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Reply

Dear Editor,

Drs. Smith et al. [1] raised several interesting issues regarding our recent publication which analyzed factors associated with aortic stiffness and its change over time in peritoneal dialysis (PD) patients. Their questions are based on their recent study [2] which was elegantly designed to prospectively observe the change of aortic stiffness over a 1-year period and analyzed factors associated with its change from patients with chronic kidney disease (CKD) stages 3 and 4. Their study shared several similarities with ours in the basic study design and follow-up period, although it was based on different CKD stages, ending up with somewhat different conclusion. While keeping in mind that our data was based on Asian PD patients at relatively younger age (mean age 50.4 years), we would like to share our thoughts on Drs. Smith’s points.

First, our study showed no association between baseline fetuin-A level and over-time change of aortic stiffness, while theirs did. We could ascribe such discrepancy to the differences in CKD stage, younger age group, and higher proportion of diabetic patients in our study. We also agree with Dr Smith et al. that the use of time-averaged values in our study could potentially suppress important changes in these variables. However, our data showed that time-averaged values were very similar to the baseline measurements. Nevertheless, the baseline triglycerides (TG) value had no correlation with over-time change of aortic stiffness, while time-averaged TG value had correlation with it (Refer to the supplementary Table 1). Therefore, it needs to be seen in the future whether control of adequate TG level may prevent progression of aortic stiffness.

Second, we employed the same fetuin-A assay kit as did Drs. Smith et al. Therefore, the differences in fetuin-A assay system might not have affected the discrepant results.

Third, another important thing to point out is that our study is based on PD patients, among whom 35% were diabetic. We agree with Drs. Smith et al. that analysis of non-diabetic and diabetic PD patients need to be separately performed. When we reanalyzed our data with non-diabetic patients only, no correlation was observed between baseline fetuin-A value and overtime change of aortic stiffness (r = −0.113, P = 0.495). However, our study cohort was relatively small, comprising 67 PD patients. Separate analysis for non-diabetics might have weakened the statistical power. Besides, whether diabetic or not, PD patients are constantly exposed to a tremendous amount of high glucose PD solutions and advanced glycation end products. Such PD-specific factors and dialysis-specific factors affected the change of aortic stiffness and could have overrided the influence of fetuin-A in our study.

In conclusion, we have shown that mean arterial pressure and time-averaged TG values were associated with overtime change of aortic stiffness, while baseline fetuin-A level was not. Nevertheless, we fully agree with Drs. Smith et al. that it is difficult to draw firm conclusions with respect to the role of fetuin-A or TG. Therefore, as we mentioned in the paper, a larger scaled study over a longer period of time is warranted to investigate the roles of fetuin-A and other biological parameters in the change of aortic stiffness.

Supplementary data

Supplementary data is available online at http://ndt.oxfordjournals.org.

Conflict of interest statement. None declared.

1Department of Internal Medicine, Gachon University of Medicine and Science, Incheon, Korea

2Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea

E-mail: khoh@snu.ac.kr


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Vancomycin catheter lock as a cause of gross overestimation of vancomycin pre-dialysis trough levels

Sir,

Vanholder et al. rightly recommended recently [1,2], in agreement with US guidelines [3], antibiotic lock solutions combined with systemic antibiotics for cases of catheter-related bloodstream infections (CRBSI) in which removal
of the tunnelled cuffed catheter (TCC) is considered impossible or undesirable. The recommended vancomycin concentration in the lock is at least 1000 times higher than the minimal inhibitory concentration of the microorganism involved [1,3], i.e. at least 2.5 mg/mL [2]. In order to ensure effective and safe systemic vancomycin treatment despite variable removal by residual renal function and dialysis sessions, measurement of pre-dialysis trough levels is also recommended [1]. However, if the catheter has been locked with a solution containing vancomycin, and predialysis serum is obtained, as usual, from the catheter lumens prior to the start of a session, the vancomycin serum level may be considerably overestimated.

We report the case of one patient on chronic haemodialysis by a TCC. She received intravenous vancomycin for a CRBSI. The TCC was further locked with a solution of vancomycin (5 mg/mL) diluted in pure heparin (5000 IU/mL) at the end of every haemodialysis (HD) session. Vancomycin pre-dialysis trough levels measured by immunoenzyme assay (Abbott Laboratories, www.abbott.com) in samples taken from the catheter at the beginning of the session were surprisingly high (47 μg/mL). She had received 2 days earlier the first dose of vancomycin (1 g) during the last 60 min of the previous dialysis session. A second blood sample drawn 50 min later from the dialysis circuit showed a level of 10.8 μg/mL.

To confirm our suspicion that this discrepancy in vancomycin levels reflected the residual high concentration in the TCC due to the interdialytic lock, rather than very rapid vancomycin removal by HD, two independent samples were drawn from the TCC and from the dialysis circuit before and 5 min after starting the HD session, respectively, in two additional patients. In both of them, vancomycin trough levels were >100 μg/mL (outside the upper range of the test) and <20 μg/mL (10.5 and 16.6 μg/mL), in samples taken from the catheter and dialysis circuit, respectively.

Our cases are reminiscent of a similar problem observed while monitoring warfarin treatment (by INR measurement) on blood samples drawn directly from HD catheters locked with pure heparin if aspiration of the endoluminal content was incomplete [4]. This problem can easily be avoided by drawing the samples directly from the dialysis circuit a few minutes after the beginning of each session. Clinicians should consider this fact for the routine interpretation of laboratory values and the prescription of drugs such as vancomycin in patients dialysed by a catheter. Otherwise, gross underdosing of systemic vancomycin could seriously increase the risk of treatment failure.

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Department of Nephrology, Cliniques Universitaires St-Luc, Université Catholique de Louvain, Brussels, Belgium
E-mail: laura.labriola@nefr.ucl.ac.be

Delphine Halleux
Laura Labriola
Michel Jadoul


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Reply

We thank Labriola et al. for their useful and meticulous clinical observation and important addition to our European Renal Best Practice (ERBP) recommendations on Catheter-Related Bloodstream Infections (CRBSI) [1,2]. It indeed is very reasonable to expect that when a vancomycin lock has been inserted into a central vein catheter, some of the drug will be left in that catheter before the start of the next dialysis, hence contaminating blood collected for vancomycin blood level estimations. Such measurements are indispensable for guiding adequate antibiotic treatment and avoiding drug toxicity. Also, the solution suggested by Dr Labriola in her letter, namely to collect samples 5 min after the start of dialysis out of the circuit, is well taken and helpful.

Of note, the ERBP recommendations on CRBSI only encourage the application of antibiotic locks with concomitant systemic antibiotic treatment, while their isolated use is formally rejected. The reason for this reluctance for single locks in absence of systemic treatment is the high risk for resistance since the procedure is almost always accompanied by a spillover of unpredictable quantities of the drug into the circulation. The publication by Soriano et al. [3], used in the ERBP recommendations to illustrate the spillover out of the catheter, at the same time quite convincingly demonstrates the problem that jeopardizes plasma level estimations from the same catheter, as not all of the drug is seeping out in between sessions. In the study by Soriano et al. [3], only femoral catheters in ambulatory patients lost almost all of their initial vancomycin contents (2.5 mg/mL) and then only at the tip.

Finally, it is reassuring to learn that the ERBP recommendations are not only read but also implemented and critically considered and that the necessary steps are taken if additional information can be offered to the medical community. This is the perfect fulfillment of the aim that the members of the ERBP Advisory Board set at the start of the ERBP initiative [4].