SciMedCentral

Journal of Chronic Diseases and Management

Short Notes

Adsorptive Hemodialysis by Polymethylmethacrylate (PMMA): an update on Hepatitis B Vaccination Immunoresponce

Ennio Duranti and Diletta Duranti*

Department of Nephrology, Dialysis Hospital of Arezzo, Italy

***Corresponding author**
Diletta Duranti, Department of Nephrology, Dialysis Hospital of Arezzo, Italy, Email: enniodil@libero.it

Submitted: 06 September 2016

Accepted: 18 November 2016

Published: 20 November 2016

Patients with end stage renal disease (ESRD), undergoing hemodialysis, present with an alteration in immune response to anti-HBV vaccination [1]. Immunodeficiency in ESRD patients is caused by a dysregulation of various types of immune cells. The receptor CD40, which is expressed on the surface of B-cells, interacts with CD40 ligand (CD40L), which is expressed on T cells, NK cells and basophils [2]. The CD40/CD40L complex modulates the proliferation of B-cells, expression of IL-12 and activation of T-cells [2]. The soluble form of CD40, sCD40, serves to regulate the interaction between CD40 and CD40L and thereby causing a reduction in lymphocyte activation and Ig production. Up to 50% of patients with end-stage renal disease (ESRD) undergoing dialysis therapy present with a reduced response to anti-hepatitis B virus (anti-HBV) vaccination [1]. Patients on hemodialysis have been shown to have higher levels of soluble CD40 (sCD40), compared to healthy subjects [9,3]. Soluble CD40 is produced by B-cells by alternative splicing of the CD40 gene and by proteolytic cleavage of membrane-bound CD40 [4]. It has been shown experimentally that sCD40 reduces immunoglobulin (Ig) production and T cell activation and this molecule has therefore been hypothesized to have an immunodepressant effect [5]. Soluble CD40 is a glycoprotein and exists as dimeric and higher oligomeric forms of 50 and 150 kDa [6]. Due to its high molecular weight, sCD40 cannot be removed effectively by standard diffusive or convective dialysis therapy.

Dialysis membranes in polymethylmethacrylate (PMMA) have been shown to effectively reduce the levels of sCD40 [7]. Reduction of sCD40 levels by hemodialysis was shown to correlate with an improvement in the response rate to anti-HBV vaccination [7]. We have shown previously, that dialysis with PMMA strengthens the response to anti- HBV vaccination and that this lasted effectively over time, even after discontinuation of PMMA [8-9]. 47 % of patients who were dialyzed with PMMA membranes were able to develop a protective immune response against HBV (anti-HBs antibody levels > 10UI/L), whereas only 13% of control group (13%) who were dialysed with other membranes, developed a protective response.

The sCD40 level was found to vary considerably from patient to patient. Even if in the small patient population presented in our studies, we found no significant difference between the PMMA group and the control group. After the second month of dialysis we observed a tendency towards a decrease in the PMMA group, although this was not significant. When the data from patients undergoing dialysis with PMMA membranes were divided into responders and non-responders, the decrease in serum sCD40 levels after the second month was even more noticeable in the responder group.

A possible explanation to the noticed drop in sCD40 levels after the second month of dialysis could be its removal by the PMMA membrane. This drop would be enough to generate Ig and thereby to mount a protective response against HBV. However, the removal of sCD40 would also cause an increase in lymphocyte activation by CD40/CD40L, leading to proliferation of B-cells and thereby an increase in sCD40 expression, thus explaining the subsequent increase in sCD40 levels after 3 months of dialysis. Further studies are required to fully elucidate the mechanism of sCD40 regulation.

In our works [8,9] we underlined that PMMA is the only membrane able to absorb medium and large molecules, including sCD40 and high-molecular weight protein bound uremic toxins (PBUTs) involved in other major comorbidities such as uremic pruritus, anemia, and amyloidosisecc. In addition to altered immune-response.

In fact the synthetic membranes normally used in the convection therapy are usually asymmetrical (ie high – flux polysulphone) : although they are 30 micron thick only one micron is responsible for the separation and the remaining thickness has exclusively structural functions . Such membranes can be represented as 2-D membranes able to separate solutes by means of convection and diffusion only. On the contrary the PMMA membranes are characterized by symmetrical structures with larger, longer and winding pores that together with ionic treatment of the inner surface may enhance the adsorptive mechanism. For example, PMMA membranes remove beta – 2-microglobulin and IL-6 by adsorption, whereas high – flux polysulphone membranes by filtration [10,11].

Therefore, following this line of thought super-flux dialyzers

with high convection and adsorption such as the PMMA-BK series could be widely used in clinical situations where large quantities of High Molecular Weight Toxins (HMWT) or PBUTs are produced including septic patients with acute renal failure in which it is necessary to control at the same time uremia, fluid status and the removal of cytokines [12].

We wondered whether there could be a rationale for an occasional use of PMMA in order to maintain better immune competence during and after every vaccination and also strengthen the immune system of dialyzed patients.

So, in conclusion, PMMA membranes should become the first choice treatment for immune depressed patients, as well as for patients awaiting kidney transplantation in which a good response to anti- HBv is recommended. Looking at recent findings sCD40 removal could play, in the near future, a role in HD patients improving endothelial function and preventing some dialysis co morbidities (i.e. artery coronary disease) [13].

In addition we should resolve the important doubt whether continuous or periodic use of PMMA (i.e. one or two sessions per month) could improve immune dysfunction in all dialysis patients who seem to be particularly immune compromised. Further studies are needed to clarify the possible role of periodical – intermittent dialysis sessions with PMMA adsorptive membranes in the removal of HMWT that are produced daily.

REFERENCES

1. Eleftheriadis T, Antoniadi G, Liakopoulos V, Kartsios C, Stefanidis I. Disturbances of acquired immunity in hemodialysis patients. Semin Dial. 2007; 20: 440-451.
2. Van Kooten C, Banchereau J. CD40-CD40 ligand. J Leukoc Biol. 2000; 67: 2-17.
3. Schwabe RF, Engelmann H, Hess S, Fricke H. Soluble CD40 in the serum of healthy donors, patients with chronic renal failure, haemodialysis and chronic ambulatory peritoneal dialysis (CAPD) patients. Clin Exp Immunol. 1999; 117: 153-158.
4. Contin C, Pitard V, Itai T, Nagata S, Moreau JF, Déchanet-Merville J, et al. Membrane-anchored CD40 is processed by the tumor necrosis factor-alpha-converting enzyme. Implications for CD40 signaling. J Biol Chem. 2003a; 278: 32801-32809.
5. Fanslow WC, Anderson DM, Grabstein KH, Clark EA, Cosman D, Armitage RJ. Soluble forms of CD40 inhibit biologic responses of human B cells. J Immunol. 1992; 149: 655-660.
6. van Kooten C, Gaillard C, Galizzi JP, Hermann P, Fossiez F, Banchereau J, et al. B cells regulate expression of CD40 ligand on activated T cells by lowering the mRNA level and through the release of soluble CD40. Eur J Immunol. 1994; 24: 787-792.
7. Contin-Bordes C, Lacraz A, Precigout V. Potential role of the soluble form of CD40 in deficient immunological function of dialysis patients: new findings of its amelioration using polymethylmethacrylate (PMMA) membrane. NDT Plus. 2010; 3: 20-27.
8. Duranti E, Duranti D. Polymethylmethacrylate strengthens antibody response in hemodialysis patients not responding to hepatitis B vaccine: preliminary data. Minerva medica. 2011; 102: 469-474.
9. Ralli Chiara1, Imperiali Patrizio1, Gabbrilelli Claudio, Conti Paolo, Lombardi Marco, Sidoti Antonino, et al. Hemodialysis with Polymethylmethacrylate Restores the Response to Hepatitis B Vaccination in Chronic Dialysis Patients: Hypothesized Mechanism of Action. Arch Renal Dis Manag. 2016; 2: 1-4.
10. Campistol JM, Torregrosa JV, Ponz E, Fenollosa B. Beta-2-microglobulin removal by hemodialysis with polymethylmethacrylate membranes. Contrib Nephrol. 1999; 125: 76-85.
11. Kawanishi H. Intensive and critical care medicine. 2000; 12: 7-8.
12. Pavlak K, Misliwiec M, Pavlak D. Hepatitis C virus sieropositivity and TNF superfamily receptors: sCD40, sFAS the new putative determinants of endothelial dysfunction in hemodialysis patients. Thromb Res. 2010; 126: 393-398.
13. Contin C, Pitard V, Delmas Y, Pelletier N, Defrance T, Moreau JF, et al. Potential role of soluble CD40 in the humoral immune response impairment of uraemic patients. Immunol. 2003; 110: 131-140.

Cite this article

Duranti E, Duranti D (2016) Adsorptive Hemodialysis by Polymethylmethacrylate (PMMA): an update on Hepatitis B Vaccination Immunoresponce. J Chronic Dis Manag 1(1): 1005.