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Acute and chronic influence of hemodialysis according to the membrane used on phagocytic function of neutrophils and monocytes and pro-inflammatory cytokines production in chronic renal failure patients

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Abstract

This work evaluated the phagocytic capacity of monocytes and neutrophils, and tumor necrosis factor-α, interleukin 6, 1 and 8 serum levels in chronic renal failure patients under peritoneal dialysis and hemodialysis treatment, compared with chronic renal failure patients without dialysis treatment and healthy individuals, in order to contribute to a better understanding of the action of these therapies on the evolution of chronic renal failure patients. All patients with chronic renal failure (under dialysis or not) showed decreased phagocytic capacity of neutrophils and monocytes. All those in hemodialysis (cellulose acetate or polysulfone membranes) showed a decreased phagocytic capacity. The phagocytic index for neutrophil was 13 times lower than that of the control group for both membranes, whereas for monocytes, only those using polysulfone membrane showed a significant decrease of 4.9 times in phagocytic capacity. There was an acute stimulation of the phagocytosis by neutrophils after a single session of dialysis with both types of membrane, while only cellulose acetate membrane decreased the phagocytic index of monocytes after the hemodialysis session. Patients using cellulose acetate showed a chronic increase in tumor necrosis factor-α serum levels, while those using polysulfone showed a chronic increase in interleukin 6. After a single hemodialysis procedure, no acute effect of the treatment on tumor necrosis factor-α

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and interleukin 6 levels was identified. The decreased phagocytic function of neutrophils and monocytes may account for the high levels of susceptibility of chronic renal failure patients to infections with pyogenic bacteria and tuberculosis. Furthermore, inflammatory activity may occur with both types of membrane studied, suggesting that it will be useful for these patients to evaluate some anti-inflammatory or anti-cytokine therapies against tumor necrosis factor-α and interleukin 6, in order to avoid cardiovascular complication.

Keywords: Phagocytosis; Neutrophils; Monocytes; Chronic renal failure; CAPD; Hemodialysis; Interleukin 1 (IL-1); Interleukin 6 (IL-6); Interleukin 8 (IL-8); Tumor necrosis factor-α (TNF-α)

Introduction

Infections and cardiovascular diseases remain the leading causes of complications and death in end-stage renal disease patients (Hörl, 1999; Kaysen, 2001; Minnaganti and Cunha, 2001), and it is still not clear how to prevent these complications. This is due in part to the small understanding of its pathophysiology, their relationship with background renal disease, and the currently available therapy. Infections in these patients are mainly caused by pathogens that depend on phagocyte functions for blood and tissue clearance (Greenberg and Silverstein, 1993; Khan and Catto, 1993). Chronic inflammation also appears to be highly prevalent in these patients and is strongly related to clinical outcome (Owen and Lowrie, 1998; Caglar et al., 2002), enhancing mainly cardiovascular risk and mortality (Zimmermann et al., 1999).

Immunodeficiencies and chronic inflammation in chronic renal failure patients (CRFP) have been related to multiple factors, including underlying uremic condition, increased cytokine production, type of dialysis treatment, and certain co-morbid conditions, such as malnutrition, atherosclerosis, and chronic infections (Kimmel et al., 1998; Kalantar-Zadeh and Kopple, 2001; Caglar et al., 2002) often associated in these patients, and that may influence the immune system functions. The hemodialysis procedure has also been suggested as a potential source of inflammatory stimuli (Caglar et al., 2002).

The impairment of humoral and cellular immunity, phagocyte functions and deregulated cytokine productions in chronic renal failure patients have been considered to concur to increased susceptibility to infectious diseases, high morbidity and mortality and decreased vaccine responses (Kimmel et al., 1998; Gastaldello et al., 2000; Pesanti, 2001). A chronic inflammatory state due to the enhanced production of cytokines, as tumor necrosis factor-α (TNF-α), and interleukines 1 (IL-1), 6 and 8, has been related to blood cell stimulation by using non-biocompatible membrane during hemodialysis treatment (Macdonald et al., 1993; Ryan et al., 1993; Engelberts et al., 1994; McKenna et al., 1994; Girndt et al., 1995; Memoli et al., 2002; Santos et al., 2003). However, the acute and chronic influence of the type of treatment and the type of membrane on phagocyte functions and cytokine production still remains unclear.

The cellular sources of inflammatory cytokines enhanced in chronic renal failure patients are mainly neutrophils and monocytes, and the major function of these cells and the initial stimuli to production of cytokines is phagocytosis (Cassatela et al., 1997). The evaluation of phagocytic function of neutrophils of chronic renal failure patients has shown conflicting results (Lewis and van Epps, 1987; Vanholder et al., 1993; Cohen et al., 1997; Anding et al., 2003; Rao et al., 2004). Some investigators have found phagocytosis to be normal, whereas others have shown deficiencies. Meanwhile, phagocytosis by