

9. Ardissino G, Tetsa S, Possenti I, Tel F, Paglialonga F, Salardi S, et al. Discontinuation of eculizumab maintenance treatment for atypical hemolytic uremic syndrome: a report of 10 cases. *Am J Kidney Dis.* 2014;64:633-7, <http://dx.doi.org/10.1053/j.ajkd.2014.01.434>.
10. Fakhouri F, Fila M, Provot F, Delmas Y, Barbet C, Chatelet V, et al. Pathogenic variants in complement genes and risk of atypical hemolytic uremic syndrome relapse after eculizumab discontinuation. *Clin J Am Soc Nephrol.* 2017;12:50-9, <http://dx.doi.org/10.2215/CJN.06440616>.

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<https://doi.org/10.1016/j.nefro.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.<sup>1-3</sup> This response is worse in patients with reduced renal function, older and malnourished patients<sup>1,2</sup> or those with vitamin D (VD) deficiency<sup>3</sup> which is common in dialysis patients.<sup>3,4</sup> 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  $151 \pm 161$  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.<sup>5</sup> We now know that VD deficiency is associated with an increase in the rate and poor prognosis of infectious diseases<sup>3,4,6,7</sup> and absence of response to treatment of viral hepatitis with more chronic liver disease and hepatocellular carcinoma.<sup>8</sup> We also know that sun exposure is associated with the viral response to treatment of hepatitis C,<sup>9</sup> and that VD status is related to the persistence of HBsAb 20 years after primary vaccination.<sup>7</sup> The supplementation with VD in dialysis patients reduces respiratory infections and peritonitis in peritoneal dialysis patients.<sup>4</sup>

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? *Nefrología.* 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.<sup>3,6,10</sup> VD induces antibacterial products such as cathelicidin,<sup>3,4</sup> inhibits production of interferon gamma and interleukin-2 (IL-2), and stimulates production of IL-4, IL-5, and IL-10 by Th<sub>2</sub> cells.<sup>6,10</sup> This, together with the presence of VDR in both dendritic cells<sup>6</sup> and T and B lymphocytes, including memory cells,<sup>7</sup> suggests that VD supplementation would not only improve the innate immune response to vaccination but also the intensity of the systemic humoral immune response.<sup>6,7</sup> 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<sub>3</sub> in daily or weekly doses.<sup>1,6,7,10</sup>

In chronic kidney disease (CKD), poor response to vaccination is mainly due to a defect of helper T cells function,<sup>1,2</sup> 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.

## REFERENCES

- Pin M, Compte MT, Angelet P, Gallego C, Gutierrez C, Martínez-Vea A. Evaluación a largo plazo de la respuesta inmunológica a la vacuna de la hepatitis B en 136 pacientes en hemodiálisis. *Nefrología*. 2009;29:415–20.
- Cordova E, Miglia I, Festuccia F, Sarlo MG, Scornavacca G, Punzo G, et al. Hepatitis B vaccination in haemodialysis patients: an underestimated problem. Factors influencing immune responses in ten years of observation in an Italian haemodialysis centre and literature review. *Ann Ig*. 2017;29:27–37, <http://dx.doi.org/10.7416/ai.2017.2129>.
- Zitt E, Sprenger-Mähr H, Knoll F, Neyer U, Lhotta K. Vitamin D deficiency is associated with poor response to active hepatitis B immunisation in patients with chronic kidney disease. *Vaccine*. 2012;30:931–5, <http://dx.doi.org/10.1016/j.vaccine.2011.11.086>.
- Parikh C, Gutgarts V, Eisenberg E, Melamed ML. Vitamin D and clinical outcomes in dialysis. *Semin Dial*. 2015;28:604–9, <http://dx.doi.org/10.1111/sdi.12446>.
- Niels Ryberg Finsen – Biographical. Nobelprize.org. Nobel Media AB 2014. Available from: [http://www.nobelprize.org/nobel\\_prizes/medicine/laureates/1903/finsen-bio.html](http://www.nobelprize.org/nobel_prizes/medicine/laureates/1903/finsen-bio.html) [accessed 06.05.18].
- Lang PO, Aspinall R. Vitamin D status and the host resistance to infections: what it is currently (not) understood. *Clin Ther*. 2017;39:930–45, <http://dx.doi.org/10.1016/j.clinthera.2017.04.004>.
- Jafarzadeh A, Keshavarz J, Bagheri-Jamebozorgi M, Nemati M, Frootan R, Shokri F. The association of the vitamin D status with the persistence of anti-HBs antibody at 20 years after primary vaccination with recombinant hepatitis B vaccine in infancy. *Clin Res Hepatol Gastroenterol*. 2017;41:66–74, <http://dx.doi.org/10.1016/j.clinre.2016.06.005>.
- Hoan NX, Tong HV, Song LH, Meyer CG, Velavan TP. Vitamin D deficiency and hepatitis viruses-associated liver diseases: a literature review. *World J Gastroenterol*. 2018;24:445–60, <http://dx.doi.org/10.3748/wjg.v24.i4.445>.
- Hernández-Álvarez N, Pascasio JM, Quintero E, Fernández I, García-Eliz M, de la Revilla J, et al. Effect of season and sunlight on viral kinetics during hepatitis C virus therapy. *BMJ Open Gastroenterol*. 2017;4:e000115, <http://dx.doi.org/10.1136/bmjgast-2016-000115>.
- Sadarangani S, Whitaker J, Poland GA. “Let there be light”: the role of vitamin D in the immune response to vaccines. *Expert Rev Vaccines*. 2015;14:1427–40, <http://dx.doi.org/10.1586/14760584.2015.1082426>.

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<https://doi.org/10.1016/j.nefro.2018.11.016>