local manufacture of the solutions and competitive policies among the providers. The cost for CAPD is now a bit lower than HD. In the near future, the National Health Security Office (NHSO) will include RRT in the benefits package for poor people. Because of its low infrastructure requirements, consistent quality, cost advantages and applicability to a wide range of patients, the NHSO may announce a 'PD first' policy and allow recruited cases to receive PD for only a small co-payment.

In clinical practice, ESRD patients usually undergo a counseling process that is run by a well-trained nurse and supervised by a nephrologist. Patients with ischemic heart disease and especially those with compromised cardiac function and vascular disease are preferentially offered CAPD. Once the patient and their family have accepted CAPD, a CAPD nurse further assesses the patient, and all related factors, including psychological status, hygiene habits and caregiver status, are reviewed. Once the final decision is made, a nephrologist or surgeon inserts a Tenckhoff catheter. Then, the current practice is to conduct training and care programs with the patient. All CAPD patients are cared for by nephrologists and renal nurses. The current ratio of nurses to PD patients is 1:25 to 1:50.

Regarding the outcome of CAPD, the peritonitis rate has decreased with meticulous technique and the use of double-bag systems. The peritonitis rate for double-bag systems at my facility (Srinagarind Hospital) is one episode in 36 patient-months compared with one episode in 30 patient-months for single-bag systems. The targets for Kt/V and creatinine clearance are 1.8 and 60 L/week, respectively. Patient and technique survival curves for CAPD and HD patients reported in the Thailand Replacement Therapy (TRT) Registry 2003 report are shown in Figures 1 and 2. Unexpectedly, the survival rates for CAPD and HD were almost the same.

A number of CAPD patients have given up the therapy because of catheter problems. Good initial placement of the catheter is therefore essential for CAPD to succeed. The lack of surgeons dedicated to this relatively minor surgery has led to less than optimal catheter survival.

Figure 1. Patient Survival on PD and HD in Thailand (2001).

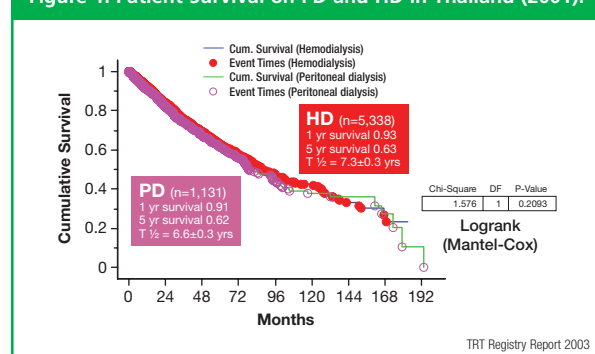
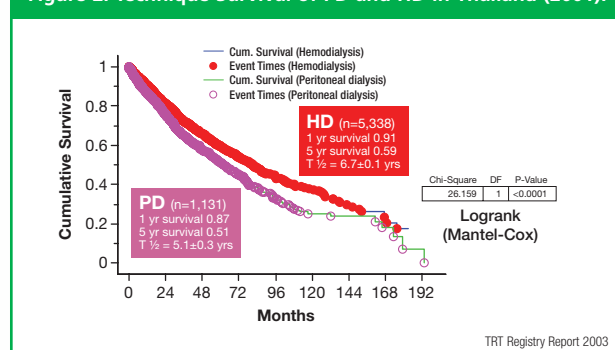


Figure 2. Technique Survival of PD and HD in Thailand (2001).



Patient compliance has been generally excellent. After the initial adjustment, most patients feel good because they can go about their life as usual and are not bound to the machine frequently.

In conclusion, although CAPD penetration is quite low in Thailand and PD is mainly used by the elderly and those with serious comorbidities, the outcome of CAPD is acceptable and comparable to HD. In the near future, a higher rate of PD utilization is expected due to an anticipated policy change from the government.

From the Editorial Office



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This is the first issue of the ISPD Asian Chapter Newsletter since Dr. Fu-Keung Li, our previous editor, left the post. I would like to take this opportunity to thank Dr. Li for his enormous effort in establishing the Newsletter, which is rapidly gaining wide acceptance amongst our Asian colleagues.

If you want to communicate PD news or PD data to other Asian colleagues through the newsletter, or have comments or suggestions regarding the newsletter, please send your message to the Newsletter Editor. You are most welcome to distribute this newsletter electronically or in printed form to your colleagues or other interested people. If you or your colleagues want to receive this newsletter directly from our editorial office, please send your e-mail address to: meeting.hk@asia.cmpmedica.com.

News from ISPD

(Please look up the full details in www.ispd.org)

The 11th Congress of the ISPD, 25-29 August 2006, Hong Kong

The program has been finalized and is available at www.ispd2006.org. Become a member of the ISPD and you will receive a discount on the registration fee of US \$65 – US \$100. If you are from a *developing country*, joining the 'Institutional Membership' at the cost of a single member can allow 10 members from the same institute to pay the registration fee at our members' rate. Download the membership registration form from www.ispd.org. **Join Now!**

Asian Chapter Scholarship

Dr. Sung-Gyun Kim from Anyang, Korea, was awarded a scholarship to train in clinical PD under Dr. Wai-Kei Lo, Tung Wah Hospital, Hong Kong. Dr. Kim is the fourth recipient of this scholarship, following awardees from Malaysia, Vietnam and Laos.

If you need financial support for clinical PD training in an expert PD center, whether in your home country or elsewhere in Asia/Australia, you may apply for this scholarship. A list of welcoming PD training centers and details of the scholarship application are available at www.ispd.org under Asia Chapter.

Deadlines for applications for each round: twice a year, on 30 June or 31 December. *The next deadline is 30 June 2006.*

The Next Asian Chapter Meeting

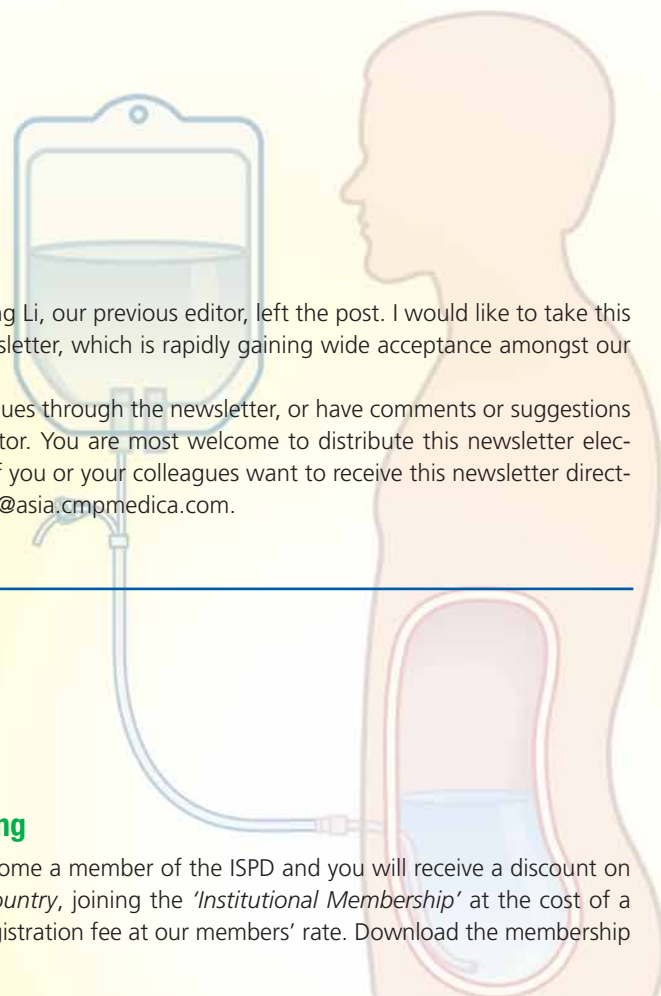
The next, that is, the 3rd Asian Chapter Meeting will be held in November 2007 in Hiroshima, Japan. The 4th Asian Chapter Meeting, to be held in 2009, will be open for bidding in late 2006. Any interested party may contact Dr. Wai-Kei Lo at: wkloc@hkucc.hku.hk.

ISPD New Council Election

The ISPD Nomination Committee has produced a *slate of nominations for new council members and executives as listed below*:

President: **W.K. Lo** (Hong Kong)
President Elect: **J. Burkart** (USA)
Secretary: **O. Heimbürger** (Sweden)
Treasurer: **I. Teitelbaum** (USA)
Council Members: **R. Mehrotra** (USA), **S.S. Naga** (Egypt), **V. Price** (nursing, Canada),
A. Rodriguez (Portugal), **F. Schaefer** (pediatrics, Germany), **T. Wang** (China)

Any member of the ISPD can submit alternative nominees to the secretary within 60 days of the publication of this advertisement. Submissions should be accompanied by a written, brief resume of nominees' qualifications and verification of their willingness to serve. The election will take place during the 11th Congress of the ISPD in Hong Kong.



Research Update in PD

Peritonitis, aminoglycosides and residual renal function

The ISPD treatment guidelines for PD peritonitis 2000 recommended the use of cefazolin plus ceftazidime as the initial therapy in patients with residual renal function (RRF). A recent randomized controlled trial, however, has aroused uncertainty about this recommendation. Lui et al studied 102 PD patients with peritonitis and compared intraperitoneal cefazolin plus netilmicin versus cefazolin plus ceftazidime. The authors found that both regimens had identical primary cure rates and relapse rates. Irrespective of the treatment regimen, RRF and daily urine volume were reduced significantly at day 14 but returned to near baseline levels at day 42. Most importantly, the degree of reduction in RRF and urine volume did not differ between the two regimens.

Comments: Aminoglycosides are much less expensive than third-generation cephalosporins. The pendulum has swung and there is likely to be a resurgence in the use of aminoglycosides as the first-line antibiotic, particularly amongst those clinicians who believe that two cephalosporins do not make a logical combination.

* Lui SL, et al. Cefazolin plus netilmicin versus cefazolin plus ceftazidime for treating CAPD peritonitis: effect on residual renal function. *Kidney Int* 2005;68:2375-2380.

Ghrelin and anorexia in PD patients

Anorexia and malnutrition confer significant morbidity and mortality to patients with end-stage kidney disease. Two recent studies shed light on the role of ghrelin, an appetite-stimulating gut hormone, in anorexia of PD patients. In the first study by Perez-Fontan et al, the physiologic effect of glucose-based PD solution was explored. It was found that 3.86% glucose-based PD exchange resulted in a significant decrease of plasma ghrelin levels. On the other hand, ghrelin secretion is partially refractory to the acute inhibitory effect of oral feeding. In the second study, nine PD patients with mild to moderate malnutrition were given subcutaneous ghrelin in a randomized placebo-controlled design. It was found that administration of subcutaneous ghrelin significantly increased the group mean absolute energy intake, and the increase in energy intake seemed to persist for over 24 h after intervention. There were no significant adverse events with this treatment.

Comments: These papers further support the concept that the gastrointestinal tract is an endocrine organ, and there is important cross-talk between the gut and the brain. Although ghrelin itself requires subcutaneous administration, a small-molecule agonist for oral use will probably be available in the future.

* Perez-Fontan M, et al. Acute plasma ghrelin and leptin responses to oral feeding or intraperitoneal hypertonic glucose-based dialysate in patients with chronic renal failure. *Kidney Int* 2005;68:2877-2885.

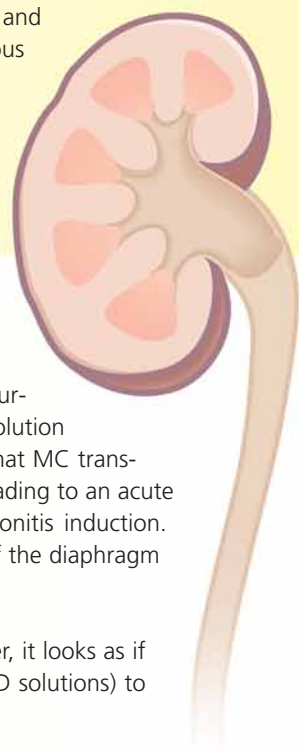
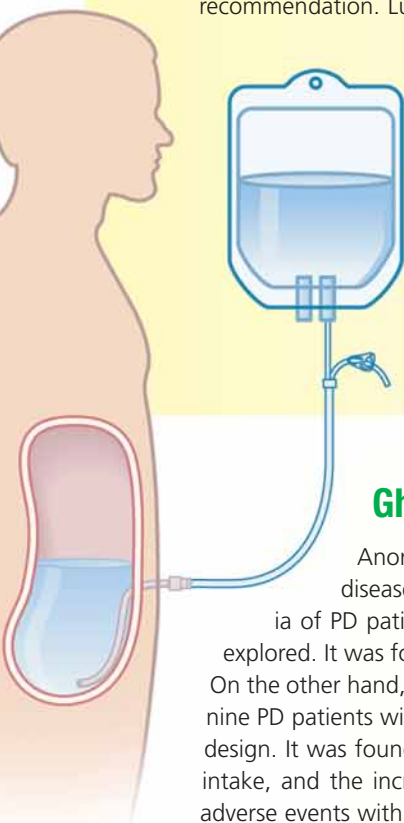
* Wynne K, et al. Subcutaneous ghrelin enhances acute food intake in malnourished patients who receive maintenance peritoneal dialysis: a randomized, placebo-controlled trial. *J Am Soc Nephrol* 2005;16:2111-2118.

News about mesothelial cell transplantation

Mesothelial cell (MC) transplantation has been suggested to improve mesothelial repair after surgery, recurrent peritonitis and peritoneal dialysis. A recent study evaluated MC transplantation during the resolution phase of experimentally induced peritonitis in rats. In this series of experiments, Hekking et al found that MC transplantation after peritonitis resulted in incorporation of these cells into the parietal mesothelial lining, leading to an acute transient submesothelial thickening, which was not seen in transplanted animals without prior peritonitis induction. In addition, trapping of transplanted MC in the milky spots of omental tissue and lymphatic stomata of the diaphragm seemed to increase microvascular permeability.

Comments: Although this is an animal study, it shows that MC transplantation is a realistic goal. However, it looks as if we still need to tackle the underlying peritoneal inflammation (due to infection and unphysiological PD solutions) to ensure a successful transplant.

* Hekking LH, et al. Apparent successful mesothelial cell transplantation hampered by peritoneal activation. *Kidney Int* 2005;68:2362-2367.



From the PD Industry

Improving patient outcomes through product design

Since the inception of peritoneal dialysis, we have witnessed a stream of product design improvements that have played important roles in improving patient outcomes. Noteworthy innovations include double-bag, disconnect and advanced connector systems that have continuously driven down peritonitis rates worldwide^{1,2}.

These developments have been pivotal to the success of peritoneal dialysis therapy as it is well established that peritonitis can lead to catheter removal, hospitalization and technique failure³. Peritonitis is now recognized also as a primary inflammatory insult to the peritoneal membrane, and thus is likely a primary contributing factor to membrane failure⁴.

There are several important design principles that are prerequisites for clinical success with PD solution delivery systems. A primary design principle is the assurance of non-turbulent fluid flow during the 'flush and drain' procedure. Another critical design principle is the minimization of touch contamination of the fluid path during the exchange procedure. The latter is achieved in the Ultrabag system using a combination of a shrouded male luer connector and a female counterpart on the patient connector side, as shown in the Figure. This design ensures that touch contamination of either connector is efficiently excluded from the fluid flow path during the connection procedure.

The superiority of this system over others has been demonstrated *in vitro* using high levels of bacterial challenge. Kubey et al

have shown that the Ultrabag connector design completely prevented the transfer of bacteria into the fluid path from a heavily contaminated patient connector (10^2 - 10^3 cfu) in 90% of performed connections, and that the drain and flush procedure was also capable of removing $>10^3$ bacteria placed in the fluid path⁵.

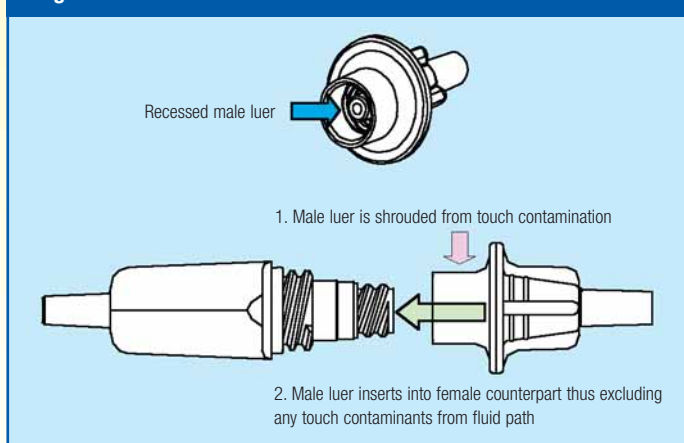
This *in vitro* performance has now been evaluated in the clinical setting. Several Asian randomized controlled trials with incident CAPD patients have now been reported describing impressively low peritonitis rates with such systems⁶⁻⁸. The Table summarizes the design and results of these studies, which were conducted in Hong Kong, Malaysia and Singapore.

Table.

Reference	Description	Systems	Peritonitis rates
2002 Li et al ⁶	Multicenter 110 patients	UltraBag Stay safe	1 in 45.0 pt months 1 in 36.8 pt months
2005 Wong et al ⁸	Multicenter 270 patients	UltraBag ANDY-Disc	1 in 35.0 pt months 1 in 22.9 pt months*
2005 Tan et al ⁷	Single center 64 patients	UltraBag ANDY-Disc	1 in 63.2 pt months** 1 in 42.9 pt months

* Therapeutic equivalence to UltraBag not established; ** $p < 0.002$

Figure.



The latest 2005 ISPD peritoneal dialysis-related infection recommendations state that a rate of peritonitis of, at most, 1 in 18 patient-months should be achieved, but point to the fact that rates of 1 in 40-50 patient-months have been reported, and thus centers should strive to meet such standards⁹. These randomized controlled trials clearly demonstrate that such peritonitis rates are achievable using delivery systems that have been developed and validated using the design principles described above.

By Clifford J. Holmes Ph.D. Renal Division, Baxter Healthcare,
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Baxter

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2. Li PK, et al. Comparison of double-bag and Y-set disconnect systems in continuous ambulatory peritoneal dialysis: a randomized prospective multicenter study. *Am J Kidney Dis* 1999;33:535-540.
3. Piraino B, et al. Peritoneal dialysis-related infections recommendations: 2005 update. *Perit Dial Int* 2005;25:107-131.
4. Topley N. Membrane longevity in peritoneal dialysis: impact of infection and bio-incompatible solutions. *Adv Ren Replace Ther* 1998;5:179-184.
5. Kubey W, Straka P, Holmes CJ. An *in vitro* bacterial touch contamination risk assessment of two CAPD twinbag systems. *Blood Purif* 2001;19:62-67.
6. Li PK, et al. Comparison of clinical outcome and ease of handling in two double-bag systems in continuous ambulatory peritoneal dialysis: a prospective, randomized, controlled, multicenter study. *Am J Kidney Dis* 2002;40:373-380.
7. Tan SH, et al. A prospective comparison of peritonitis between two disconnect systems in a single centre. *Nephrology* 2005;10(suppl):A69-A70.
8. Wong HS, et al. A randomized, multicenter, open-label trial to establish the therapeutic equivalence between ANDY-Disc and UltraBag in patients on CAPD (CAPD-2 Trial). *Perit Dial Int* 2005;25(suppl 2):S5.

From the PD Industry

Low-GDP fluid preserves residual renal function

Residual renal function (RRF) has a major impact on the quality of life as well as the survival of patients on peritoneal dialysis. Preservation of RRF has therefore become an important goal in PD therapy. A growing body of evidence shows that RRF is better preserved in patients using the new generation of PD fluids with very low concentrations of glucose degradation products (GDPs).

The fate of GDPs in the body

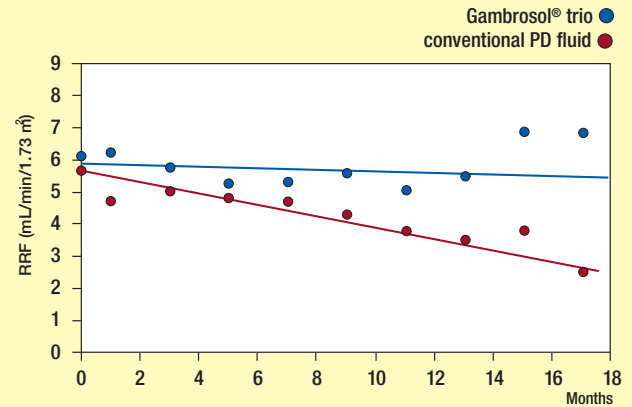
Conventional PD fluids, i.e. glucose-containing solutions, heat-sterilized in single-compartment bags, contain high levels of toxic GDPs. When such fluids are infused into the peritoneal cavity, the GDPs disappear from the dialysate during the dwell, causing carbonyl stress. Highly reactive GDPs, such as formaldehyde, bind to peritoneal tissue, while others, such as 3-DG, are transported into the circulation along with the glucose molecules. When reaching the blood, the GDPs may undergo structural changes and react with proteins, forming so-called advanced glycation endproducts (AGEs) (Ledebro *et al. Contrib Nephrol*, 2003).

Elevated levels of AGEs have been detected in the systemic circulation in patients exposed to PD fluid with a high content of GDPs (Zeier *et al. KI*, 2003). Furthermore, it has been found that increased carbonyl stress, measured as accumulation of AGEs in different tissues, can be associated with decreasing RRF. AGEs are proinflammatory molecules believed to play a role in the progression of atherosclerosis. Thus, the AGE-associated effect on RRF could be mediated through low-grade inflammation in vascular tissue.

Residual renal function decline in PD patients

The blood purification provided by the RRF is a vital complement to the dialytic clearance, and the renal contribution should therefore be preserved as long as possible. The possible effect on RRF of different PD fluids was studied in a group of PD patients, comparing a fluid with low-GDP level, Gambrosol® trio, with conventional fluids.

Figure. Residual Renal Function in PD patients treated with conventional PD fluid or with Gambrosol® trio



Thailand Replacement Therapy Registry Data for 2001.

After 18 months on PD, an intermediate analysis revealed a highly significant ($p < 0.0001$) difference in RRF decline between the groups. Patients using Gambrosol® trio maintained their RRF better than those using conventional fluids (Haag-Weber *et al. JASN*, 2003). It could also be seen that RRF was stable or increasing in a larger share of patients treated with Gambrosol® trio compared with the group treated with conventional fluids. The improved preservation of renal function when fluids with low GDP content are used has recently been confirmed by other groups of investigators.

Residual renal function and mortality

A decline in RRF by 1 mL/min/1.73 m² has been found to be associated with a 12% increase in the relative risk of death (Bargman *et al. JASN*, 2001). Thus, the use of PD fluids with low levels of GDPs could be a major contributor to improved survival of PD patients. This was confirmed by a recent retrospective analysis of 2,000 patients treated with low-GDP fluid for 2 years (Lee *et al. PDI*, 2005).

The preservation of RRF in patients on PD is one of the major goals of therapy and the use of low-GDP fluids is an important tool to achieve this.

By Gambro Corporate Research and Global Marketing PD.



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4. Bargman J, Thorpe K, Churchill DN and the CANUSA Peritoneal Dialysis Study Group: Relative contribution of residual renal function and peritoneal clearance to adequacy of dialysis: a reanalysis of the CANUSA study. *J Am Soc Nephrol* 2001;12:2158-2162.
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