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Residual renal function assessment with cystatin C

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Abstract Su Jin Kim and coworkers from Korea published an important study on the relationship of residual renal function (RRF) and cystatin in pediatric peritoneal dialysis (PD) patients in this issue of Pediatric Nephrology, both in anuric patients and patients with RRF. Based on a lack of correlation between cystatin C and standard small solute-based dialysis adequacy parameters such as Kt/Vurea but a significant correlation with RRF, the authors concluded that cystatin C may be a good tool to monitor RRF. The editorial reviews the available literature in adults, the different handing between urea and cystatin C, and the determinants of cystatin C clearance in dialysis patients. In adults, cystatin C levels are determined predominantly by RRF, but not exclusively. In anephric hemodialysis and PD patients, there is a correlation with standard weekly Kt/Vurea. Cystatin C levels will also depend on ultrafiltration. Despite these factors that affect cystatin C levels beyond RRF, cystatin C is a useful parameter for monitoring PD patients that may be more closely related to long-term outcomes than small solute adequacy parameters.

Keywords Cystatin C · Residual renal function · Peritoneal dialysis · Hemodialysis · End-stage renal disease · Ultrafiltration

Introduction

Practicing pediatric nephrologists have felt for some time that prescribing more dialysis should improve outcomes. In adults, the result of the National Cooperative Dialysis Study showed a survival benefit with increased dialysis prescription [1]. Disappointingly, no survival benefits with further increase in small solutes clearances once a certain threshold level was reached, which were demonstrated in two major adult trials: the Effects of Increased Peritoneal Clearances on Mortality Rates in Peritoneal Dialysis: ADEMEX, a Prospective, Randomized, Controlled Trial (ADEMEX) and the Effect of Dialysis Dose and Membrane Flux in Maintenance Hemodialysis (HEMA) studies [2, 3]. However, residual renal clearance as the major predictor of survival in dialysis patients (both hemodialysis and peritoneal dialysis) was demonstrated in carefully conducted re-analyses of both studies [4, 5]. As a result, it is important to monitor and to preserve residual renal function (RRF) in dialysis patients, as it is a strong predictor for patient survival in this adult population and presumably also in children. The Kidney Disease Outcomes Quality Improvement (KDOQI) clinical practice guideline recommends monitoring of RRF periodically in patients with end-stage renal disease [6].

As pointed out in the study from Su Jin Kim and coworkers from Korea [7] in this issue of Pediatric Nephrology, gold-standard measurements of RRF using inulin clearance or nuclear medicine techniques such as 99mTc DTPA or 51Cr EDTA clearance studies are cumbersome and invasive.
than in high-flux hemodialysis patients [12]. Beta-2 microglobulin, albeit less in PD patients affected by dialytic clearance just like the low-molecular-weight protein (13.2 kDa) produced at a constant rate, may be that the cystatin C level and single pool Kt/Vurea in a dialysis patient is somewhat analogous to the hemoglobin A1C level in its relationship to plasma glucose value in the diabetic. In other words, the marker may reflect cumulative middle molecule clearance over time. The stability may be useful in that a given cystatin C level may allow the rough estimation of both dialytic and residual renal functional clearance, providing the total standard weekly Kt/Vurea is known.

Studies in children remain scarce. With this context, we read the Korean study on pediatric PD patients [7] with great interest. In this study, nine patients who were anuric did not demonstrate any correlation between the peritoneal Kt/Vurea or the peritoneal weekly creatinine clearance. The total Kt/Vurea was within a very narrow range in this group (1.8–2.5). By contrast, the total weekly creatinine clearance was 49.8 (range 36.2–66.3) L/week/1.73 m², suggesting a much wider range of dialysis prescriptions than indicated by the total Kt/Vurea. For all patients, 24-h urine and dialysate collections were performed at home, but in the anuric group no collections were performed. Data on the proportion of the nine patients who had both native kidneys removed were not provided. By contrast, in the patients with RRF, there was a significant negative correlation between the cystatin C concentrations and the renal Kt/Vurea ($r=-0.793$, $p<0.001$). The authors concluded that serum cystatin C could be an appropriate marker for RRF, independent of total and peritoneal Kt/Vurea.

Based on their observations, this conclusion is reasonable. However, it is more likely that cystatin C levels are somewhat affected by dialysis dose, as the determinants of cystatin C concentrations during dialysis remain to be fully established.
It is known that the intra-patient variability of cystatin C levels is less than that of creatinine in children with CKD [15]. In a recent study on 15 functionally anephric patients who underwent cystatin C profiling during high-flux hemodialysis, we established that cystatin C reduction ratio depended on normalized blood liters processed and fluid removal during hemodialysis. Those two parameters explained 81% of the cystatin C variance. As outlined above, cystatin C values will be affected by volume status because of the smaller volume of distribution of cystatin C. In contrast to creatinine, cystatin C variance is less than that of creatinine in children with CKD [15]. In a recent study on 15 functionally anephric patients who underwent cystatin C profiling during high-flux hemodialysis, we established that cystatin C reduction ratio depended on normalized blood liters processed and fluid removal during hemodialysis. Those two parameters explained 81% of the cystatin C variance. As outlined above, cystatin C values will be affected by volume status because of the smaller volume of distribution of cystatin C. In contrast to creatinine, cystatin C variance is less than that of creatinine in children with CKD [15]. In a recent study on 15 functionally anephric patients who underwent cystatin C profiling during high-flux hemodialysis, we established that cystatin C reduction ratio depended on normalized blood liters processed and fluid removal during hemodialysis. Those two parameters explained 81% of the cystatin C variance. As outlined above, cystatin C values will be affected by volume status because of the smaller volume of distribution of cystatin C. In contrast to creatinine, cystatin C variance is less than that of creatinine in children with CKD [15]. In a recent study on 15 functionally anephric patients who underwent cystatin C profiling during high-flux hemodialysis, we established that cystatin C reduction ratio depended on normalized blood liters processed and fluid removal during hemodialysis. Those two parameters explained 81% of the cystatin C variance. As outlined above, cystatin C values will be affected by volume status because of the smaller volume of distribution of cystatin C. In contrast to creatinine, cystatin C variance is less than that of creatinine in children with CKD [15]. In a recent study on 15 functionally anephric patients who underwent cystatin C profiling during high-flux hemodialysis, we established that cystatin C reduction ratio depended on normalized blood liters processed and fluid removal during hemodialysis. Those two parameters explained 81% of the cystatin C variance. As outlined above, cystatin C values will be affected by volume status because of the smaller volume of distribution of cystatin C. In contrast to creatinine, cystatin C variance is less than that of creatinine in children with CKD [15]. In a recent study on 15 functionally anephric patients who underwent cystatin C profiling during high-flux hemodialysis, we established that cystatin C reduction ratio depended on normalized blood liters processed and fluid removal during hemodialysis. Those two parameters explained 81% of the cystatin C variance. As outlined above, cystatin C values will be affected by volume status because of the smaller volume of distribution of cystatin C. In contrast to creatinine, cystatin C variance is less than that of creatinine in children with CKD [15]. In a recent study on 15 functionally anephric patients who underwent cystatin C profiling during high-flux hemodialysis, we established that cystatin C reduction ratio depended on normalized blood liters processed and fluid removal during hemodialysis. Those two parameters explained 81% of the cystatin C variance. As outlined above, cystatin C values will be affected by volume status because of the smaller volume of distribution of cystatin C. In contrast to creatinine, cystatin C variance is less than that of creatinine in children with CKD [15]. In a recent study on 15 functionally anephric patients who underwent cystatin C profiling during high-flux hemodialysis, we established that cystatin C reduction ratio depended on normalized blood liters processed and fluid removal during hemodialysis. Those two parameters explained 81% of the cystatin C variance. As outlined above, cystatin C values will be affected by volume status because of the smaller volume of distribution of cystatin C. In contrast to creatinine, cystatin C variance is less than that of creatinine in children with CKD [15].

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