Oral Diseases (2008) 14, 8–9. doi:10.1111/j.1601-0825.2007.01431.x

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COMMENTARY

Chronic inflammation in dialysis patients – periodontal disease, the new kid on the block

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Despite significant technical advances, annual mortality in chronic dialysis patients is as high as 20% with cardiovascular disease and infection being the leading causes of death. Chronic inflammation is highly prevalent in dialysis patients and chronic kidney disease (CKD) *per se* is a pro-inflammatory state (Zimmermann *et al*, 1999; Kaysen, 2001). Impaired renal function results in a reduced clearance of cytokines, an accumulation of advanced glycosylation end products (AGEs), and an impaired immune response to infections. Dialysis patients frequently experience the breakdown of important anatomical barriers by indwelling central venous dialysis catheters, repeated puncture of arterio-venous fistulas, and vascular grafts. In addition, patients are exposed to the surface of foreign materials such as dialyzer membranes and blood lines, causing problems of biocompatibility. Poor bacteriological water quality with high endotoxin levels may result in an inflammatory response (Rahmati *et al*, 2004). Dependent on the dialysis technology used, backfiltration may be a relevant problem, resulting in the transfer of endotoxins to the patient. In CKD patients treated with peritoneal dialysis, catheter-related peritonitis and bio-incompatible dialysate are important sources of inflammation. Transfer of endotoxins and bacteria from the gut to the systemic circulation has been proposed as another potential source of inflammation (Kotanko *et al*, 2006).

Recently, periodontal disease (PDD) has been recognized as another potential source of chronic inflammation in CKD patients. The current state of PDD in CKD is comprehensively reviewed by RG Craig in this issue of *The Journal*. Several strands of epidemiological evidence indicate that the prevalence of PDD is increased in CKD patients (Naugle *et al*, 1998; Bots *et al*, 2006). A recent report of 253 end-stage renal disease (ESRD) patients on hemodialysis maintenance therapy from Taiwan found age, smoking status, diabetes, dialysis vintage, decreased serum albumin, blood urea nitrogen, and increased C-reactive protein (CRP) values associated with increasing severity of periodontitis. When the data were analyzed by multiple regression analysis, age, diabetes, smoking, albumin, and dialysis vintage were found independently associated with periodontitis severity (Chen *et al*, 2006). In a cohort of 154 chronic hemodialysis patients at two locations, North Carolina and New York City, a significant association between low serum albumin levels and severity of PDD was shown (Kshirsagar *et al*, 2007). It is conceivable that the uremic milieu as such contributes to the high prevalence of PDD in CKD, although the results of observational studies are not clear on that issue.

Two recent studies in non-renal patients reported that effective PDD therapy may decrease systemic markers of inflammation such as interleukin-6 (IL-6) and CRP. These effects were the greatest for those subjects with the most favorable response to periodontal therapy, as measured by clinical indices, and remained significant after correction for age, gender, body mass index, and smoking status (D'Aiuto *et al*, 2004, 2005). Most importantly, it was demonstrated in a recent landmark study that not only surrogate markers but also indicators of endothelial function can be improved with intensive periodontal treatment (Tonetti *et al*, 2007). This study is particularly important in renal patients, as in this group endothelial dysfunction is highly prevalent (Ochodnicky *et al*, 2006).

Although periodontal disease is moving into the focus of nephrologists caring for CKD patients, prevention, diagnosis and treatment of PDD have not yet received prominent attention they deserve, in the major national and international CKD guidelines. Clearly, a multidisciplinary approach is mandatory in the generally multimorbid CKD patients and investigations in CKD should include an assessment of oral health. Studies relating PDD to hard endpoints are very much needed but outcome studies are notoriously affected by small patient numbers. Taken together, published studies on PDD in CKD patients comprise data on more than 500 patients. Thus, it may be rewarding to form a consortium encompassing all the major groups working in that field to share PDD data and to relate the severity

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Received 15 September 2006; revised 12 December 2006; accepted 20 January 2007

of PDD to clinical outcomes, most importantly cardiovascular morbidity and mortality. Moreover, only few data on the dynamics of PDD in CKD patients are available and studies of the natural history of PDD in renal patients are needed. Most importantly, intervention studies with evidence based intensive periodontal treatment protocols are necessary in the CKD population. Eventually, PDD treatment may prove to add further to our armamentarium combating chronic inflammation in CKD patients.

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