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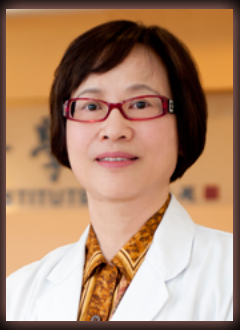

Comparing Risk of New Onset Diabetes Mellitus in Chronic Kidney Disease Patients Receiving Peritoneal Dialysis and Hemodialysis Using Propensity Score Matching

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Chronic kidney disease (CKD) patients are at risk for developing new-onset diabetes mellitus (NODM) after hemodialysis (HD) and peritoneal dialysis (PD). It is not clear if the incidence for NODM is different in patients receiving HD and PD. Our original hypothesis was PD patients might have higher incidence of NODM than HD patients, as PD patients were exposed daily to high glucose load and subsequently may develop obesity and metabolic syndrome. This study compared the risk of NODM in PD and HD patients. All HD and PD patients in Taiwan Renal Registry Database from 1997 to 2005 were included. The risk of NODM was analyzed in PD patients and compared to a group of propensity score matched HD patients with 1:4 ratios. A total of 2548 PD patients and 10192 HD patients who had no DM at the initiation of dialysis were analyzed. The incidence for NODM was 3.7 per 100 patient- year for HD and was 2.4 per 100 patient- year for PD patients. HD patients are more at risk for developing both early type NODM (patients who developed NODM ≤ 6 months after dialysis; adjusted odds ratio of 1.41, 95% CI: 1.12–1.78, $p<0.001$); and late type NODM (patients who developed NODM after more than 6 month of dialysis; adjusted hazard ratio of 2.01, 95% CI: 1.77–2.29, $p<0.001$). The development of NODM was associated with an increased risk of mortality (HR 1.42, 95% CI 1.32–1.52, $p<0.001$).

Discussion and Conclusions

In this observational cohort study, the incidence of NODM was less in PD than HD cohort (2.4 vs. 3.7/ per 100 patient- year). Compared to PD patients, HD patients had a 41% increased risk for developing early type and 2-fold increased risk for developing late type NODM. Most of the new onset diabetes was diagnosed within 2 years of dialysis and few patients developed NODM after 5 years of dialysis.

The association between HD and risk of NODM was independent of patient's age, gender, comorbid hypertension, hematocrit, and serum albumin. A propensity score matching was critical in this investigation, because younger patients are more likely to be treated with PD and have less chance of having NODM. The propensity score matched HD cohort had a similar age, primary renal disease and comorbidities when compared to PD cohort. As the risk of NODM was significantly higher in propensity score matched HD cohort, patient selection bias were minimized. Our original hypothesis was PD patients may have higher incidence of NODM than HD patients. But, to our surprise, this is not true. Actually, HD cohort had higher risk of developing DM after dialysis. What is the mechanism behind these important findings? We speculated the elevated NODM risk in HD patients may be explained by chronic inflammation induced by blood membrane interaction during HD. HD can induce chronic subclinical inflammation indicated by increased cytokine production, such as C-reactive protein and interleukins-6. Chronic inflammation plays a critical role in the development of DM. In addition, less risk for NODM among PD patients may be related to their better daily physical

FROM THE EDITORIAL OFFICE

Dear All,

Welcome back from the ISPD 2014 meeting at Madrid. It was a great success. We are particularly happy to have Professor Philip Li from Hong Kong being elected as the new ISPD President.

In this issue, we are delighted to have Prof. CC Huang from Taiwan to discuss the issue of new-onset diabetes in dialysis patients. In addition, Dr. W Fang will discuss the management of peritoneal dialysis during the break-in period, and the group led by Dr. R Ram from India will share their experience of re-initiation of dialysis after catheter removal for refractory peritonitis.

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Sincerely,
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Erratum

Dr. Chui-Woo YANG, together with his co-workers, who wrote the article "Body mass index and mortality in peritoneal dialysis" in the August 2014 issue of the ISPD-APC newsletter, comes from Seoul, Korea (rather than Taiwan, as mentioned in the Editor's notes of the newsletter). We are sorry for the mistake.

activities than HD patients. In contrast to ambulatory PD patients, after each HD treatment, most patients felt extremely tired and lost their energy. Gradually, they became sedentary. This study reminds us to encourage more physical activity for our dialysis patients.

The other point to be mentioned is our finding of "development of NODM in dialysis patients is associated with an increased risk of mortality". Therefore, we need to monitor blood glucose or HbA1C regularly for non-DM patients after they have entered the dialysis program and control blood glucose properly for NODM patients. For those who developed NODM, one may control blood glucose with either oral anti-diabetic medications or insulin. For PD patients with NODM, high glucose concentration dialysis solutions should be avoided. Non-glucose based solutions, such as Icodextrin or amino acid solutions are good alternatives if they are available in your country. One word of caution, in PD patients who received Icodextrin, blood glucose monitoring devices and test stripes using glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ), or glucose-dye-oxidoreductase (GDO)-based, or glucose dehydrogenase flavin-adenine dinucleotide (GDH-FAD)-based methods should not be used to avoid a false elevation of blood glucose reading.

In conclusion, HD patients are more at risk for developing new-onset DM compared to a group of propensity score matched PD patients. The development of NODM in dialysis patients is associated with an increased risk of mortality. The risk of new onset diabetes was higher in the first 2 years after dialysis. Regular blood glucose and/or HbA1C monitoring are suggested for early detection and management of NODM in dialysis patients. Icodextrin and amino acid solutions may be used for better glycemic control in PD patients with NODM.

Commentary on Reinitiation of Peritoneal Dialysis after Catheter Removal for Refractory Peritonitis

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Introduction

In India, peritoneal dialysis (PD) is preferred as a renal replacement therapy in 18-20% of patients. Only a handful of nephrologists follow the paradigm of 'peritoneal dialysis first'. The majority of nephrologists in India would guide their patients whose catheters were removed for refractory peritonitis to haemodialysis. The reasons would be the fear of adhesions and PD after initial two years, with the loss of residual renal function might not provide benefit vis-a-vis haemodialysis. It is indeed a fact that a high proportion of patients whose catheters are removed are unable to successfully reinitiate peritoneal dialysis due to irreversible peritoneal injury. We examined the outcomes of patients reinitiated on PD after refractory peritonitis. This is the first of its report from India.

Methods

We reviewed all patients with end-stage renal disease who were initiated on continuous ambulatory peritoneal dialysis at our Institute in south India between 1998 and 2012. We identified patients whose catheters were removed and the PD was reinitiated. We analyzed the reasons and outcome. We compared data of patients who could be reinitiated on PD with those who could not be reinitiated and also the data of patients who successfully continued PD after reinitiation with those who suffered technique failure.

Results

Between 1998 and December 2012, 650 end-stage renal disease (ESRD) patients were initiated on peritoneal dialysis at our Institute. There were 159 patients (31.7 % of 501 peritonitis episodes) in whom the peritonitis was refractory and the catheter was removed: 49 bacterial peritonitis patients (17.7 % of 276 episodes), 13 tuberculous (81.2 % of 16 episodes), 68 fungal (100 % of 68 episodes), and 29 culture-negative (20.5 % of 141 episodes). None of these patients had exit-site/tunnel infection. All 159 patients in whom the catheter was removed were informed about the option of reinitiating PD. The decision whether or not to reinitiate PD was up to the patient. An attempt to reinitiate PD was made in 38 (23.8 % of 159) patients. It was successful in 31 (81.7 %) patients. The mean age of the 31 patients successfully reinitiated on PD was 53.8 years (range 8–72). There were 22 (70.9 %) males. The median duration of PD before the catheter was removed was 24 months (range 3–108). The interval between catheter removal and reinitiation of PD was 50.4 ± 12.8 days (range 32–90). The median duration of follow up PD after reinitiation was 12 months (range 2–60). The causes of ESRD of the patients reinitiated on PD were: diabetes mellitus in 16 (51.6 %), hypertension in 7 (22.5 %), autosomal dominant polycystic kidney disease, chronic glomerulonephritis and vesicoureteric reflux in 2 (6.4 %) patients each, and genitourinary tuberculosis and chronic interstitial nephritis in 1 (3.2 %) each. The organisms causing peritonitis were fungal in 7 patients (22.5 %), Pseudomonas aeruginosa in 4 (12.9 %), Escherichia coli in 3 (9.6 %), Staphylococcus aureus, Coagulase-negative staphylococcus and Mycobacterium. tuberculosis in 2 (6.4 %) each, and Acinetobacter baumannii and Klebsiella pneumoniae in 1 (3.2 %) each. The cause was culture negative in 9 (29 %) patients. In seven patients, PD could not be reinitiated due to adhesions. All seven were regularly followed. One of them developed sub-acute intestinal obstruction after 6 months and was operated.

Another developed a lump in the abdomen after 3 months, due to fluid collection in adhesions that required repeated drainage. The remaining 121 patients continued on haemodialysis. They were followed for a median period of 12 months. The outcomes of these patients were: 16 (13.2 %) dropped out; 4 (3.3 %) underwent renal transplantation; 31 (25.6 %) died; and 49 (40.4 %) continued on haemodialysis.

We compared the patients in whom PD could be reinitiated (31; 81.7 %) with those in whom it could not be done (7; 18.4 %). Patients of both groups had the catheter removed for refractory peritonitis on either day 5 or 6. There was no significant difference between these

two groups in terms of age, sex, cause of ESRD, organisms causing peritonitis, previous peritonitis episodes or duration of PD prior to catheter removal.

The outcome of patients reinitiated on PD was: patients on regular follow up without peritonitis: 13 (41.9 %), died while on PD: 11 (35.4 %), ultrafiltration failure: 1 (3.2 %), catheter removed due to refractory peritonitis: 6 (19.3 %). In the six patients in whom the catheter was removed due to technique failure, the PD was continued for 18.4 ± 9.6 months. There was no significant difference between the group in which the technique failed and the group with regular PD after reinitiation.

There were five patients, who had the catheter inserted for a third time, after a second episode of refractory peritonitis. Of these five patients, the culture was negative in two patients, Escherichia coli was isolated in two more patients, while in the fifth patient it was fungal peritonitis. The duration of PD on the third catheter was 13.2 ± 5.0 months (range 6–18).

In 21 patients the peritoneal equilibration test (PET) could be performed after reinitiation of PD. There was no change in transporter status in ten patients, while in ten there was a change and in one it was unknown as PET was not done prior to catheter removal. More patients converted to high and high-average transporter status than to low and low-average transporter status.

Discussion

There were only four studies in the past on reinitiation of PD after refractory peritonitis. The present study demonstrated that reinitiating PD is feasible in a developing country, and also that reinitiation of PD is possible after an episode of Pseudomonas aeruginosa and fungal peritonitis. In our programme the decision of reinitiation of PD was not influenced by us, but was taken by the patient. Removal of the catheter on day 5 or 6, a mean interval of 50.4 days after the removal of catheter, use of peritoneal scintigraphy to rule out adhesions and reinsertion of the catheter by open surgery might have contributed to successful reinitiation of PD in our patients.

Management of Peritoneal Dialysis Patients with Short Break-in Period

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The proportion of end-stage renal disease (ESRD) patients on peritoneal dialysis (PD) has increased very fast in China over the last decade[1]. PD has a survival advantage compared with hemodialysis (HD) patients in the first few years, and also has many other advantages including cost savings, preservation of residual renal function, relative high quality of life, and greater capacity to serve more ESRD patients due to its lower infrastructure requirements[2,3]. Therefore, PD is the preferred modality of RRT in many dialysis units in China as it can meet the great demand for dialysis treatment of the rapidly increasing ESRD population. Renji Hospital, Shanghai Jiaotong University School of Medicine is one of the first hospitals to adopt PD in China and has run its PD program for 30 years and currently has in excess of 450 PD patients. It is a recognized high-quality PD unit in China with a high PD utilization rate, excellent patient and technique survival, low peritonitis rate and a well-documented good quality of life of the treated patients[4,5].

Despite improvements in catheter survival over the last few years, catheter-related complications still occur, causing significant morbidity and in some cases forcing the removal of the catheter. International guidelines recommended that catheter insertion should be performed at least 2 weeks before starting PD[6,7]. However in our center, quite a few patients have to start urgently on dialysis because of late referral or unexpected deterioration of residual renal function. In a recent analysis we showed that, during 2001-2010, a total of 657 catheters were inserted in our centre. Among them, only 176 (26.7%) patients had a break-in period longer than 2 weeks, 137 (20.9%) patients started PD within 7-14 days after catheter insertion and 344 (52.4%) patients received PD treatment with a break-in period less than 7 days. Although majority of our patients initiated PD with a short break-in period, the catheter outcome was acceptable: 35 (5.3%) patients developed catheter-related complication, and only 8 (1.2%) needed surgical intervention, and 10 (1.5%) had to be transferred to HD due to catheter dysfunction, others recovered with conservative treatment[8].

We believe several key factors contribute to this low prevalence of catheter dysfunction in our centre: Firstly, peritoneal catheter insertion are performed by appropriately trained and experienced nephrologists in a dedicated renal operation room, which helps in reducing unnecessary surgical consultations and facilitates timely interventions. Nephrologists are, indeed, reported to be ideally suited to perform catheter insertion with excellent catheter outcome data, because of their better understanding of renal patients and the pathophysiology of the disease process[9]. Secondly, establishing appropriate protocols is another essential. The protocol for catheter insertion in our centre includes: 1) Administration of prophylactic antibiotic at the time of catheter insertion, a cephalosporin or vancomycin is used in our centre; 2) Placing the catheter in a downward direction with the superficial cuff 2-3 cm from the exit site, as this has been shown to reduce the risk of exit-site/tunnel infections; 3) Catheter function is tested by filling and draining PD fluid before tunneling the catheter; 4) Bowel preparation to avoid constipation before and after surgery, as constipation is associated with catheter malfunction and Gram-negative peritonitis; 5) Appropriate catheter care after insertion, including anchoring the catheter to immobilize the exit site and minimize entry of bacteria into the tunnel track. Thirdly, appropriate management of patients during break-in period is important. After catheter insertion, dressing of the wound should be kept intact for a week unless complicated by leaking or bleeding. Our PD nurse usually change dressing under aseptic technique weekly for the first 2-3 weeks because too often changing may expose more risk for infection before the sinus wound healed. For patients with break-in period longer than 1 week, nurses flush the tube with PD fluid once a week to prevent catheter obstruction. When start PD, for

patients who need to initiate PD urgently, low intra-peritoneal volume (0.75L-1.2L) is generally used, and then gradually increase to 2L per exchange within 2 weeks after catheter insertion. 3 or 4 exchanges are performed daily for CAPD patients, and for APD patients, 6 or 7 cycles are prescribed, and is converted to standard CAPD with 2L intra-peritoneal volume within 2 weeks after catheter insertion. In patients with a break-in period of 2 weeks or longer, PD is usually started with 2L except small patients who could not tolerate 2L fluid in their peritoneal cavities. It is also necessary to monitor closely the patient's symptom and sign at dialysis initiation. When signs of catheter dysfunction occurred, the cause of catheter dysfunction is determined by some combination of physical examination, abdominal radiography, and peritoneography, as required. In patients who develop catheter dysfunction, conservative therapy is given initially: supine position and a lower infusion volume for leaks; abdominal massage, administration of aperients or enemas, or ambulation for malposition; clot dislodgement with heparin or urokinase for obstruction; and administration of aperients or enemas for omental wrap. If conservative treatment failed, surgical intervention or transfer to HD is considered and performed.

In summary, dedicated operator, establishing and utilizing standardized protocols, careful management of patients during break-in period, start PD with low intra-peritoneal volume for patients who need urgent PD, and appropriate conservative therapy for catheter dysfunction are all the important factors contribute to low prevalence of catheter dysfunction in our centre.

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35th Annual Dialysis Conference
January 31 - February 3, 2015
Ernest N. Morial Convention Center
New Orleans, Louisiana
Website: medicine.missouri.edu/dialysis/

International Society of Nephrology World Congress of Nephrology 2015
March 13-17,2015
Cape Town, South Africa
Website: http://www.theisn.org/itemid-666

7th Asia-Pacific Chapter meeting of the International Society for Peritoneal Dialysis
September 17-19, 2015
Daegu, Korea
Website: apcm-ispd2015.org

12th European Peritoneal Dialysis (EuroPD) Meeting
October 2-5, 2015
ICE Krakow Congress Centre, Poland
Website: www.europd.com