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Racial differences in the association between injectable vitamin D dose and mortality in incident hemodialysis patients

Introduction

- Observational studies have reported an association between injectable (IV) vitamin D use and reduced mortality in incident hemodialysis (HD) patients.
- Few studies have examined whether racial differences exist in the association between IV vitamin D dose and mortality.
- The purpose of this study was to assess whether the effect of IV vitamin D dose in an incident population is consistent between whites and blacks.

Methods

- Retrospective cohort study
- Study population:
  - Medicare white and black HD patients incident in 1999-2000, surviving 90 days after HD initiation, and with Medicare as primary payor.
  - Survived three months including the month of day 90, continuously enrolled in Medicare, and on HD therapy.
  - Patients were excluded if they received a transplant or peritoneal dialysis any time before follow-up start, were aged 20 and younger at follow-up start, or did not reside in the 50 states or Washington D.C.
- Exposure: IV vitamin D use and cumulative IV vitamin D dose during 3-month interval
  - Identified based on HCPCS level II codes in Medicare Part A outpatient revenue files (calcitriol: J0635-J0636; doxercalciferol: J1270; paricalcitol: J2500-J2501)
  - Three-month cumulative IV vitamin D dose was calculated as calcitriol and calcitriol-equivalent (paricalcitol, doxercalciferol), using the following dose-conversion ratios:
    - paricalcitol to calcitriol = 4.6 to 1, determined by the slope from a linear regression model with zero intercept on the percentiles of monthly paricalcitol and calcitriol doses
    - doxercalciferol to calcitriol = 3.1 to 1, determined using the same method
- Outcome: all-cause mortality.
- We used the first three months including the month of day 90 as a baseline period, and followed these patients from month four to December 31, 2004 to track all-cause mortality (max. follow-up: 5.75 years).
- Patient characteristics at baseline included demographics, primary cause of kidney failure, provider type, vascular access type, and comorbidities.
- A Cox proportional hazards model was used to assess the time-varying effect of IV vitamin D use and 3-month cumulative dose on the risk of all-cause death, by race and time on IV vitamin D, adjusting for baseline characteristics, comorbidity, and time-varying hospital days over the 3-month moving interval in the follow-up period.

Results

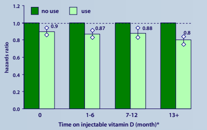
- Median follow-up time was 1.9 years for whites and 2.9 years for blacks.
- At baseline, IV vitamin D use was 54% for blacks and 43% for whites. More blacks (14%) received >40 mcg of IV vitamin D (calcitriol equivalent) than whites (6%).
- Overall, IV vitamin D use and higher cumulative dose over the 3-month interval was associated with decreased risk of all-cause death, with an apparent stronger protective effect in blacks.
- The hazard ratio pattern across time on IV vitamin D, however, was not consistent across race groups.
  - The protective effect of IV vitamin D use increased with increasing time on IV vitamin D among whites, but presented a bell-shape pattern among blacks.
  - At higher cumulative doses, the protective effect of IV vitamin D was erratic with increasing time on IV vitamin D for both race groups.
  - At lower cumulative doses, a bell-shaped pattern across time on IV vitamin D was shown for blacks with no evident pattern for whites.

Patient characteristics at baseline, by cumulative IV vitamin D dose level, and for whites and blacks

	Whites						Blacks					
		Cumulative IV vitamin D dose at 3-month baseline (mcg)						Cumulative IV vitamin D dose at 3-month baseline (mcg)				
	All (n=50,500)	0 (n=28,689)	0<-15 (n=6,307)	15<-30 (n=6,185)	30<-40 (n=6,394)	>40 (n=2,925)	All (n=26,427)	0 (n=12,127)	0<-15 (n=3,230)	15<-30 (n=3,538)	30<-40 (n=3,876)	>40 (n=3,656)
Age												
20-44	7.9	8.3	8.7	7.1	6.1	7.8	17.8	20.1	19.3	17.0	13.6	13.9
45-64	24.9	26.7	24.3	22.3	20.4	24.0	38.8	40.5	38.4	37.6	35.9	38.1
65-74	32.1	31.7	31.0	32.2	34.3	33.8	24.9	22.6	23.9	25.9	27.8	29.5
75+	35.1	33.4	36.0	38.3	39.3	34.4	18.4	16.8	18.4	19.5	22.7	18.5
Gender												
Male	54.9	55.3	53.3	52.3	56.9	56.0	47.7	50.2	46.7	44.8	44.7	45.9
Female	45.1	44.7	46.7	47.7	43.1	44.0	52.3	49.8	53.3	55.2	55.3	54.1
Primary cause of ESRD												
Diabetes	46.2	45.3	45.9	46.5	49.2	47.9	44.9	43.6	44.1	46.0	47.9	45.5
Hypertension	27.0	26.6	26.7	28.5	27.2	27.6	35.9	34.6	36.3	36.7	37.1	38.0
GN	8.3	8.4	8.7	8.4	8.1	7.8	6.6	6.7	7.3	6.8	5.8	6.7
Other	18.5	19.7	18.7	16.6	15.5	16.8	12.6	15.1	12.2	10.5	9.2	9.8
Provider												
Profit	67.5	64.8	66.5	71.8	71.6	78.3	68.7	63.4	66.4	71.9	73.3	80.0
Nonprofit	26.7	27.7	29.5	24.4	24.9	18.6	25.0	28.0	27.7	24.0	22.7	16.5
Missing or unkown	5.8	7.5	4.0	3.8	3.5	3.1	6.3	8.7	5.9	4.1	4.0	3.5
Vascular access type												
Catheter	32.2	31.6	34.5	34.9	30.6	31.1	26.0	23.7	30.6	29.0	27.9	24.6
Fistula	17.2	15.1	18.3	19.4	21.9	21.7	11.4	8.9	11.6	13.4	13.9	15.3
Graft	25.1	22.0	27.3	28.1	32.0	29.4	25.4	19.8	25.5	29.3	32.8	32.6
Unknown	25.4	31.3	19.9	17.7	15.5	17.8	37.1	47.6	32.4	28.3	25.5	27.5
Hospitalization days												
0	65.2	66.1	60.0	58.6	69.6	71.2	67.2	69.3	58.6	60.2	68.5	73.5
1-<3	7.6	6.8	8.3	8.2	9.4	8.5	7.4	6.2	8.4	8.5	9.0	7.9
3-<7	10.0	9.3	10.6	11.3	10.8	11.2	9.2	8.0	10.3	10.5	10.6	9.3
7-<14	8.2	7.9	9.2	10.0	7.6	5.8	7.7	7.0	9.8	9.3	8.6	5.9
14+	9.0	9.8	11.9	11.9	2.6	3.3	8.5	9.6	12.9	11.5	3.3	3.4
Comorbidity												
ASHD	44.4	43.8	45.6	46.8	44.5	41.9	25.0	23.9	27.2	27.0	26.5	23.1
CHF	46.3	46.1	47.1	48.7	45.4	44.3	36.7	35.0	40.3	40.0	37.8	34.6
CVA/TIA	15.2	15.5	15.1	16.3	14.0	13.4	14.0	13.6	16.0	16.1	13.2	12.4
Diabetes	56.2	55.2	57.0	56.4	59.2	57.2	55.5	52.4	56.9	57.9	59.9	57.4
PVD	28.8	28.9	30.5	30.5	27.9	22.6	18.3	17.6	19.0	20.5	18.9	17.2
Cardiac, other	11.3	11.4	13.1	12.7	9.3	8.2	9.2	9.0	11.9	11.2	7.6	7.2
COPD	16.3	16.6	16.5	17.0	15.1	14.1	8.2	7.8	9.5	9.2	8.2	7.4
Dysrhythmia	20.6	20.2	22.7	22.6	19.5	18.0	11.1	10.9	11.7	12.2	10.8	10.6
Cancer	9.2	9.0	9.9	9.2	9.5	9.3	5.8	5.9	6.3	5.8	5.3	5.3
GI bleeding	4.3	4.5	5.1	4.9	3.0	3.2	4.1	4.2	5.6	5.2	2.6	2.8
Liver disease	9.7	8.4	10.3	12.0	11.9	11.0	8.2	7.2	9.0	10.1	9.0	8.1

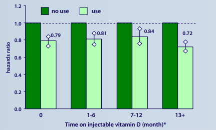
Hazards ratio for all-cause mortality for IV vitamin D use vs no use among whites

adjusted for baseline patient characteristics at baseline and time-varying hospital days



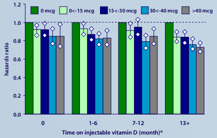
Hazards ratio for all-cause mortality for IV vitamin D use vs no use among blacks

adjusted for baseline patient characteristics and time-varying hospital



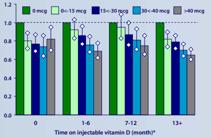
Hazards ratio for all-cause mortality for cumulative IV vitamin D dose vs no use among whites

adjusted for baseline patient characteristics and time-varying hospital



Hazards ratio for all-cause mortality for cumulative IV vitamin D dose vs no use among blacks

adjusted for baseline patient characteristics and time-varying hospital days



* Defined as number of months using IV vitamin D over the time period from the month of day 90 of ESRD leading up to the month before each moving 3-month interval during which cumulative IV vitamin D dose was evaluated.

Conclusions

- Our study results suggest that:
  - Blacks tend to receive IV vitamin D more often and at higher quarterly doses.
  - IV Vitamin D use and higher cumulative quarterly doses are generally associated with reduced risk of all-cause death, with an apparent stronger protective effect in blacks.
  - However, the hazard ratio pattern across time on IV vitamin D was not consistent across race groups, which may be due to the presence of unmeasured covariates.
- Limitations:
  - Residual confounding may exist.
  - Misclassification bias is possible due to lack of laboratory values in dataset.
- Observational studies are unlikely to completely account for residual confounding in patients exposed to vitamin D vs. those not exposed. Inconsistent IV vitamin D dose and time-exposure effects across race groups suggests the need for a randomized clinical trial to determine if apparent effect differences are a result of a true treatment effect or an effect of a biased population.

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