MANAGEMENT OF A RAPIDLY GROWING PERITONEAL DIALYSIS POPULATION AT THE FIRST AFFILIATED HOSPITAL OF SUN YAT-SEN UNIVERSITY

Xueqing Yu,^{1,2} Xiao Yang,^{1,2} and Naya Huang^{1,2}

Department of Nephrology,¹ The First Affiliated Hospital, Sun Yat-sen University, and Key Laboratory of Nephrology,² Ministry of Health, Guangzhou, PR China

Managing a rapidly growing peritoneal dialysis program with more than 1000 patients involves multiple challenges, labor constraints, logistics, and excessive geographic distance. This paper describes how Sun Yat-sen University, Guangzhou, China, manages those issues, while simultaneously improving quality of the care and, subsequently, clinical outcomes.

Perit Dial Int 2014; 34(S2):S31–S34 www.PDConnect.com
doi: 10.3747/pdi.2013.00122

KEY WORDS: PD programs; management; CQI; Southern China.

Peritoneal dialysis (PD) is a well-accepted modality of renal replacement therapy for end-stage renal disease (ESRD). This home-based therapy offers many inherent advantages, including preservation of residual renal function, maintenance of hemodynamics, improved quality of life, and lower cost than in-center hemodialysis (1). The rapid growth of the ESRD population in the presence of limited resources highlights the need for strategies to maximize the use of PD while simultaneously improving clinical outcomes. Those objectives remain a challenge for nephrologists in developing countries (2).

The Department of Nephrology at The First Affiliated Hospital of Sun Yat-sen University is one of the first independent nephrology departments that was established in southern China. It pioneered the use of PD in China and has become one of the largest units in the world, with a PD population exceeding 1000. Here, we share our experiences of the development and management of a large and rapidly growing PD center in China.

Correspondence to: X. Yu, Department of Nephrology, The First Affiliated Hospital of Sun Yat-sen University, 58th Zhongshan Road II, Guangzhou 510089 PR China.
yuxq@mail.sysu.edu.cn

Received 8 May 2013; accepted 11 June 2013

A RAPIDLY GROWING PD PROGRAM

In 1963, we pioneered PD for the management of acute renal failure in China. Continuous ambulatory PD for the treatment of ESRD, introduced by Moncrief and Oreopoulos in 1978, was soon thereafter adopted by our team. We continued developing the continuous ambulatory PD technique until, by 2005, we had established a standardized PD program of catheter insertion, patient education, training, treatment, and PD follow-up. Since the early 1980s, we have provided continuing medical education courses on PD to senior nephrologists from all over the country, under the sponsorship of the Ministry of Health of China.

The number of patients undergoing PD at our center increased to 968 in 2011 from 297 in 2005. We are currently following 1040 patients. The 841 new patients who started treatment with PD between 2006 and 2009 had 1-, 2-, 3-, and 4-year patient survival rates of 94%, 87%, 83%, and 76% respectively (3). Death-censored technique survival rates for those patients were 98%, 95%, 91%, and 90% respectively, and the overall rate of peritonitis was 1 episode in 68.5 patient-months (3). During the same 4-year period, the 1-year overall catheter survival rate was 94%. The average patient survival time on PD in 2009, 2010, and 2011 was 30.0, 30.1, and 33.1 months respectively (3).

CHARACTERISTICS OF THE PD PROGRAM

In our opinion, PD is still underused, despite being the preferred modality of renal replacement therapy for ESRD in China's large rural population. A key prerequisite for addressing patient training and nurse specialization is the development of a functional PD team.

The PD Team: A team consisting of skilled, dedicated, collaborative, and hardworking medical staff is the cornerstone of our PD program's success. Our team includes

3 nephrologists who oversee pre-dialysis counseling, perform catheter insertions, and provide medical services in the inpatient wards. An additional 3 nephrologists are responsible for patient follow-up, outpatient treatment, and quality management. The team also includes 12 PD nurses led by a senior nurse. In our experience, the nurse-to-patient and nephrologist-to-patient ratios required to manage our large PD program are 1:90–100 and 1:340–350 respectively. To make follow-up more efficient, we have formed teams of 3 or 4 well-trained primary nurses working under the direct supervision of 1 designated PD nephrologist. This system ensures the mutual accountability of doctors and nurses, and plays an important role in safeguarding high standards for PD care.

A multidisciplinary approach, supported by various subspecialties, is required to maximize PD outcomes. The essential components include provision of an inpatient ward, a hemodialysis center, a kidney transplantation center, and a kidney laboratory. Based on multiple proactive international collaborations and practice-sharing, we have also been able to develop a program that takes into account the specifics of the Chinese environment.

Clinical Governance and Continuous Quality Improvement: Our patient management procedures are based primarily on guidelines set out by the International Society for Peritoneal Dialysis and the U.S. National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (4–7). We have also developed standard protocols based on our own experience in PD management. Catheter insertion is performed by nephrologists, and all patients undergo a 4- to 5-day training program, with retraining being offered as needed. The patients are seen at clinical units every 1–3 months, and a 24-hour on-call service is provided in case of emergency.

To further optimize the overall quality of the PD program, we adopted a clinical governance program, which is a systematic approach aimed at maintaining and improving the quality of patient care within a given health system (8). We used international guidelines to establish goals for key performance indicators, taking current center size and clinical outcomes into account, and including an assessment of treatment satisfaction by the patients. Experience has shown that our key performance indicators play a critical role in achieving the management objectives and success of the program (9).

To continuously improve PD practice, we conduct routine daily clinical meetings, weekly PD team discussions, and monthly PD symposia to measure, identify, and modify performance. For instance, in the summer of 2007, we noticed an unexpectedly high rate of peritonitis.

We identified the possible underlying causes, and by analyzing the data, we identified 17 episodes of *Escherichia coli* infection among 72 episodes of peritonitis, which accounted for 58.6% of all infections caused by gram-negative bacteria. We then implemented measures to educate patients about diet and hygiene, with the aim of preventing seasonal gastrointestinal problems. Regular monitoring shows that those measures have been effective in controlling the increased incidence of summertime peritonitis. The total annual number of peritonitis episodes has also declined (Figure 1).

We promoted the widespread use PD by improving technique quality. The good reputation of our PD program has thus attracted many ESRD patients from various parts of China. We actively encourage patients with new-onset ESRD to be treated with PD as the first choice of renal replacement therapy—especially patients who have good residual renal function and who live in suburban areas. That approach has resulted in a continuous increase in incident and prevalent PD patients over time.

Patient Characteristics and Satellite Centers: The number of incident PD patients has grown steadily, especially since about 2009. More than 80% of our patients are unplanned starters who have received limited pre-dialysis education, and approximately two thirds of the PD patients seen at our center live outside the city, which makes management a challenge. To address those issues, we established a PD “satellite center” program across Guangdong Province. The program provides standardized training for doctors and nurses in satellite hospitals, with the objective of increasing the use and quality of PD, reducing the incidence of peritonitis, and lowering the drop-out rate. The program was initiated in January 2008, and by the end of 2010, 13 units had been accepted as satellite centers. We provide courses covering all aspects of PD therapy for the nephrologists and nurses working in the satellite centers, and to date, 26 physicians and 32 nurses have been trained.

Figure 1 — Peritonitis rate from 2006 to 2011.

Clinical outcome parameters have significantly improved in the satellite centers since training was initiated. The number of patients receiving PD in satellite centers has increased to 2544 in 2010 from 1010 in 2007. The annual drop-out rate has declined from 28.2% to 18.2%, and the average peritonitis rate in the cohort has declined to 1 episode in 54.5 patient-months from 1 episode in 39.4 patient-months. Over the same period, the 1-year death-censored technique survival rate increased to 93.0% from 88.7%, and the 1-year patient survival rate increased to 84.2% from 82.0%. Average time on PD rose to 26.1 months from 16.3 months (10).

The PD satellite center model not only meets a need for adequate management of suburban patients, but also promotes high-quality PD therapy across the province and enhances uptake of the PD technique, as independently reported (11).

Optimization of PD Through Research Activities: We aim to continuously improve the quality and management of PD by undertaking research to solve clinical problems and improve therapeutic outcomes. Our dedication to research is documented by our more than 30 published papers, including 3 authored by nurses (12–14).

In recent years, our research has focused on preservation of residual renal function, protection of peritoneal function, and the pathogenesis and prevention of peritonitis (15–22). In 2009, we received a grant to study the pathogenesis of PD-related *E. coli* peritonitis. That ongoing study has investigated the role of serotypes, genotypes, virulence factors, and the innate and adaptive immune responses of the host, ultimately providing a basis for prevention and intervention. We are also involved in a large-scale of randomized controlled trial to compare the survival rates of ESRD patients receiving either PD or hemodialysis treatment. That trial is scheduled to end in 2016. It is being coordinated by our hospital and Shanghai Renji Hospital, and will enroll 1370 patients with ESRD from more than 20 Chinese hospitals.

Functional deterioration of the peritoneal membrane has been reported to be an obstacle to the long-term application of PD (23). To identify preventive and therapeutic measures, we therefore explored the mechanisms of peritoneal structural injury and malfunction during PD. Our findings indicated that transforming growth factor β 1 (TGF- β 1), and its signaling pathway protein (SMAD) both play a key role in the pathogenesis of peritoneal fibrosis. Using a gene transfection technique, we also showed that upregulation of an inhibitory protein (Samd7) significantly attenuates the initiation and progression of peritoneal fibrosis, and thus might have

potential clinical value (24–26). Furthermore, in an acute model of peritonitis induced by *E. coli* in rats, we demonstrated that upregulation of Smad7-enhanced inflammation results in deterioration of peritoneal function (22). Those findings suggest that TGF- β 1 might protect against acute peritoneal inflammation and peritoneal fibrosis. A more specific way of preventing peritoneal fibrosis can therefore be explored. Signaling pathways such as heat shock protein 72 and c-Jun N-terminal kinase have been found to be involved in the regulation of peritoneal fibrosis induced by TGF- β 1 and might be candidates for therapies aimed at preventing fibrosis (27–30).

Taken together, those findings indicate that TGF- β 1 and SMAD play an important role in the development of peritoneal fibrosis. The studies also identify part of the molecular mechanism involved in the pathogenesis of peritoneal fibrosis and provide a scientific basis for further research. Indeed, an independent review stated that “the combination of inhibition of TGF-signaling and inflammatory response by Smad7 overexpression suggested that this is a promising approach to limiting peritoneal fibrosis in PD and is an important area for future research” (31).

SUMMARY

An excellent team, implementing standardized procedures in PD treatment and management, together with continuous quality improvement and clinically-oriented scientific research has, in our opinion, contributed to the success of our PD center.

ACKNOWLEDGMENTS

We thank Dr. Anders Tranæus for his kind revision of the manuscript and Dr. Qiang Yao from Baxter China for her assistance with the manuscript. We also thank the doctors and nurses in our center for their careful management of our patients.

DISCLOSURES

The authors have no financial conflicts of interest to disclose.

REFERENCES

1. Bargman JM. Advances in peritoneal dialysis: a review. *Semin Dial* 2012; 25:545–9.
2. Finkelstein FO, Abu-Aisha H, Najafi I, Lo WK, Abraham G, Pecoits-Filho R, *et al*. Peritoneal dialysis in the developing world: recommendations from a symposium at the ISPD meeting 2008. *Perit Dial Int* 2009; 29:618–22.
3. Yang X, Mao HP, Guo QY, Yu XQ. Successfully managing a

- rapidly growing peritoneal dialysis program in Southern China. *Chin Med J (Engl)* 2011; 124:2696–700.
4. Piraino B, Bernardini J, Brown E, Figueiredo A, Johnson DW, Lye WC, *et al.* ISPD position statement on reducing the risks of peritoneal dialysis-related infections. *Perit Dial Int* 2011; 31:614–30.
 5. Blake PG, Bargman JM, Brimble KS, Davison SN, Hirsch D, McCormick BB, *et al.* on behalf of the Canadian Society of Nephrology Work Group on Adequacy of Peritoneal Dialysis. Clinical practice guidelines and recommendations on peritoneal dialysis adequacy 2011. *Perit Dial Int* 2011; 31:218–39.
 6. Li PK, Szeto CC, Piraino B, Bernardini J, Figueiredo AE, Gupta A, *et al.* on behalf of the International Society for Peritoneal Dialysis. Peritoneal dialysis-related infections recommendations: 2010 update. *Perit Dial Int* 2010; 30:393–423. [Erratum in: *Perit Dial Int* 2011; 31:512]
 7. National Kidney Foundation. K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. *Am J Kidney Dis* 2003; 42(Suppl 3):S1–201.
 8. Goodman NW. Clinical governance. *BMJ* 1998; 317:1725–7.
 9. Johnson DV. Reaching standards of care in peritoneal dialysis. *ISPD Asian Chapter Newsletter* 2010; 8:2–3.
 10. Jiang Z, Yu XQ. Advancing the use and quality of peritoneal dialysis by developing a peritoneal dialysis satellite center program. *Perit Dial Int* 2011; 31:121–6.
 11. Lo WK. Improving peritoneal dialysis outcomes through networking based on experienced centers of excellence. *Perit Dial Int* 2011; 31:131–3.
 12. Lin J, Guo Q, Ye X, Li J, Yi C, Zhang X, *et al.* The effect of social support and coping style on depression in patients with continuous ambulatory peritoneal dialysis in southern China. *Int Urol Nephrol* 2013; 45:527–35.
 13. Li J, Guo Q, Ye X, Lin J, Yi C, Mao H, *et al.* Prevalence and risk factors of sleep disturbance in continuous ambulatory peritoneal dialysis patients in Guangzhou, southern China. *Int Urol Nephrol* 2012; 44:929–36.
 14. Ye XQ, Chen WQ, Lin JX, Wang RP, Zhang ZH, Yang X, *et al.* Effect of social support on psychological-stress-induced anxiety and depressive symptoms in patients receiving peritoneal dialysis. *J Psychosom Res* 2008; 65:157–64.
 15. Yang Q, Li R, Zhong Z, Mao H, Fan J, Lin J, *et al.* Is cystatin C a better marker than creatinine for evaluating residual renal function in patients on continuous ambulatory peritoneal dialysis? *Nephrol Dial Transplant* 2011; 26:3358–65.
 16. Yang X, Ye R, Kong Q, Yang Q, Dong X, Yu X. CD40 is expressed on rat peritoneal mesothelial cells and upregulates ICAM-1 production. *Nephrol Dial Transplant* 2004; 19:1378–84.
 17. Yang X, Ye RG, Kong QY, Yang QQ, Gao Y, Zhong JH, *et al.* CD40 ligand expression on macrophages during peritonitis in continuous ambulatory peritoneal dialysis patients. *Adv Perit Dial* 2000; 16:213–15.
 18. Wu J, Yang X, Zhang YF, Wang YN, Liu M, Dong XQ, *et al.* Glucose-based peritoneal dialysis fluids downregulate toll-like receptors and trigger hyporesponsiveness to pathogen-associated molecular patterns in human peritoneal mesothelial cells. *Clin Vaccine Immunol* 2010; 17:757–63.
 19. Wu J, Yang X, Zhang YF, Zhou SF, Zhang R, Dong XQ, *et al.* Angiotensin II upregulates Toll-like receptor 4 and enhances lipopolysaccharide-induced CD40 expression in rat peritoneal mesothelial cells. *Inflamm Res* 2009; 58:473–82.
 20. Zhang YF, Yang X, Zhang YJ, Sun YL, Zou XL, Kong QY, *et al.* Peroxisome proliferator-activated receptor-gamma is expressed by rat peritoneal mesothelial cells: its potential role in peritoneal cavity local defense. *Am J Nephrol* 2006; 26:602–11.
 21. Yang X, Yang QQ, Guo QY, Yi CY, Mao HP, Lin JX, *et al.* *Aeromonas salmonicida* peritonitis after eating fish in a patient undergoing CAPD. *Perit Dial Int* 2008; 28:316–17.
 22. Wang X, Nie J, Jia Z, Feng M, Zheng Z, Chen W, *et al.* Impaired TGF-beta signalling enhances peritoneal inflammation induced by *E. coli* in rats. *Nephrol Dial Transplant* 2010; 25:399–412.
 23. Davies SJ, Mushahar L, Yu Z, Lambie M. Determinants of peritoneal membrane function over time. *Semin Nephrol* 2011; 31:172–82.
 24. Nie J, Hao W, Dou X, Wang X, Luo N, Lan HY, *et al.* Effects of Smad7 overexpression on peritoneal inflammation in a rat peritoneal dialysis model. *Perit Dial Int* 2007; 27:580–8.
 25. Nie J, Dou X, Hao W, Wang X, Peng W, Jia Z, *et al.* Smad7 gene transfer inhibits peritoneal fibrosis. *Kidney Int* 2007; 72:1336–44.
 26. Sun Y, Zhu F, Yu X, Nie J, Huang F, Li X, *et al.* Treatment of established peritoneal fibrosis by gene transfer of Smad7 in a rat model of peritoneal dialysis. *Am J Nephrol* 2009; 30:84–94.
 27. Liu Q, Mao H, Nie J, Chen W, Yang Q, Dong X *et al.* Transforming growth factor β 1 induces epithelial-mesenchymal transition by activating the JNK-Smad3 pathway in rat peritoneal mesothelial cells. *Perit Dial Int* 2008; 28(Suppl 3):S88–95.
 28. Liu Q, Zhang Y, Mao H, Chen W, Luo N, Zhou Q, *et al.* A crosstalk between the Smad and JNK signaling in the TGF- β -induced epithelial-mesenchymal transition in rat peritoneal mesothelial cells. *PLoS One* 2012; 7:e32009.
 29. Li S, Zhou Y, Fan J, Cao S, Cao T, Huang F, *et al.* Heat shock protein 72 enhances autophagy as a protective mechanism in lipopolysaccharide-induced peritonitis in rats. *Am J Pathol* 2011; 179:2822–34.
 30. Zhu F, Li T, Qiu F, Fan J, Zhou Q, Ding X, *et al.* Preventive effect of Notch signaling inhibition by a gamma-secretase inhibitor on peritoneal dialysis fluid-induced peritoneal fibrosis in rats. *Am J Pathol* 2010; 176:650–9.
 31. Fraser D. Smad7: at the interface of TGF-beta and proinflammatory signaling. *Perit Dial Int* 2007; 27:523–5.