Impact of vitamin D level on infections in patients with multiple sclerosis treated with disease-modifying therapies: A pilot study

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Background

- Disease-modifying therapies (DMTs) are the cornerstone of treatment in multiple sclerosis (MS) to control disease activity and decrease relapses.
- Because of their immunomodulatory effects, DMTs may predispose patients to more infections.
- High doses of vitamin D (≥2000 IU per day) are proposed to have immunomodulatory effects, and are a commonly used adjunctive therapy in MS.
- There is a potential for increased infections with concurrent vitamin D and DMT use.
- This pilot study will aim to evaluate the impact of vitamin D on infections in patients with MS on concurrent DMTs.

Objectives

Primary objective:

- Asses and characterize the relationship between vitamin D levels and the development of infections.

Secondary objective:

- Describe and characterize the use of vitamin D and assess the safety and tolerability of using this regimen.

Methods

Design:

- Single center, retrospective, chart review
- Goal n=100 (convenience sample)
- Charts from BH MS Clinic from Nov. 1st, 2014 – Mar. 31st, 2018

Table 1: Inclusion and exclusion criteria for study participants.

Inclusion	Exclusion
▪ Receiving DMT and high-dose vitamin D (≥2000 IU daily) ▪ DMTs of interest: fingolimod, natalizumab, dimethyl fumarate ▪ Vitamin D level ▪ ≥19 years old	▪ Immunocompromising conditions or treatment ▪ Hyperparathyroidism ▪ IBS or IBD ▪ Primary progressive MS (PPMS) ▪ History of renal stones or dysfunction ▪ History of cardiac arrhythmias

Table 2: Patient characteristics.

	Low vitamin D level (n=16)*	Normal vitamin D level (n=18)^	High vitamin D level (n=1)#
Mean age ± SD – yr	46 ± 12	48 ± 8	32
Female – no. (%)	11 (69)	13 (72)	1 (100)
RRMS – no. (%)	16 (100)	15 (83)	1 (100)
Mean disease duration ± SD – yr	13 ± 10	10 ± 9	6
Mean EDSS ± SD	4 ± 2	3 ± 2	1.5
DMT used – no. (%)			
Fingolimod	4 (25)	2 (11)	-
Natalizumab	5 (31)	1 (6)	-
Dimethyl fumarate	7 (44)	15 (83)	1 (100)
Mean duration of DMT use ± SD – y	3 ± 2	2.5 ± 1	4
Mean vitamin D dose ± SD – IU/day	3231 ± 1365	4583 ± 3735	20 000
Mean serum 25(OH)D levels ± SD – nmol/L	80 ± 16	140 ± 20	248

Table 3: Infections and gastrointestinal (GI) adverse events.

	Low vitamin D level (n=16)*	Normal vitamin D level (n=18)^	High vitamin D level (n=1)#
Patients experiencing ≥1 infection – no. (%)	8 (50)	8 (44)	0
Patients experiencing ≥1 infection requiring healthcare visit	8 (50)	7 (39)	-
Patients experiencing ≥1 GI adverse event – no. (%)	1 (6)	2 (11)	0
Nausea	-	2 (11)	-
Diarrhea	-	1 (6)	-
Constipation	1 (6)	1 (6)	-

*Low level: <100 nmol/L; ^normal level: 100 – 200 nmol/L; #high level: >200 nmol/L.

Table 4: Spearman's rank correlations between vitamin D level, vitamin D dose, infections, and infection severity.

	Spearman's Rho	
	Infections (n=35)	Infection Severity (n=35)
Vitamin D level	-0.152*	0.153*
Vitamin D dose	-0.161*	0.050*

*Values not statistically significant.

Discussion & Limitations

- Although there was no correlation between vitamin D dose or level and infections or infection severity, the use of high-dose vitamin D appears to be well-tolerated.
- Single-center design limits generalizability to a wider population.
- Accuracy of data collection is limited by the completeness of information provided in patient charts.
- Insufficient power to detect statistically significant correlations due to small sample size.
- Lack of a DMT-only comparator arm makes it difficult to assess the impact of vitamin D supplementation vs. DMTs alone on infections and GI adverse events.
  - Practice patterns at the BH MS Clinic indicate that almost all patients on DMTs receive vitamin D supplementation.
- Effect of vitamin D on infections and adverse events is confounded by disease symptoms and DMT received.

Conclusions

- The use of high doses of vitamin D appears to be well-tolerated.
- Our study did not show a correlation between vitamin D dose or level and infections or infection severity.
- Due to the limitations of this study, further studies are needed to determine the impact of vitamin D on infections.
- Future studies should aim to:
  - Include a larger number of patients (e.g. by expanding the timeframe for retrospective data collection or conducting the study prospectively)
  - Improve the reliability of outcome data reporting (e.g. by asking patients to record infective symptoms and adverse events in a prospective study design)

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