

Hepatitis B Vaccination Response: Does Hemodialysis Start Time Matter?



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Introduction

- Hepatitis B vaccine (HBVacc) administration in chronic hemodialysis (HD) patients is important.
- Due to the fact that HD patients regularly undergo extracorporeal therapy, they are at a higher risk of contracting hepatitis B (HepB). Abnormalities in innate and adaptive immune responses as a result of uremia and other comorbidities associated with end stage kidney disease (ESKD), mean that HD patients have a lower HBVacc response rate than their healthy counterparts.
- It was previously found that patients who start HD early in the morning have significantly disturbed sleep-wake patterns.
- Given the known association between sleep and vaccination response in the healthy population, we wanted to study if HD treatment start time had an effect on HBVacc response in HD patients.²

Methods

- Chronic HD patients in Fresenius Medical Care North America (FMCNA) clinics were followed starting from January 2010 to December 2015. Engerix B and Recombivax HB are the two vaccines used by FMCNA. Vaccination doses are administered when a patient is in the clinic to receive HD. In order to be included in our analysis, patients had to receive a complete HBVacc series which is defined in Figure 1.
- HBV was deemed successful if a HepB antibody (HbsAb) titer of ≥ 10 IU/mL was detected up to a year after the completed vaccination. In addition to the titer the following parameters were collected: age, race, gender, HD vintage, diabetes status, body surface area (BSA), hepatitis C status, albumin, and hemoglobin.
- Patients were stratified into two groups based on HD treatment start times: If 90% of a patient's treatments during the observation period began before 8:30 am, patient's were part of the "early group," and if 90% of a patient's treatments during the observation began later, they were a part of the "late group."

Results

- 19,969 patients had completed per protocol HBVacc during the observation period. Cohort descriptive statistics and the results of the univariate and multivariate regressions are listed in Table 1.
- HBVacc response rates of early vs late group was 74% vs 72% ($p=0.003$; $\Delta=2\%$, 95% C.I. (0.7%, 3.3%)).

Discussion

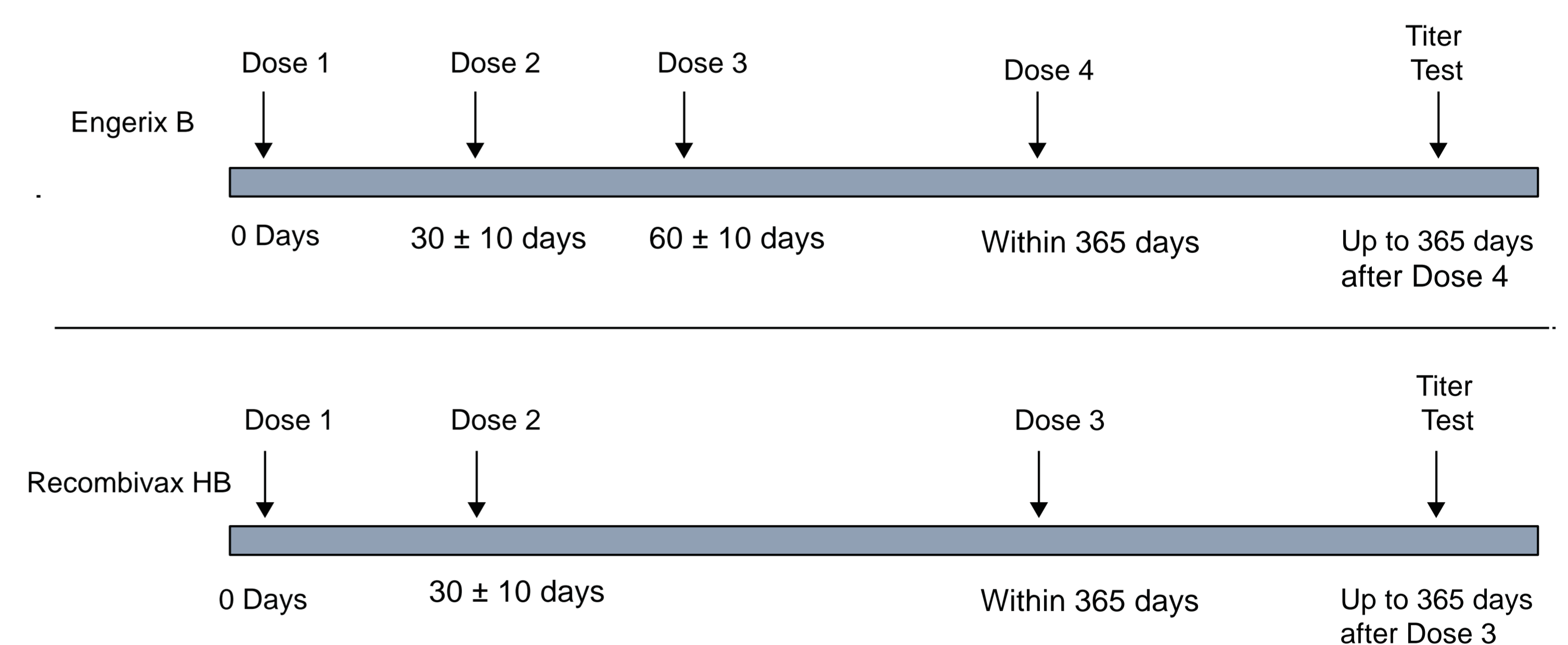
- Early HD start time is associated with HBVacc response, but this effect disappears in the multivariate regression model. In our study cohort, those with an early HD start time were younger, more likely to be male, and had a longer HD vintage – all of which were associated with HBVacc response. In order to truly detect if there is an advantage to being vaccinated earlier in the day vs later, randomly controlled prospective studies or observational studies with very careful matching are required.

Table 1

Parameter	Cohort Descriptive [Mean (SD)]				Δ (95% C.I.)	Univariate Regression α (95% C.I.)	Multivariate Regression (N=15,119) OR (95% C.I.)
	All (N=19,969)	Early (N=6,613)	Late (N=13,356)				
Vaccine type: Engerix B	90%	94.8%	95.2%	-0.41 (1.06, 0.26)	1.56 (1.39, 1.75)**	1.70 (1.45, 1.99)**	
Albumin [g/L]	3.82 (0.35)	3.85 (0.33)	3.80 (0.36)	0.04 (0.03, 0.05)	2.47 (2.29, 2.67)**	2.48 (2.22, 2.77)**	
Age [years]	64.90 (13.96)	63.03 (13.35)	65.82 (14.17)	2.79 (-3.20, -2.38)	0.97 (0.97, 0.98)**	0.97 (0.97, 0.98)**	
Race: White	69.4%	66.8%	70.7%	-3.89 (-5.23, -2.46)	0.65 (0.61, 0.69)**	0.76 (0.70, 0.83)**	
Body Surface Area [m ²]	1.90 (0.27)	1.95 (0.27)	1.88 (0.26)	0.07 (0.06, 0.08)	0.82 (0.74, 0.92)*	0.38 (0.33, 0.45)**	
Hemoglobin [g/dL]	11.22 (0.77)	11.27 (0.79)	11.20 (0.75)	0.07 (0.05, 0.09)	0.93 (0.90, 0.96)**	0.87 (0.83, 0.91)**	
Sex: Male	5.5%	61.2%	55.7%	5.46 (4.0, 6.91)	1.15 (1.09, 1.21)**	1.38 (1.27, 1.50)**	
HD Vintage [years]	0.86 (1.60)	1.2 (1.83)	0.69 (1.46)	0.51 (0.46, 0.56)	1.15 (1.09, 1.20)**†	1.14 (1.07, 1.21)**†	
Hepatitis C positive	5.8%	6.4%	5.4%	0.98 (0.21, 1.76)	1.02 (0.89, 1.16)	0.88 (0.75, 1.03)	
Diabetes mellitus	61.5%	61.9%	61.2%	0.70 (-0.70, 2.15)	1.11 (1.05, 1.18)*	1.15 (1.06, 1.25)*	
90% of treatments starting before 8:30a.m.	33.1%	-	-		1.11 (1.04, 1.18)*	0.99 (0.92, 1.08)	

†square root of vintage; * $p<0.05$, ** $p<0.0001$; OR, odds ratio

Figure 1. Hepatitis B Vaccination Schedule for Engerix B and Recombivax HB



References

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2. Lange, T., et al., Sleep after vaccination boosts immunological memory. J Immunol, 2011. 187(1): p. 283-90.

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