12. Koda Y, Nishi S, Miyazaki S *et al*. Switch from conventional to high-flux membrane reduces the risk of carpal tunnel syndrome and mortality of hemodialysis patients. *Kidney Int* 1997; 52: 1096–1101
13. Traut M, Haufe CC, Eismann U *et al*. Increased binding of beta-2-microglobulin to blood cells in dialysis patients treated with high-flux dialyzers compared with low-flux membranes contributed to reduced beta-2-microglobulin concentrations. Results of a cross-over study. *Blood Purif* 2007; 25: 432–440
14. Ayli M, Ayli D, Azak A *et al*. The effect of high-flux hemodialysis on dialysis-associated amyloidosis. *Ren Fail* 2005; 27: 31–34
15. Koda Y, Nishi S, Miyazaki S *et al*. Switch from conventional to high-flux membrane reduces the risk of carpal tunnel syndrome and mortality of hemodialysis patients. *Kidney Int* 1997; 52: 1096–1101
16. Schwalbe S, Holzhauer M, Schaeffer J *et al*. Beta 2-microglobulin associated amyloidosis: a vanishing complication of long-term hemodialysis? *Kidney Int* 1997; 52: 1077–1083

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Frequencies of hepatitis B and C infections among haemodialysis and peritoneal dialysis patients in Asia-Pacific countries: analysis of registry data

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Abstract

Background. The impact of dialysis modality on the rates and types of infectious complications has not been well studied. The aim of the present investigation was to evaluate the rates of hepatitis C virus (HCV) and hepatitis B virus (HBV) infections in peritoneal dialysis (PD) and haemodialysis (HD) patients in the Asia-Pacific region.

Methods. The study included the most recent period-prevalent data recorded in the national or regional dialysis registries of the 10 Asia-Pacific countries/areas (Australia, New Zealand, Japan, China, Taiwan, Korea, Thailand, Hong Kong, Malaysia and India), where such data were available. Longitudinal data were also available for all incident Australian and New Zealand patients commencing dialysis between 1 April 1995 and 31 December 2005. Rates of HCV and HBV infections were compared by chi-square, Poisson regression and Kaplan–Meier survival analyses, as appropriate.

Results. Data were obtained on 201 590 patients (HD 173 788; PD 27 802). HCV seroprevalences ranged between 0.7% and 18.1% across different countries and were generally higher in HD versus PD populations (7.9% $\pm$ 5.5% versus 3.0% $\pm$ 2.0%, $P = 0.01$). Seroconversion rates on dialysis were also significantly higher in HD patients (incidence rate ratio PD versus HD 0.33, 95% CI 0.13–0.75). HCV infection was highly predictive of mortality in Japan (relative risk 1.37, 95% CI 1.15–1.62, $P = 0.003$) and in Australia and New Zealand (adjusted hazards ratio 1.29, 95% CI 1.05–1.58). HBV infection data were limited, but less clearly influenced by dialysis modality.

Conclusions. Dialysis modality selection significantly influences the risk of HCV infection experienced by end-stage renal failure patients in the Asia-Pacific region. No such association could be identified for HBV infection.

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Keywords: end-stage renal failure; environmental transmission; haemodialysis; hepatitis B; hepatitis C

Introduction

Dialysis modality has been identified as a major risk factor for infection with hepatitis B virus (HBV) and hepatitis C virus (HCV), with significantly higher rates of seroconversion observed in HD compared with peritoneal dialysis (PD) [1–5]. In one South American study, haemodialysis (HD) treatment (but not blood transfusion) was the only risk factor significantly associated with HBV and HCV infection (hazard ratios 22.3 and 5.7, respectively), suggesting that both viruses were transmitted mainly through the HD environment [2]. However, significant variability in HBV and HCV prevalence has been reported across South America, North America, Europe and Asia [1,4,6–9] and even across dialysis units within the same country [4,7,8]. Recent recommendations for adoption of universal infection control practices [10], HBV vaccination for all susceptible dialysis patients, use of newer generation anti-HCV antibody assays, more rigorous screening of blood donors for hepatitis viruses, reduction of blood transfusion requirements with greater utilization of erythropoiesis-stimulating agents (ESA) and reduction of dialyzer reuse are likely to lead to reductions in hepatitis transmission in dialysis units [4,6]. Indeed, the prevalence of HBV infection in HD patients in the United States of America progressively fell from 7.8% to 1.0% between 1976 and 2002 [11]. Similarly, the prevalence of HCV infection fell from 10.4% to 7.8% from 1995 to 2002 [11]. In contrast, there is limited evidence that the prevalence of HCV remains high in some Asian countries [5,12], although this has not been well studied.

The aim of the present investigation was to evaluate the impact of dialysis modality on the prevalences and incidences of HCV and HBV infections in dialysis patients in Asia-Pacific countries using available contemporaneous registry data.

Materials and methods

Study population

The study included the most recent period-prevalent cohort of all dialysis patients from the national registries of eight Asia-Pacific countries/areas (Australia 2005, New Zealand 2005, Japan 2002, Taiwan 2004, Korea 2005, Thailand 2003, Hong Kong 2001, Malaysia 2006). For two countries without national renal replacement therapy registries (China and India), infection epidemiologic data were obtained from published or unpublished results of regional registries (Shanghai and Hyderabad, respectively) [13,14]. Some data were obtained from registry publications [5,13,15]. Longitudinal data were also available for all incident Australian and New Zealand patients commencing dialysis between 1 April 1995 and 31 December 2005.

Dialysis modality was generally assigned at initiation of dialysis, except for the Australian and New Zealand patients where dialysis modality was assigned according to the modality they were receiving on Day 90. The prevalence of HBV infection was defined as the percentage of all PD or HD patients who tested positive for HBV surface antigen (HBsAg) during the registry data collection period. The incidence of HBV infection was defined as the percentage of all patients receiving PD or HD during the data collection period who seroconverted from negative to positive for HBsAg. Similar definitions were used for the prevalence and incidence of HCV infection, based on the results of screening with anti-HCV assays. The rates of HCV seroconversion were compared between PD and HD using data recorded for all Australian and New Zealand patients commencing chronic dialysis between 1 April 1995 and 31 December 2005. Dialysis (HD and PD) patients in all participating countries/regions were screened for anti-HCV antibodies every 6 months. Data were not available on blood transfusions, but blood donors were screened for anti-HCV antibodies prior to blood donation in all participating countries/regions.

Statistical analysis

Results were expressed as frequencies and percentages for categorical variables and mean ± standard deviation for continuous variables. Distributions of categorical variables across the PD and HD groups were compared by the chi-square test. The risk of mortality according to HCV status was determined in Japanese dialysis patients by logistic regression. In Australian and New Zealand patients, the influence of baseline anti-HCV status and *de novo* anti-HCV seroconversion during dialysis on all-cause mortality was assessed by multivariate Cox proportional hazards model analysis. *De novo* anti-HCV status was assessed as a time-varying covariate (yes or no). The model was stratified by modality (HD, PD) and vintage (1995–1997, 1998–2000, 2001–2003, 2004–2006) to satisfy proportional hazards. Covariates included in the model were age at ESRD, gender, race (indigenous versus non-indigenous), BMI category (underweight, normal, overweight, obese), smoking status (non, current, former), late referral to a nephrologist and presence of comorbidities (chronic lung disease, coronary artery disease, peripheral vascular disease, cerebrovascular disease and diabetes). Comparison of the rates of HCV seroconversion between PD and HD patients per 100 patient-years at-risk in the Australian and New Zealand dialysis populations was performed by Poisson regression and presented as an incidence rate ratio [95% confidence interval (CI)]. The cumulative hazard of HCV seroconversion was calculated by the Kaplan–Meier method. Data were censored for renal transplantation, modality change, recovery of dialysis-independent renal function and 31 December 2005. Data were analysed using the software packages SPSS for Windows release 12.0 (SPSS Inc., North Sydney, Australia) and Stata/SE 9.2 (College Station, Tx, USA). *P*-values less than 0.05 were considered statistically significant.

Results

HCV infection

Data were obtained on 201 590 dialysis patients (HD, $n = 173788$; PD, $n = 27\ 802$). The prevalence of HCV infection across different Asia-Pacific countries ranged

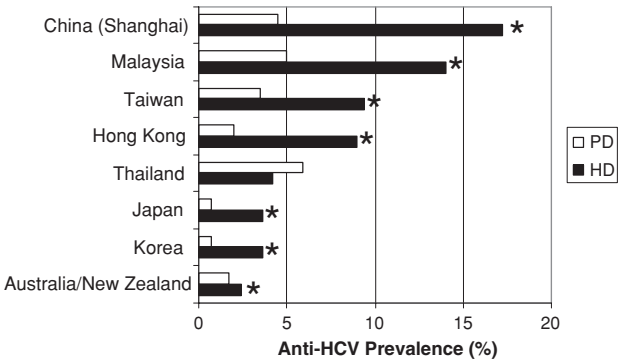

Fig. 1. Prevalence (%) of having anti-HCV antibodies amongst patients receiving PD (white bars) or HD (black bars) across different Asia-Pacific countries. *$P < 0.01$ versus PD.

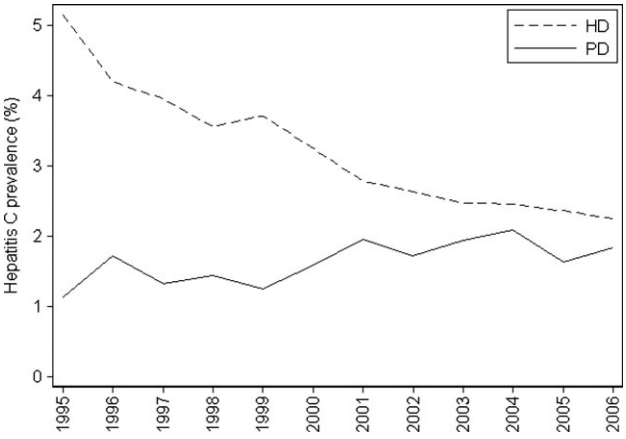

Fig. 2. Prevalence (%) of having anti-HCV antibodies in dialysis patients in Australia and New Zealand 1995–2006.

between 0.7% and 18.1% (Figure 1). For most countries, the frequency of HCV infection was significantly higher in HD patients than in PD patients (7.9% ± 5.5% versus 3.0% ± 2.0%, $P = 0.01$). In Australia and New Zealand, the prevalence of having anti-HCV antibodies in HD patients fell progressively over the period 1995–2006 and approached the prevalence observed in PD patients (Figure 2). Data for HCV RNA positivity were only available for Japanese patients (HD 2.9% versus PD 0.7%, $P < 0.001$). Three percent of HCV RNA positive patients had no detectable anti-HCV antibodies, whilst 26% of anti-HCV antibody positive patients had no detectable HCV RNA.

The annual incidence of HCV infections ranged from 0% in Thai PD patients to 18.1% in Indian HD patients (Figure 3). Rates were generally lower in PD patients than in HD patients, but were potentially confounded by the shorter technique survival of PD patients (and therefore much shorter number of years at risk). Therefore, in an attempt to better define the rate of HCV seroconversion in PD versus HD, the incidence rates of Australian and New Zealand HD and PD patients who seroconverted from negative to positive for anti-HCV antibody per 100 patient-years at risk were calculated during the period 1995–2005 (censored for renal transplantation, dialysis modality change

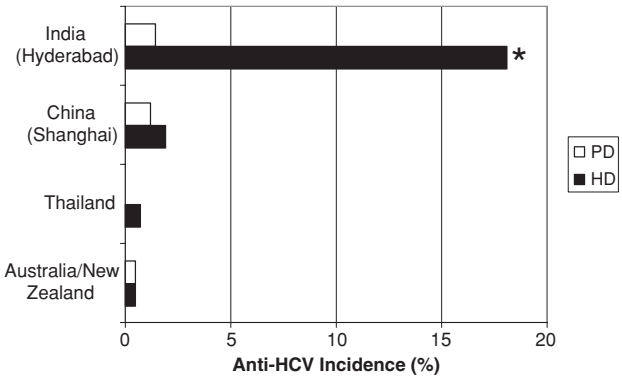

Fig. 3. Annual incidence of anti-HCV antibody amongst patients receiving PD (white bars) or HD (black bars) across different Asia-Pacific countries. *$P < 0.05$ versus PD.

and recovery of dialysis-independent renal function). HD patients had 0.1 HCV seroconversions per 100 patient-years at risk (95% CI 0.07–0.13), whilst PD patients experienced only 0.03 HCV seroconversions per 100 patient-years at risk (95% CI 0.02–0.07) ($P < 0.05$). The incidence rate ratio (PD versus HD) was 0.33 (95% 0.13–0.75).

The proportions of patients dying from hepatitis were not significantly different between PD and HD patients in Korea (4% versus 6%, $P = 0.24$), Hong Kong (0% versus 0.15%, $P = 0.43$) and Australia/New Zealand (0.04% versus 0.03%, $P = 0.76$), although numbers were too small to exclude a type 2 statistical error. In Japan, the presence of the anti-HCV antibody was significantly more common in HD patients and was an independent predictor of mortality (relative risk 1.37, 95% CI 1.15–1.62, $P = 0.003$). Similarly, in Australia and New Zealand, all-cause mortality was predicted by both the presence of anti-HCV at baseline (adjusted hazards ratio 1.29, 95% CI 1.05–1.58, $P = 0.016$) and the development of anti-HCV antibodies during the course of dialysis (adjusted hazards ratio 1.27, 95% CI 1.04–1.55, $P = 0.017$).

HBV infection

Limited HBV infection data were available from seven Asia-Pacific countries (HD, $n = 160\,711$; PD, $n = 28\,952$). The prevalence of HBsAg positivity ranged between 1.3% and 14.6% and was generally comparable between PD and HD populations in China, Malaysia, Hong Kong and Thailand, higher in PD patients in Japan and Taiwan and lower in PD patients in Korea (Figure 4). Incidence data were only available for Thailand and were not statistically significantly different between HD and PD patients (0.4% versus 0%). In Japan, HBV e antigen (HBeAg) positivity was reported in 0.4% of HD patients and 0.3% of PD patients ($P =$ ns).

Discussion

The present study of Asia-Pacific Dialysis Registry data clearly demonstrated that dialysis modality differentially affected the risk of hepatitis infection in ESRF

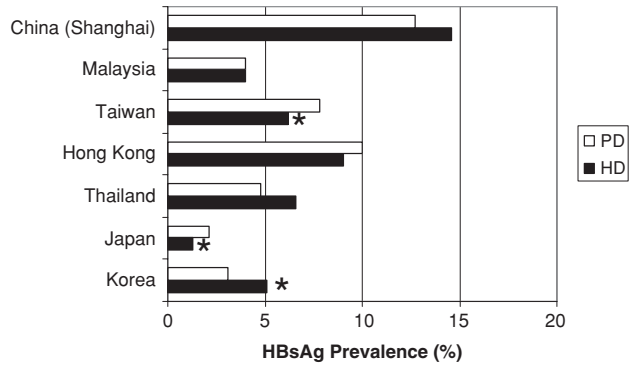

Fig. 4. Prevalence of HBsAg positivity amongst patients receiving PD (white bars) or HD (black bars) across different Asia-Pacific countries.

patients. On the one hand, HD was associated with higher HCV prevalences than PD patients (7.9% ± 5.5% versus 3.0% ± 2.0%, $P = 0.01$), higher HCV seroconversion rates and a shorter time to HCV seroconversion. On the other hand, no consistent differences were observed in the prevalences and incidences of HBV infections between PD and HD, although the available country data were limited.

The prevalences of HCV infection observed in dialysis patients in the present study were considerably higher than those in the corresponding general populations of many Asian countries (range 1.0–2.9%) [16], and likely contributed to higher rates of complications (hepatic cirrhosis and hepatocellular carcinoma) and death [17]. The consistent findings of higher rates of anti-HCV positivity in HD patients compared with PD patients across the Asia-Pacific region are in keeping with those of earlier studies in other parts of the world, which reported hazard ratios for HCV infection in HD between 1.6 and 5.7 [1–3,18–21]. In contrast, a more recent study of 5179 medical records of dialysis patients from the Thailand Renal Replacement Therapy Registry failed to find any independent predictive value of dialysis modality on HCV seroprevalence or incidence [5]. The apparent disparity in results compared with those of other Asia-Pacific countries may represent a type 2 statistical error in the former investigation due to relatively small numbers of PD patients (320 or 6.2%). Alternatively, the inter-country variability in HCV seroprevalences according to dialysis modality may reflect variable clinical practices, such as dialyzer reuse, blood transfusion policies or adherence to infection control guidelines for dialysis units. Recently, the KDIGO (Kidney Disease: Improving Global Outcomes) guidelines for the prevention, diagnosis, evaluation and treatment of hepatitis C in chronic kidney disease strongly recommended that HD units employ strict infection-control procedures designed to prevent transmission of HCV pathogens [22]. Nearly all Asia-Pacific countries had published national guidelines for HCV and HBV infection control measures in dialysis units, the key points of which generally included (a) HBV vaccination for susceptible patients and staff; (b) isolated dialysis machines/areas/rooms for hepatitis patients without sharing the same staff; (c) staff barrier protection (protective glasses/one−off gloves) and (d) avoidance of blood transfusions. However, data on the degree of adherence of different dialysis units to these clinical practice guidelines have not been published.

An important and novel observation of this study was the identification of a persistent, clinically significant incidence of HCV seroconversion despite having general infection control policies (including isolation) in place. The HCV seroconversion rate was higher in HD patients than in PD patients. This result underscores the limitations of infection control policies and the need for ongoing audit of HCV infection rates. Previous studies have identified a number of risk factors for HCV infection in dialysis units including dialysis modality, HD treatment duration, HD unit HCV seropositive prevalence, total transfused blood volume, lack of effective isolation of the infected patient, higher comorbid illness burden, history of prior renal transplantation and greater frequency of invasive procedures (e.g. surgery and endoscopy) [2,4,19,21,23–25]. The postulated reasons for a lower incidence of HCV infection in PD patients include reduced blood transfusion requirements [2] and the more isolated practice of dialysis at home with minimized visits to the renal unit (every 1–3 months rather than three times weekly). A number of studies suggest that environmental transmission within dialysis units is a major risk factor for HCV transmission and underpins the higher HCV seropositive prevalence in HD patients [2,21]. This contention is supported by the observations of Pascual and coworkers [26] who demonstrated a higher incidence of HCV infection among hospital HD patients rather than individuals performing home HD.

Importantly, the presence of anti-HCV antibodies predicted increased mortality in both the Japanese and Australian dialysis patient populations. The development of anti-HCV antibodies during the course of dialysis in Australia and New Zealand was also predictive of an increased risk of mortality, although this covariate may have acted as a marker of the general quality of care provided at individual units, rather than directly causing mortality.

In contrast to the findings of a significantly increased risk of HCV infection in HD compared with PD, no such clear distinction was possible to discern with respect to HBsAg positivity. Even though HBV infection shares many transmission risk factors in common with HCV (including blood transfusions and nosocomial exposure) [1,2], apparent dissociation of infection risks between the two blood-borne viruses has been described in other studies [3,5] and may be potentially related to rigorous HBV vaccination programmes [6], and/or stricter isolation/separation polices for in-centre HD patients. An alternative possibility is that the data may be potentially confounded by the fact that choice of dialysis modality is influenced by knowledge of a particular patient's hepatitis serologic status. For example, a patient with documented HBV infection may be encouraged to dialyze at home (generally by PD) to minimize the possibility of spread to other patients. Given that the risk of blood-borne transmission is substantially higher for HBV than for HCV, the influence of hepatitis serologic status on dialysis modality selection may be greater for HBV. Although such limitations can be partially circumvented by examining incidence data, such data were poorly recorded for hepatitis B by most Asia-Pacific Registries.

The strengths of our study lie in its large cohort size across multiple Asian and Pacific countries and rigorous statistical analyses. Moreover, the robustness of the findings in relation to the impact of dialysis modality on infection rates, especially for HCV infection, in spite of marked country-to-country variations in PD utilization (range 4.2%–81%) suggested that modality selection bias was not likely to be a major confounding factor. The external validity of our results was thus greatly enhanced.

Nevertheless, the study had a number of limitations. Because of the retrospective nature of the analysis and the fact that the patient coverage of different dialysis registries varied between 57.5% (Korea) and 100% (Australia and New Zealand), the potentials for both recall and ascertainment biases were present. For China and India, data were only available for a single region (Shanghai and Hyderabad, respectively) and may not have been the representative of the country as a whole. Furthermore, the strength of registry analyses with respect to their extent of coverage must be balanced against their main weakness, which is a limited depth of coverage. Most registries collected fairly sparse data on infectious outcomes and did not collect information on blood transfusions, hospitalizations, individual unit management protocols or the severity of comorbidities, so that residual confounding or unidentified associations could not be entirely excluded. There were also coding differences between registries (e.g. timing of dialysis modality assignment) and many could only provide data on prevalent patients rather than incident patients, thereby raising the possibilities of Neyman and informative censoring biases. In common with other registries, all Asia-Pacific dialysis registries were voluntary and there were no external audits of data accuracy. Finally, the possibility of differential screening for, and reporting of, infectious complications according to dialysis modality could not be entirely excluded (e.g. HBV and HCV infected patients might be more strongly encouraged to choose home dialysis modalities).

In conclusion, the present Asia-Pacific registry analyses demonstrate that dialysis modality selection is an independent predictor of the rates, types and times of occurrence of hepatitis infections in end-stage renal failure patients. Specifically, HD patients experience a markedly increased risk of early HCV infection, which in turn is predictive of hepatic cirrhosis, hepatocellular carcinoma and mortality. In contrast, no consistent relationship was observed between dialysis modality selection and HBV seroprevalence. Shared decision making by health professionals and patients in relation to dialysis modality selection and mitigation of infection risk should be informed by the above findings and local hepatitis infection seroprevalence data. The large country-to-country variability in HCV seroprevalence and seroconversion also suggests a need for more consistent, rigorous adherence to infection control guidelines to minimize environmental transmission.

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Conflict of interest statement. Professor Johnson, Dr Huang, Dr Han, Dr Jha, Dr Wang and Dr Kawaguchi have received consultancy fees and lecture fees from Baxter Healthcare Pty Ltd and are members of the Baxter Asia-Pacific Consultant Advisory Board. Professor Johnson is a current recipient of a Baxter Extramural Grant. Dr Yao and Dr Tranaeus are employees of Baxter Healthcare Pty Ltd.

References

1. Pereira BJ, Levey AS. Hepatitis C virus infection in dialysis and renal transplantation. *Kidney Int* 1997; 51: 981–999
2. Cendoroglo NM, Draibe SA, Silva AE *et al*. Incidence of and risk factors for hepatitis B virus and hepatitis C virus infection among haemodialysis and CAPD patients: evidence for environmental transmission. *Nephrol Dial Transplant* 1995; 10: 240–246
3. Sayiner AA, Zeytinoglu A,Ozkahya M *et al*. HCV infection in haemodialysis and CAPD patients. *Nephrol Dial Transplant* 1998; 14: 257
4. Sulowicz W, Radziszewski A, Chowaniec E. Hepatitis C virus infection in dialysis patients. *Hemodial Int* 2007; 11: 286–295
5. Thanachartwet V, Phumratanaprapin W, Desakorn V *et al*. Viral hepatitis infections among dialysis patients: Thailand registry report. *Nephrology (Carlton)* 2007; 12: 399–405
6. Tang S, Lai KN. Chronic viral hepatitis in hemodialysis patients. *Hemodial Int* 2005; 9: 169–179
7. Fabrizi F, Bunnapradist S, Martin P. HBV infection in patients with end-stage renal disease. *Semin Liver Dis* 2004; 24(Suppl 1): 63–70
8. Fissell RB, Bragg-Gresham JL, Woods JD *et al*. Patterns of hepatitis C prevalence and seroconversion in hemodialysis units from three continents: the DOPPS. *Kidney Int* 2004; 65: 2335–2342
9. Fabrizi F, Lunghi G, Ganeshan SV *et al*. Hepatitis C virus infection and the dialysis patient. *Semin Dial* 2007; 20: 416–422
10. Centers for Disease Control and Prevention. Recommendations for preventing transmission of infections among chronic hemodialysis patients. *Morb Mort Wkly Rep* 2004; 50: 1–43
11. Finelli L, Miller JT, Tokars JI *et al*. National surveillance of dialysis-associated diseases in the United States, 2002. *Semin Dial* 2005; 18: 52–61
12. Wang SM, Liu JH, Chou CY *et al*. Mortality in hepatitis C-positive patients treated with peritoneal dialysis. *Perit Dial Int* 2008; 28: 183–187
13. Taduri G, Murty KV, Pillalamarri NP *et al*. Avoidance of hepatitis C transmission: a major advantage for PD in an Indian center. *Perit Dial Int* 2005; 25: 605–606
14. Yao Q, Zhang W, Qian J. Peritoneal dialysis in Shanghai. *Perit Dial Int* 2008; 28: S42–S45
15. Leung N, Chu C, Tam JS. Viral hepatitis C in Hong Kong. *Intervirology* 2006; 49: 23–27
16. Shepard CW, Finelli L, Alter MJ. Global epidemiology of hepatitis C virus infection. *Lancet Infect Dis* 2005; 5: 558–567
17. Nakayama E, Akiba T, Marumo F *et al*. Prognosis of anti-hepatitis C virus antibody-positive patients on regular hemodialysis therapy. *J Am Soc Nephrol* 2000; 11: 1896–1902
18. Barril G, Traver JA. Decrease in the hepatitis C virus (HCV) prevalence in hemodialysis patients in Spain: effect of time, initiating HCV prevalence studies and adoption of isolation measures. *Antiviral Res* 2003; 60: 129–134
19. Meyers CM, Seeff LB, Stehman-Breen CO *et al*. Hepatitis C and renal disease: an update. *Am J Kidney Dis* 2003; 42: 631–657
20. Gorriz JL, Miguel A, Garcia-Ramon R *et al*. Prevalence and risk factors for hepatitis C virus infection in continuous ambulatory peritoneal dialysis patients. *Nephrol Dial Transplant* 1996; 11: 1109–1112
21. Chauveau P. Epidemiology of hepatitis C virus infection in chronic haemodialysis. *Nephrol Dial Transplant* 1996; 11(Suppl 4): 39–41
22. Kidney Disease Improving Global Outcomes. KDIGO clinical practice guidelines for the prevention, diagnosis, evaluation and treatment of hepatitis C in chronic kidney disease. *Kidney Int Suppl* 2008; 73: S1–S99

23. Olmer M, Bouchouareb D, Zandotti C *et al*. Transmission of the hepatitis C virus in an hemodialysis unit: evidence for nosocomial infection. *Clin Nephrol* 1997; 47: 263–270
24. Pereira BJ. Hepatitis C virus infection in dialysis: a continuing problem. *Artif Organs* 1999; 23: 51–60
25. Zeuzem S, Teuber G, Lee JH *et al*. Risk factors for the transmission of hepatitis C. *J Hepatol* 1996; 24: 3–10
26. Pascual J, Teruel JL, Mateos M. Nosocomial transmission of HCV in a haemodialysis unit during 2 years of prospective follow-up. *J Am Soc Nephrol* 1992; 3: f386

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Hypokalaemia: an independent risk factor of enterobacteriaceae peritonitis in CAPD patients

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Abstract

Background. Hypokalaemia is a relatively common complication in uraemic patients undergoing continuous ambulatory peritoneal dialysis (CAPD). The hazards of hypokalaemia are multiple and have been correlated with patient morbidity and mortality. Whether it is associated with increased risk of peritonitis remains to be addressed.

Methods. We retrospectively analysed our CAPD patients who had complicating peritonitis in a 2-year period. The influence of hypokalaemia on the clinical features of peritonitis was assessed. From September 2003 to August 2005, 140 unselected patients undergoing CAPD treatment and followed up in our hospital were recruited for the study. Hypokalaemia was defined as a serum potassium level <3.5 mmol/l. The impact of hypokalaemia on several clinical parameters, including the nutrition status, dialysis adequacy, occurrence of peritonitis and the etiologic pathogens, was analysed.

Results. During the study period, 462 determinations (23.6%) were below quantity <mmol/l. The overall peritonitis rate was 30.6 patient-month per episode (total 64 episodes). The prevalence of peritonitis was significantly higher in patients with hypokalaemia (6.9%) compared to those without hypokalaemia (2.1%, $P < 0.001$). Hypokalaemia was also associated with lower serum albumin ($P < 0.001$), serum phosphate ($P < 0.001$), total serum cholesterol ($P = 0.049$) and normalized protein nitrogen appearance ($P < 0.001$). There was no correlation between serum potassium level and daily PD exchange volume, total Kt/V, urine volume or daily ultrafiltration volume. The peritoneal equilibration test was not significantly different between patients with and without hypokalaemia. When the aetiologic organisms of peritonitis were grouped according to their usual site of colonization, *Enterobacteriaceae* appeared to be much more prevalent than epidermal microorganisms (53.1% versus 18.8%, $P = 0.004$) in the hypokalaemia group. However, this was not the case in patients with normal serum potassium.

Conclusion. CAPD patients with hypokalaemia are associated with a higher prevalence of peritonitis and poor nutritional status. *Enterobacteriaceae* were the predominant organisms causing peritonitis in the group with hypokalaemia. This unique and novel finding implies the translocation of these organisms from intestinal mucosa into the peritoneal cavity. A pathogenic mechanism linking malnutrition and hypokalaemia is also proposed.

Keywords: CAPD; enteric peritonitis; *Enterobacteriaceae*; hypokalaemia; malnutrition

Introduction

Hypokalaemia is a relatively common feature in end-stage renal disease (ESRD) patients undergoing peritoneal dialysis (PD). The prevalence of hypokalaemia is ∼10–36% in PD patients [1–3]. The consequences of hypokalaemia have as yet not been well defined. In a recent study [4], Szeto *et al*. found that hypokalaemia was associated with poor nutritional status, severe comorbidity and a decreased patient survival. In another study [5], hypokalaemia was a poor prognostic sign in peritonitis of PD patients. It is frequently associated with malnutrition and may in turn

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