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Javier Naranjo Muñoz[a,*], Ana Garcia Garcia-Doncel[a], María Elisa Montero Escobar[a], Florentino Villanego Fernandez[a], Irene Millán Ortega[b], Manuel Ceballos Guerrero[a]

[a] *Servicio de Nefrología, Hospital Universitario Puerta del Mar, Cádiz, Spain*
[b] *Servicio de Anatomía Patológica, Hospital Universitario Puerta del Mar, Cádiz, Spain*

[*] *Corresponding author.*
E-mail address: javiernaranjo08@gmail.com (J. Naranjo Muñoz).

https://doi.org/10.1016/j.nefroe.2019.01.008

Does vitamin D influence hepatitis B surface antibodies in non-vaccinated patients on haemodialysis?☆

¿Influye la vitamina D en los anticuerpos de superficie de la hepatitis B en pacientes no vacunados en hemodiálisis?

The prevention of hepatitis B virus infection is one of the main goals in haemodialysis (HD) centres. Vaccination is recommended, but only 50%–85% of patients develop antibodies (HBsAb) but in less quantities and shorter permanence over time.[1–3] This response is worse in patients with reduced renal function, older and malnourished patients[1,2] or those with vitamin D (VD) deficiency[3] which is common in dialysis patients.[3,4] We are aware of seasonal variations in VD, but variations of HBsAb titres have not hitherto been described.

In the HDHD NephroCare Fresenius Medical Care centre (FMC)-Reus, we conducted a retrospective observational study with the aim of assessing the relationship between VD and HBsAb. We divided the study into 2 annual semesters, terminating in April and October, when most of the laboratory determinations were obtained and which, in turn, coincided with the lowest and highest annual sun exposure. Nonvaccinated patients were included, before or during their stay in the centre, had at least 1 determination of HBsAb in each consecutive period, and one determination of 25-hydroxycholecalciferol. Vaccinated patients were excluded, in addition to those with laboratory results with non-numerical values and patients on holiday. The data was obtained over 40 months, from July 2014 to October 2017.

We obtained results in 20 patients: 90 determinations (between 2 and 9, an average of 5 determinations per patient). HBsAb levels were between 8 and 635 UI/ml, with a mean value of 151 ± 161 UI/ml. Ten patients (50%) had mean values higher than 100 UI/l. Due to the limited size of the study population, the values of the monthly medians were influenced by the entry of patients with different antibody levels. For example, the entry in November of one patient with levels of 566 UI/ml increased the mean estimated for that month. The values were grouped by semesters regardless of the year in which they were obtained, observing an insignificant increase of levels in the warm semester (Table 1). The 25-hydroxycholecalciferol results were obtained from 94 determinations (between 2 and 8, an average of 5 determinations per patient). The values of 25-hydroxycholecalciferol were significant higher during the warm semester (Table 1).

The action of VD against infections earned Dr Ryberg Finsen the Noble Prize in 1903.[5] We now know that VD deficiency is associated with an increase in the rate and poor prognosis of infectious diseases[3,4,6,7] and absence of response to treatment of viral hepatitis with more chronic liver disease and hepatocellular carcinoma.[8] We also know that sun exposure is associated with the viral response to treatment of hepatitis C,[9] and that VD status is related to the persistence of HBsAb 20 years after primary vaccination.[7] The supplementation with VD in dialysis patients reduces respiratory infections and peritonitis in peritoneal dialysis patients.[4]

Most immune cells produce CYP27B1, express VD receptors (VDR), and are regulated by VD via the endocrine, autocrine

DOI of original article:
https://doi.org/10.1016/j.nefro.2018.11.004.
☆ Please cite this article as: Arruche M, Varas J, Rincón A, Ramos R, Moreno D, Cabré C. ¿Influye la vitamina D en los anticuerpos de superficie de la hepatitis B en pacientes no vacunados en hemodiálisis? Nefrologia. 2019;39:442–443.

Table 1 – Descriptions of the analysed cohort.

		Complete cohort	Cold semester	Warm semester	p
HBsAb (UI/ml)	Mean (IQR)	81.23 (40.55–200.34)	79.79 (33.93–271.09)	82.91 (43.12–156.53)	0.681
	Minimum	8.24	12.06	8.24	
	Maximum	635	566.1	635	
VD (ng/ml)	Mean (IQR)	12.90 (10.04–19.92)	11.6 (8.28–14.45)	19 (12.45–27.80)	<0.001
	Minimum	5.4	5.4	6.1	
	Maximum	69.8	43.7	69.8	

HBsAb: hepatitis B surface antibody; IQR: interquartile range; VD: vitamin D.
The *p*-value shown compares the means between the warm and cold semesters using the Mann–Whitney *U* test.

and paracrine systems.[3,6,10] VD induces antibacterial products such as cathelicidin,[3,4] inhibits production of interferon gamma and interleukin-2 (IL-2), and stimulates production of IL-4, IL-5, and IL-10 by Th_2 cells.[6,10] This, together with the presence of VDR in both dendritic cells[6] and T and B lymphocytes, including memory cells,[7] suggests that VD supplementation would not only improve the innate immune response to vaccination but also the intensity of the systemic humoral immune response.[6,7] The disparate results obtained in intervention studies with VD in immunity may not be due to serum levels of VD, but to methodological and pharmacological differences (of the vaccine and VD) and the different polymorphisms of the VDR and the VD transporter protein, with perhaps a better response in deficient patients with VD_3 in daily or weekly doses.[1,6,7,10]

In chronic kidney disease (CKD), poor response to vaccination is mainly due to a defect of helper T cells function,[1,2] which is also the case in VD deficiency, which is widely present in patients on haemodialysis. This could be the connection point between immune response and VD in HD.

In this study, we observed the seasonal variation of HBsAb, supporting the idea of its direct relationship with sun exposure and VD. However, we were unable to demonstrate a statistical difference, due to the small sample size and the wide range of HBsAb titres. Larger studies would be necessary to confirm the role of sun exposure and VD as adjuvants in the immune response in HD patients.

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Mercedes Arruche[a,*], Javier Varas[b], Abraham Rincón[b], Rosa Ramos[b], Darío Moreno[c], Carmen Cabré[d]

[a] *Fresenius Medical Care, Reus, Spain*
[b] *Fresenius Medical Care, Madrid, Spain*
[c] *Fresenius Medical Care, Aranda de Duero, Spain*
[d] *Nefrología-Hemodiálisis, Clínica Fuensanta, Madrid, Spain*

[*] *Corresponding author.*
E-mail address: marrucheh@senefro.org (M. Arruche).

https://doi.org/10.1016/j.nefroe.2018.11.016