

HBV Vaccination in the Patient with Chronic Renal Disease

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Abstract

Patients undergoing hemodialysis often present with a reduced response to anti-hepatitis B virus (anti-HBV) vaccination. The soluble form of CD40 (sCD40) is elevated in hemodialysis patients and this has been shown to correlate with lack of response to anti-HBV vaccination. Due to its high molecular weight, conventional dialyzers cannot clear sCD40. Dialysis membranes in polymethylmethacrylate (PMMA) can reduce the levels of sCD40. We have used PMMA membranes in patients who were non-responders to anti-HBV vaccination (anti-HB antibody level <10 UI/L after 2 vaccinations circles). Interestingly, we found that significantly more patients in the PMMA group were able to mount a response to vaccination, compared to the control group.

Keywords: Hepatitis B vaccination; Hemodialysis; Immunodepression; PMMA; sCD40

Short Communication

50% of patients with chronic kidney disease undergoing hemodialysis, present an alteration in the immune response that determines a significant reduction of the response to vaccination for hepatitis B. The mechanisms that are at the base of these profound alterations of the immune system are not so clear today; the phenomena of bio-incompatibility of dialysis membranes and the accumulation of some uremic toxins can constitute two important pathogenic phases in the development of immunological dysfunction in dialysis. It also plays a role the different dysregulation types of immune cells, in addition to CD40 receptor, expressed on the surface of B lymphocytes, which interacts with the ligand CD40 (CD40L), expressed on T lymphocytes, on the "Natural Killer" (NK) lymphocytes and on the basophils. The CD40/CD40L complex modulates the proliferation of B lymphocytes, the expression of interleukin 12 (IL-12) and activation of T lymphocytes [1-3]. The soluble form of the CD40 (sCD40), goes to interact in the formation of the complex CD40 and CD40L thus inhibiting activation of lymphocytes and consequent production of immunoglobulins, necessary for the development of the antibody titer. Given that patients on hemodialysis have higher levels of sCD40, in comparison to healthy subjects, this glycoprotein reduces the production of immunoglobulins and activation of T lymphocytes with an immuno-depressing effect. The sCD40, produced by B lymphocytes, exists in the dimeric and oligomeric form arriving at molecular weights of 50 and 150 kDa [4-6]. Precisely because of the high molecular weight and of its size, it cannot be eliminated by hemodialysis based on standard filtration-purification mechanisms: diffusive and/or convective mechanisms. So to remove high and medium weight molecules, "not dialysable", it is necessary to consider a third mechanism for their effective purification, i.e. Adsorption. Dialysis membranes in polymethylmethacrylate (PMMA) demonstrated their ability to effectively reduce serum levels of sCD40 and the first clinical evidences had suggested that the decrease in serum was associated with a considerable increase of the percentage of

seroconversion to vaccination for hepatitis B in chronic uremic patients. Subsequently further studies confirmed that the reduction of sCD40 levels, during hemodialysis treatment was related with an improvement in the percentage response to anti-HBV vaccination. So hemodialysis performed with PMMA membranes has been shown to strengthen the response to hepatitis B vaccination and to maintain that effect over time, even later at the suspension of PMMA membrane use for the dialysis session. In a study conducted by us recently, the 47% of hemodialysis patients treated with PMMA membranes has been able to develop a protective immune response against HBV (anti-HB antibody level >10 UI/L), while only 13% of patients in the control group, dialyzed with others conventional membranes, has developed a protective antibody response [7-9]. The PMMA membrane is the only one able to adsorb significantly, molecules of medium and heavy weight, including sCD40. The adsorption action is effective moreover for bound uremic toxins to high molecular weight proteins (PBTU) involved in other relevant comorbidities typical of the uremic patient as uremic pruritus, anemia and amyloidosis [10]. A hemodialysis treatment that of for self is born to be a treatment for purification of the uremic toxic, can in reality have a decisive action in the apheresis of additional molecules. It is configured then the concept of a dialysis-apheresis which has certain characteristics and precise indications, for a therapy proposal of personalized hemodialysis. We believe that there is a logical basis for the use of PMMA membrane in order to maintain a better immune competence, during and after every vaccination, and for strengthening the immune system of hemodialysis patients. Therefore, in conclusion, PMMA membranes should become the first choice for immunosuppressed patients, as well as for patients awaiting transplantation of kidney for which one a good response to anti-HBV is mandatory [8,9]. Looking at recent discoveries, removal of the CD40 could play, in next future, a role in patients in hemodialysis, improving endothelial function and preventing some dialysis comorbidities (as, for example, the coronary and cardiovascular diseases [11-13]. In this scenario, the dialytic membrane is in fact a fundamental element in the prescription of the hemodialysis therapy.

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