Research Article

Higher dietary intake of vitamin D may influence total cholesterol and carbohydrate profile independent of body composition in men with Chronic Spinal Cord Injury

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Study Design: A case-control design.

Objectives: To determine the effects of dietary vitamin D intake on insulin sensitivity (Si), glucose effectiveness (Sg), and lipid profile in individuals with spinal cord injury (SCI).

Methods: 20 male, paraplegic (T3-L1) with chronic (> one year) motor complete SCI (AIS A or B) were recruited. Three-day dietary records were analyzed for dietary vitamin D (calciferol), and participants were assigned to one of two groups, a high vitamin D intake group and a low vitamin D intake group based on the mid-point of vitamin D frequency distribution. Individuals in both groups were matched based on age, weight, time since injury and level of injury. Sg, Si and lipid profiles were measured of the two groups.

Results: The high vitamin D group had an average intake of 5.33 ± 4.14 mcg compared to low vitamin D group, 0.74 ± 0.24 mcg. None of the 20 participants met the recommended guidelines for daily vitamin D intake. The higher vitamin D group had a significantly lower ($P = 0.035$) total cholesterol (148.00 ± 14.12 mg/dl) than the lower vitamin D group (171.80 ± 36.22 mg/dl). Vitamin D adjusted to total dietary intake was positively correlated to improvement in Si and Sg ($P < 0.05$).

Conclusion: The findings suggest that persons with SCI consume much less than the recommended guidelines for daily vitamin D intake. However, a higher dietary intake of vitamin D may influence total cholesterol and carbohydrate profile as demonstrated by a significant decrease in total cholesterol and improvement in glucose homeostasis independent of body composition changes after SCI.

Keywords: Vitamin D, Cholesterol, Lipid profile, Carbohydrate, Insulin sensitivity, Body composition, Spinal cord injury

Introduction

Vitamin D₃ (cholecalciferol) is a fat-soluble vitamin activated in the skin or absorbed from dietary intake. This pro-hormone is then converted into its active form by enzymes

in the liver and kidneys. Daily dietary intake is one of the major sources of vitamin D. The Institute of Medicine recommends a daily dietary vitamin D intake of 15 µg for adults,¹ but most individuals in the spinal cord injury (SCI) population do not consume the daily intake requirement.²⁻⁴ The lower vitamin D intake in patients with SCI could be secondary to decreased dietary intake from mechanical difficulties with feeding and/or decreased access to recommended diet rich in vitamin D. Vitamin D deficiency is defined as levels of 25(OH)D < 20 ng/

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mL, and the SCI population has a higher rate of vitamin D deficiency than the able-bodied population.^{2,4,5}

Persons with SCI commonly have abnormal metabolic profiles characterized by insulin resistance, glucose intolerance, and dyslipidemia. Metabolic dysfunction has been reported to be associated with loss of muscle mass and increased fat mass, especially below the level of injury.^{6,7} Metabolic dysfunction is thought to be secondary to the higher prevalence of increased absolute and regional fat mass as well as reduced level of physical activity after SCI.⁷⁻⁹ Abnormal lipid profiles are very common in the SCI population; these profiles are characterized by low levels of high-density lipoprotein cholesterol (HDL-C) and elevated levels of low-density lipoprotein cholesterol (LDL-C) and triglycerides (TG).^{7,10-13} Bauman *et al.* showed that 37% of the SCI population have HDL-C levels below 35 mg/dL, and 18% of persons with SCI have LDL-C levels above 160 mg/dL.¹⁴ Nash *et al.* reported that 76% of individuals with paraplegia had HDL-C less than 40 mg/dl and 34% had the Adult Treatment lipid Panel III-defined metabolic syndrome.¹⁵ In a different study, Bauman *et al.* showed that up to 62% of the SCI population demonstrates decreased glucose tolerance compared to 18% of an age-matched group.¹⁶ In that same study, 22% of the subjects with SCI met diabetic criteria compared to only 6% of the control group.¹⁶

Studies are inconclusive about a direct causative effect, but vitamin D deficiency appears to play a role in the pathogenesis of metabolic dysfunction, especially Type 2 Diabetes Mellitus (T2DM).^{2,17-26} T2DM is caused by inadequate insulin secretion combined with decreased insulin sensitivity. Vitamin D deficiency has been shown to negatively impact β -cell function in the pancreas thereby reducing insulin secretion.^{18,25-27} Additionally, studies have demonstrated relationships between vitamin D deficiency and reduced insulin sensitivity^{2,17,24-30} and impaired glucose tolerance.^{24, 30} Studies have also demonstrated a link between dyslipidemia and vitamin D status.^{11,28,31-34} Vitamin D has been positively correlated with HDL-C levels,^{7,11-13,31} and low vitamin D levels are associated with high levels of total cholesterol (total-C), LDL-C, and TG.^{7,11-13,31,32}

We hypothesize that persons with a higher daily dietary vitamin D intake may have improved metabolic profiles independent of changes in body composition. Anecdotal evidence suggests a positive effect of vitamin D intake on the metabolic profile in the SCI population. The primary purpose of the current study was to investigate the effects of vitamin D intake on glucose tolerance, insulin sensitivity, and dyslipidemia independent of lean body mass in persons with chronic SCI. We hypothesized

that persons with SCI who have higher vitamin D intake will have a better metabolic profile compared to those with lower vitamin D intake.

Methods

20 healthy men with chronic motor complete SCI (American Spinal Injury Association Impairment Scale (AIS) -A or B) were enrolled in the current study as part of a large national study investigating the effects of chronic SCI (> one year) on body composition and metabolic profile. Participants were selected from a database of 72 individuals who had full metabolic profiles and three-day dietary intake records prior to enrollment (Figure 1). They were matched based on their group, and separated into either a higher or lower intake group based on their vitamin D intake. Separation into higher and lower groups was performed after establishing the frequency distribution of vitamin D and identifying the midpoint of the distribution of the 20 participants. This approach was adopted because persons with SCI usually consume less vitamin D than the recommended guidelines.

1. Study Inclusion Criteria

A. Inclusion Criteria

Previously, a database of 72 participants was compiled for a large national study investigating the effects of chronic SCI on body composition and metabolic profile. Participants were recruited from the VA/VCU Health System through word of mouth and posted flyers in the SCI clinics. Participants were included if they were 18-65 years old and had motor complete SCI (C5- L2; AIS A & B) with greater than one year duration since injury. This database contains a three-day dietary recall, full metabolic profile, and body composition for each participant. To ensure sample homogeneity and to reduce the variables influencing the metabolic profile only paraplegic (T3-L1 in this study) males, with chronic (>one year post-injury) motor complete SCI (AIS A or B) were selected (Table 1). Both groups were then closely matched based on age, weight, level and

Figure 1 Timeline of sequence of events for persons with SCI during the course of the study.

Table 1 Physical characteristics of 20 men with motor complete Spinal Cord Injury.

	Age	Body Mass (kg)	Height (cm)	BMI (kg/cm ²)	TSI(yrs.)	LOI	AIS
High Vit. D	30	63.3	181.0	19.3	11.0	T7	A
	32	84.5	173.7	28.0	2.2	T3	A
	36	142.7	178.1	45.0	1.3	T3-T4	A
	43	95.6	182.3	28.8	21.1	T10-L1	A
	46	67.4	167.5	24.0	26.2	T4	A
	65	80.7	176.2	26.0	38.9	T7	A
	60	72.7	162.9	27.4	14.1	T9	A
	47	72.0	170.7	24.7	27.6	T9	A
	49	71.3	176.8	22.8	31.6	T2	A
	57	122.0	176.1	39.3	15.5	T9-T11	A
Mean± SD	47.0±11.8	87.2±25.9	174.5±6.0	28.5±7.8	18.9±12.4	T3-L1	10A:0B
Low Vit. D	36	66.4	172.8	22.2	2.7	T6-T7	A
	34	86.0	168.6	30.3	5.2	T6	A
	36	133.1	189.9	36.9	7.1	T4	A
	47	97.4	196.5	25.2	22.2	T4-T5	A
	46	53.5	171.6	18.2	15.6	T11	A
	60	84.0	165.4	30.7	6.4	T3-T4	B
	59	82.5	167.0	29.6	37.3	T10	B
	41	106.0	181.4	32.2	19.8	T4	A
	56	91.6	187.9	25.9	5.9	T4	A
	56	82.2	177.1	26.2	29.4	L1	B
Mean± SD	47±10.1	88.3±21.6	177.8±10.7	27.8±5.3	15.2±11.8	T3-L1	7A:3B

TSI, time since injury; LOI, level of injury; AIS, American Spinal Cord Injury Association Impairment Scale.

completeness of injury to reduce the impact on metabolic outcomes.¹⁶ All of the tests described below were conducted during data collection of the initial study. All aspects related to the study design and methodology were reviewed and approved by the VA and VCU institutional review boards. Participants were asked to read and sign an informed consent statement that was approved by the local ethics committee.

B. Exclusion criteria

Participants were excluded if they had cardiovascular disease, hypertension, heavy tobacco use, alcohol abuse, or the presence of pressure ulcers greater than Grade II. Before starting, each participant underwent a general physical examination, including vital signs and a resting 12-lead electrocardiogram, to rule out any pre-existing cardiac problems.

II. Dietary logs and vitamin D assessment

For the present study, the three-day dietary records of the selected participants were analyzed for vitamin D (calciferol) intake. We have recently shown that three-day frequency is the most appropriate strategy to analyze dietary recalls in persons with SCI.³⁶ Each participant met with a dietitian and was asked to complete food dietary logs monitoring caloric intake and macronutrients for three consecutive days, including two weekdays and one weekend day. Participants were clearly instructed not to change their dietary habits and dietary logs were turned in on the body composition assessment day

(figure 1). Participants were instructed to record all liquid and food consumption and no nutritional advice was given on the size or the portion of the food. The dietary logs were returned to study personnel and analyzed using the Nutrition Data System for Research version 2014 nutritional software package under the supervision of a registered dietitian. After the analysis was completed, various micronutrient values, including average calciferol intake, were calculated for each participant.

III. Body composition assessment

Body mass was measured while subjects were seated in their wheelchairs, using a wheelchair scale^a. Height was measured in a supine lying position by placing two boards, one at the apex of the head and the other at the sole of the foot, and measuring the distance between them to the nearest 0.1 cm. BMI was calculated as mass in kilograms divided by height in meters.

A. Anthropometrics

Circumferential measurements were performed while participants were seated in their wheelchairs and wearing non-restrictive clothes. Participants were asked to take a deep breath and then exhale, and measurements were taken during the expiration phase. The waist was defined as the narrowest region below the ribcage, and the abdomen was defined as the widest region at the level of umbilicus. Measurements were reported to the nearest 0.1 cm and repeated until three measures were within a 0.5 cm range of one another.

B. Dual energy x-ray absorptiometry (DXA)

DXA was used to measure body composition in participants, specifically regional and total fat mass, fat-free mass (lean mass and bone mass), and lean mass. Total body and regional DXA scans were performed using a Lunar Prodigy Advance^b at the VAMC hospital. The scans were performed after lying flat for at least 20 minutes to minimize fluid shift. All scans were performed and analyzed by a trained certified DXA operator using Lunar software version 10.5. The coefficient of variability of two repeated scans for whole body percentage fat mass is less than 3%.

IV. Metabolic profile

Participants who met the study inclusion/exclusion criteria were instructed to abstain from exercise, alcohol, and caffeine for 24–48 hours preceding the examination. Other than using their manual wheelchairs, participants were instructed not to be engaged in any upper extremity training programs 24–48 hours prior testing. All participants were allowed to take their medications as prescribed by their physicians on the day of blood work testing, but it was optionally recommended holding medications during blood work testing not to interfere with the results. All participants were immediately instructed to get their medications at the end of the blood work.

A. Lipid profile

Following a 12-hours fast, blood lipid profiles were assessed using standard analysis procedures. A Teflon catheter was inserted into an antecubital vein in one arm, and 4 mL of blood were drawn and sent for analysis of TG, total-C, HDL-C, and LDL-C. Plasma concentrations were determined using commercially available colorimetric assays,^c and the ratio of total-C to HDL-C was calculated.

B. Insulin and glucose tolerance tests

Carbohydrate profiles were also assessed during the metabolic profile testing using a standard three-hour intravenous glucose tolerance test (IVGTT) to determine insulin sensitivity (Si) and glucose effectiveness (Sg). Briefly, an indwelling catheter with an intravenous saline drip (0.9% NaCl) was placed in an antecubital vein, and another intravenous line was placed in a contralateral hand vein between the hours of 8:00 and 8:30 to facilitate the infusion of glucose and blood sampling during the IVGTT. Glucose samples were taken at minutes –6, –4, –2, 0, 2, 3, 4, 5, 6, 8, 10, 12, 14, 16, 19, 22, 23, 24, 25, 27, 30, 35, 40, 50, 60, 70, 80, 90, 100, 120, 140, 160, and 180 after the rapid glucose injection (0.3 gm/kg IV over 30 seconds at time zero). In

addition, 20 minutes after the glucose injection, a bolus of insulin (0.02 U/kg) was injected to determine insulin sensitivity. Blood pressure and heart rate were assessed at minutes 22, 23, and 24 of the protocol. The results of the IVGTT were modeled using MinMod analysis^e. The plasma insulin concentration was measured using a commercially available radioimmunoassay kit^d.

V. Statistical analysis

Independent t-tests were used to test for the difference between variables of body composition and metabolic profile between higher and lower vitamin D dietary intake groups. Si values were log-transformed to account for normality of the data. Data were examined for outliers using Cook's D. Pearson correlations were used to determine the association between body composition and nutritional assessments after examining for outliers. Statistical analyses were performed using IBM-SPSS version 23. All values were reported as mean $\pm$ SD and statistical significance was set at alpha less than 0.05.

Results

The physical characteristic of both groups were matched based on age, weight, level and completeness of injury are presented in Table 1. The 2 groups had similar body composition (Table 3) in regards to total %fat mass ($P = 0.11$), region % fat mass ($P = 0.14$), total fat mass ($P = 0.28$), lean mass ($P = 0.27$), sitting waist circumference ($P = 0.49$) and sitting abdominal circumference ($P = 0.46$). Data for vitamin D (calciferol) intake, calcium intake, total caloric intake and percentage macronutrients (%fat, %carbohydrate and % protein) in the higher and lower vitamin D intake groups are presented in Table 2. Because the total caloric intake was 28% greater in the high vitamin D group compared to the low vitamin D, we have adjusted vitamin D intake (μg) to total dietary intake (grams). After adjustment vitamin D was still 4.5 times greater in the higher vitamin D group compared to the lower vitamin D group ($P = 0.0001$). The total caloric intake and the caloric intake adjusted body weight were statistically greater in the high vitamin D group compared to the low vitamin D group (Table 2). Moreover, total caloric intake ($r = 0.78$, $P < 0.0001$) and the caloric intake adjusted body weight ($r = 0.79$, $P < 0.0001$) were positively related to vitamin D intake.

The higher intake group had a calciferol intake of 5.33 ± 4.14 mcg, which was statistically higher ($P = 0.0025$) than the calciferol intake of 0.74 ± 0.24 mcg in the lower intake group. The higher intake group had a calcium intake of 799.25 ± 522.5 mg, and the

Table 2 Vitamin D intake, calcium intake, total caloric intake and percentage macronutrients in 20 men with motor complete SCI.

	Vitamin D (Calciferol) (μ g)	Vitamin D -IU	Calcium (mg)	Vitamin D/ Total intake (μ g/ grams)	Total Intake (grams)	Total caloric Intake (kcal)	Caloric intake/ body weight	%Fat	%Carbohydrate	% Protein
High Vitamin D	3.275	131	378.7	0.00524	624.9	686.6	10.8	27.2	61	15
	1.827	73	389.3	0.00176	1038.8	1229.0	14.5	33.2	51	18
	2.389	96	501.7	0.00288	830.8	1777.8	12.5	43.9	33	24
	5.469	219	967.3	0.00293	1865.8	1700.0	17.8	35.8	52	16
	3.562	142	630.4	0.00213	1675.0	1735.0	25.7	31.1	58	14
	7.954	318	946.7	0.00384	2069.8	1652.9	20.5	28.7	56	20
	1.657	66	430.2	0.00174	952.1	1405.8	19.3	38.0	50	15
	14.331	573	1743.2	0.00730	1962.1	2949.4	41.0	45.3	39	18
	9.781	391	1648.8	0.00414	2362.8	2290.7	32.1	38.0	40	24
	3.102	124	356.1	0.00231	1343.5	1407.0	11.5	41.5	45	16
Mean $\pm$ SD	5.3 $\pm$ 4.1	213 $\pm$ 166	799 $\pm$ 523	0.00343 $\pm$ 0.00177	1472.5 $\pm$ 595	1683 $\pm$ 609	20.6 $\pm$ 10	36 $\pm$ 6	48.5 $\pm$ 9	18 $\pm$ 4
Low Vitamin D	0.318	13	157.3	0.00059	539.2	1179.6	17.8	32.7	58	11
	1.122	45	371.6	0.00111	1008.3	1536.5	17.9	42.1	45	15
	0.491	20	622.6	0.00039	1251.5	1500.9	11.3	34.0	53	15
	0.906	36	201.1	0.00212	428.0	694.9	7.1	51.5	37	13
	0.923	37	473.8	0.00066	1389.4	1260.1	23.6	34.6	50	18
	0.767	31	507.5	0.00038	2023.0	1383.3	16.5	28.1	59	16
	0.734	29	245.0	0.00031	2388.1	676.9	8.2	38.5	44	20
	0.526	21	357.1	0.00063	830.8	1777.8	16.8	43.9	33	24
	0.768	31	245.3	0.00081	952.7	995.8	10.9	34.6	45	22
	0.841	34	218.0	0.00062	1359.6	1119.3	13.6	28.5	56	18
Mean $\pm$ SD	0.74 $\pm$ 0.24	30 $\pm$ 9	340 $\pm$ 154	0.00076 $\pm$ 0.00053	1217 $\pm$ 616	1212 $\pm$ 358	14.4 $\pm$ 5	37 $\pm$ 7	48 $\pm$ 9	17 $\pm$ 4
P-values	0.0025	0.0025	0.0157	0.0001	0.17	0.02	0.048	0.4	0.8	0.3

Table 3 Body composition assessment in 20 men with motor complete SCI based on their vitamin D intake.

	DXA Total % Fat	DXA Region % Fat	DXA Fat mass (kg)	Lean Mass (kg)	Sitting Waist Circumference	Sitting Abdominal Circumference
High Vit. D	N/A	N/A	N/A	N/A	78.2	81.8
	39.6	38.2	31.3	47.7	98.1	108.8
	49.8	49.3	68.9	67.2	126.7	156.0
	46.9	43.9	42.4	50.7	111.8	116.2
	39.2	37.6	25.3	39.5	89.3	101.3
	42.8	42.8	33.4	44.5	96.3	119.0
	40.8	40.5	29.1	40.3	90.8	103.7
	31.3	27.7	19.6	48.2	83.0	83.8
	30.3	29.9	20.7	48.4	94.2	102.9
	53.5	52.3	62.6	53.9	121.9	143.3
Mean $\pm$ SD	41.6 $\pm$ 7.8	40.2 $\pm$ 8.1	37.0 $\pm$ 17.7	48.9 $\pm$ 8.3	99.0 $\pm$ 16.1	111.7 $\pm$ 23.5
Low Vit. D	30.6	31.4	20.8	43.1	82.3	92.6
	41.8	39.7	34.2	48.6	93.8	107.7
	42.6	41.9	54.1	71.5	116.8	136.9
	30.4	33.2	31.9	60.4	98.8	107.3
	23.3	23.8	12.6	37.8	79.1	75.8
	33.9	32.8	27.6	53.8	100.7	115.8
	42.1	40.0	32.8	45.0	100.5	113.2
	50.9	49.1	51.3	49.1	113.4	131.7
	40.8	38.9	36.5	52.9	98.7	108.7
	33.8	32.7	26.9	52.8	108.5	117.8
Mean $\pm$ SD	37.0 $\pm$ 8.03	36.3 $\pm$ 7.0	32.9 $\pm$ 12.6	51.5 $\pm$ 9.4	99.3 $\pm$ 12.1	110.7 $\pm$ 17.6

lower intake group had a calcium intake of 340 ± 154 mg ($P = 0.015$).

In Table 4, it is shown that vitamin D intake adjusted to total caloric intake ($P = 0.0001$) or macronutrients of total carbohydrates ($P = 0.0002$), total protein ($P = 0.0001$), vegetable protein ($P = 0.0004$), total-C ($P = 0.015$), total saturated fats ($P = 0.0025$), total monounsaturated fats ($P = 0.0004$) and total polyunsaturated fats ($P = 0.0015$) were significantly greater in the higher intake group compared to low intake group.

I. Carbohydrate profile

The individual Si and Sg values are presented in Table 4. After log transformation, Si was not different ($P = 0.13$) between the high (0.19 ± 1.1) and low (0.16 ± 0.46) vitamin D groups even after controlling for weight and lean mass (data not shown). It is worth noting that three data points of the Si were identified as outliers in the high Vitamin D group and after exclusion of these points, Si was no longer different between both groups. Glucose effectiveness (Sg) was greater in the higher intake group, 0.03 ± 0.03 $\mu\text{g/mL}$, compared to the lower intake group 0.02 ± 0.01 ($P = 0.1257$). However, it did not attain statistical significance even after controlling for body weight ($P = 0.1337$) and lean mass ($P = 0.2044$).

II. Lipid profile

Total-C in the higher intake group was 148 ± 14.12 mg/dl compared to 171.8 ± 36.22 in the lower intake group ($P = 0.0354$). Moreover, LDL-C levels showed a trend in the higher intake group (91 ± 14.77 mg/dl) compared to the lower intake group (110.4 ± 34.96 mg/dl) without attaining a statistical significance ($P = 0.0654$). The higher intake group had a HDL-C of 34 ± 10.22 mg/dl, and the lower intake group had a HDL-C of 34.5 ± 6.69 ($P = 0.3993$). The total-C to HDL-C ratio decreased, but not significantly, between the two groups with the higher intake group having a ratio of 4.8 ± 1.35 and lower intake group having a ratio of 5.15 ± 1.40 ($P = 0.2645$). There was also no statistical difference between TG levels in the two groups with the higher intake group having 125 ± 54 mg/dl, and the lower intake group having 133 ± 77.4 mg/dl ($P = 0.3934$). The metabolic profile data was also obtained (Table 3).

III. Relationships between vitamin D intake and metabolic profile

Vitamin D intake was positively correlated to total caloric intake ($r = 0.77$; $P = 0.0001$; Figure 2a) and total caloric intake adjusted to body weight ($r = 0.77$; $P = 0.0001$; Figure 2b). Si adjusted to lean mass ($r =$

0.57 ; $P = 0.014$). Moreover, vitamin D intake adjusted to total dietary intake was positively correlated to Si adjusted to body weight ($r = 0.63$; $P = 0.004$), Si adjusted to lean mass ($r = 0.57$; $P = 0.012$), Sg ($r = 0.53$; $P = 0.016$; Figure 2c) and Sg adjusted to body weight ($r = 0.52$; $P = 0.018$; Figure 2d).

Discussion

Metabolic dysfunction following SCI is characterized by insulin resistance, glucose intolerance, and dyslipidemia. The purpose of this study was to investigate the role of dietary vitamin D intake on metabolic outcomes including carbohydrate and lipid profiles in the SCI population. The findings highlight that the daily dietary intake of vitamin D in persons with SCI does not meet the recommended guidelines for adults; the intake of the higher vitamin D intake group was only a third of the daily recommendation. Overall, the results show that after controlling for age, weight, gender, level of injury, matched based on age, weight, level and completeness of injury, and time since injury, higher vitamin D intake may improve the lipid profile, as it showed a significant reduction in total-C, and a non-significant decrease in LDL-C and TG. Moreover, high vitamin D intake is associated with greater improvement in Sg and Si, which reflects improvement in glucose homeostasis in persons with SCI.

The results suggest that the high vitamin D intake group consumed greater total caloric intake with similar macronutrients compared to the low vitamin D intake. However, the effects of vitamin D intake on the metabolic profile was still significant even after adjusting for the total dietary intake, suggesting that the effect is not derived by the total caloric consumption but by how much dietary intake is rich in vitamin D. This is important, because we were able to control for the other variables possibly influencing the metabolic and lipid profiles, strengthening the argument that vitamin D may influence these profiles independent of total caloric intake.

Vitamin D and glucose effectiveness/insulin sensitivity

We did not observe any statistical differences in Si or Sg between the two groups. It is well established that vitamin D deficiency reduces insulin secretion and increases the prevalence of T2DM.^{2,6,16–27} However, strong associations were noted between vitamin D intake and carbohydrate profile as measured by Si and Sg. A previous study showed that in 126 healthy glucose-tolerant subjects of various racial and/or

Table 4 Metabolic profile in 20 men with motor complete SCI based on their vitamin D intake.

	Fasting Glucose (mg/dl)	LDL (mg/dl)	HDL (mg/dl)	Total Cholesterol	Total Cholesterol:HDL Decimal	Total Cholesterol:HDL Ratio Fraction	TG(mg/dl)	Si	Si/weight	Si/Lean Mass	Sg	Sg/Body weight	Sg/Lean Mass
High Vit. D	79	84	54	158	2.9	2.9:1	100	20.3	0.321	N/A	0.099	0.001566	N/A
	82	93	33	143	4.3	4.3:1	86	139.7	N/A	N/A	0.045	0.000479	0.000848
	78	94	24	141	5.8	5.9:1	117	0.04	0.00	0.000621	0.019	0.000136	0.000288
	90	110	22	153	6.9	7.0:1	105	1.6	0.017	0.031431	0.017	0.000182	0.000344
	98	106	32	180	5.6	5.6:1	208	2.7	0.041	0.069325	0.017	0.000258	0.000439
	91	71	38	129	3.3	3.4:1	116	0.06	0.001	0.001440	0.031	0.000379	0.000686
	101	74	47	145	3.1	3.1:1	67	0.49	0.007	0.012126	0.010	0.000139	0.000251
	88	104	26	145	5.6	5.6:1	75	13.5	0.188	0.280050	0.036	0.000498	0.000744
	123	104	28	153	5.5	5.5:1	227	1.8	0.025	0.037221	0.020	0.000287	0.000423
	120	74	31	135	4.3	4.4:1	150	0.21	0.002	0.003994	0.017	0.000140	0.000317
Mean± SD	95.0± 15.8	91.0± 14.8	34.0± 10.2	148± 14.1	4.8± 1.2	4.8± 1.2	125± 54.2	18.0± 43.3	0.07± 0.11	0.05± 0.09	0.03± 0.03	0.0004± 0.0004	0.0005± 0.0002
Low Vit. D	80	74	42	131	3.1	3.1:1	77	4.4	0.066	0.102354	0.024	0.000369	0.000568
	78	178	35	237	6.8	6.8:1	91	2.1	0.024	0.042612	0.032	0.000370	0.000655
	106	152	34	207	6.1	6.1:1	103	0.2	0.001	0.002686	0.021	0.000156	0.000290
	102	72	39	127	3.2	3.3:1	82	4.3	0.044	0.070906	0.034	0.000349	0.000563
	86	112	38	200	5.3	5.3:1	158	1.7	0.032	0.045859	0.019	0.000355	0.000503
	106	92	25	179	7.2	7.2:1	311	0.9	0.010	0.016139	0.012	0.000150	0.000234
	85	126	35	172	4.9	4.9:1	56	3.1	0.037	0.068008	0.009	0.000113	0.000207
	101	117	28	165	5.9	5.9:1	98	3.1	0.029	0.062061	0.018	0.000172	0.000370
	91	75	25	130	5.2	5.2:1	148	0.35	0.004	0.006624	0.012	0.000131	0.000227
	105	106	44	170	3.9	3.9:1	209	1.1	0.014	0.021616	0.024	0.000295	0.000460
Mean± SD	94.0± 11.2	110.4± 34.9	34.5± 6.7	171.8± 36.2	5.2± 1.4	5.2± 1.4	133.3± 77.4	2.1± 1.5	0.03± 0.02	0.04± 0.03	0.04± 0.03	0.0002± 0.0001	0.0004± 0.0002

Figure 2 Relationships between vitamin D intake and daily caloric intake or daily caloric intake adjusted to body weight (both a & b, $r = 0.77$; $P = 0.0001$) and glucose effectiveness (Sg; c, $r = 0.53$; $P = 0.016$) as well as Sg adjusted to body weight (d, $r = 0.52$; $P = 0.018$).

ethnic backgrounds, low vitamin D levels are associated with insulin resistance and β -cell dysfunction.^{18,25–27} Other studies have shown that vitamin D concentrations are positively correlated with insulin sensitivity^{2,17,24–30} and glucose tolerance.^{24,30} Based on the aforementioned evidence, we hypothesized that a higher vitamin D intake would positively impact the metabolic profile by increasing insulin sensitivity and decreasing glucose intolerance. However, our results did not attain statistical significance because of the vast variability in insulin response to the IVGTT in the higher intake group and three outliers were identified. It is possible that this high variability in insulin response may be linked to body composition parameters similar to ectopic adiposity and regional distribution of body fat^{8,9}. Additionally, vitamin D intake for the higher intake group may not have been high enough to elicit significant changes in Si and Sg. Future studies with larger sample populations and a larger range in vitamin D intake might show significant changes to the insulin and glucose profiles in SCI populations.

Vitamin D and lipid profile

Despite consuming far less vitamin D than recommended, it appears that higher vitamin D

consumption may improve aspects of the lipid profile in persons with SCI, with a statistically significant reduction in total-C in the high vitamin D intake group. The total-C in both groups were within the normal limits. However, if the cardiovascular disease risk prediction model is used from the highly-regarded Framingham Heart Study, one can see that a statistically significant reduction in total-C can decrease risk of cardiovascular disease.³¹ Additionally, a study showed that a 0.5 mmol/L reduction in total-C results in a 10.4% reduction in coronary heart disease event rates.³² That total-C reduction is less than in our study where we had a 23.8 mg/dl or 0.62 mmol/l decrease in total-C in the high intake group. Another study found that coronary heart disease risk is progressively higher at every cholesterol level from 160 mg/dl.³³ This finding supports that the lower total-C in the high intake group compared to the low intake group is important in decreasing risk of heart disease. A potential reason for the total-C being within normal limits was that individuals from the database did not have abnormal lipid profiles and were overall young. Previous studies have shown vitamin D levels to be inversely related to LDL-C and TG levels.^{7,11–13,34,35} Our results agree with a recent meta-analysis which demonstrated the effects of vitamin D on lipid profile

in T2DM patients.³⁴ The findings showed that higher vitamin D levels corresponded to decreased serum levels of total-C, LDL-C, and TG, and negligible changes to HDL-C serum levels.³⁴

Vitamin D may improve lipid profile independent of changes in body composition

Interestingly, the improvement in lipid profile was still present after controlling for body weight. This was surprising because the correlation between vitamin D deficiency and obesity is well-documented.^{2,4,24,37–39} The prevalence of vitamin D deficiency is 24% higher in overweight subjects and 35% higher in obese subjects.⁴ This has been attributed to vitamin D storage in adipose tissue or being diluted throughout the enlarged fat mass, and thus being less available for use in the body, as shown in multiple studies involving able-bodied populations.^{2,24,37–39} We propose that vitamin D can improve the lipid profile independent of body mass via its role as a regulator of inflammation. Obesity causes chronic systemic sub-acute inflammation;^{40,41} obesity and diets high in fat³⁶ can both induce lipid accumulation in the liver (liver steatosis) leading to increased production of inflammatory cytokines⁴⁴ and chronic hepatic inflammation.^{44–46} Hepatic inflammation can induce hyperlipidemia due to decreased liver lipid catabolism.⁴⁶ Vitamin D deficiency has been shown to exacerbate liver steatosis through the activation of innate immune system pathways,⁴³ and in diabetic patients, vitamin D treatments have been shown to reduce inflammation.^{38,47} We propose that higher vitamin D intake may improve lipid profiles by decreasing hepatic inflammation and improving liver function. However, additional studies will need to be completed to evaluate this hypothesis after SCI.

Furthermore, adiponectin, a protein involved in glucose and lipid metabolism, has also been shown to decrease inflammation and liver steatosis and improve insulin sensitivity.⁴² The exact relationship between vitamin D and adiponectin is unclear, but a positive association between vitamin D and adiponectin serum levels has been demonstrated. This association was independent of body mass⁴³ and may also play a role in the improved lipid profile possibly induced by higher vitamin D intake.

Increasing vitamin D serum levels metabolism and body composition

Increasing vitamin D intake in the SCI population could be a relatively easy way to positively impact many different variables simultaneously. Vitamin D plays a role in both muscle repair/hypertrophy and bone mineral homeostasis;^{48–51} low vitamin D levels might slow or

limit the muscle and bone hypertrophy induced by exercise. Additionally, people with dyslipidemia are predisposed toward insulin resistance, and there is evidence that dyslipidemia may play a role in inducing insulin resistance and T2DM. Environmental stressors, like inflammation, may impair vitamin D action on insulin release from the pancreas.²⁴ Inflammation caused by obesity and vitamin D deficiency can induce insulin resistance.^{41,42,45} However, increasing vitamin D serum levels in patients with T2DM has been shown to decrease the serum levels of numerous markers of systemic inflammation.⁴⁷

Limitations

There were a number of limitations with this study. The sample size was small because every effort was considered to carefully match participants in both groups to minimize the effects of SCI characteristics on the studied variables. We have included only persons with paraplegia; however, we have 3–4 participants in each group that were T4 and above who may have suffered from isolated sympathetic preganglionic neuronal injury. This may have influenced our results considering the role of sympathetic nervous system on the metabolic profile. However, we evenly matched individuals based on the level of injury between both groups to minimize the effects of sympathetic variability on the metabolic profile. Additionally, serum vitamin D levels were not evaluated and vitamin D intake may not be related to serum vitamin D levels. Bauman *et al.* noted that the range of 25(OH)D for their chronic SCI sample was 10.2–19.6 ng/mL.⁵² We would expect our population to have a similar 25(OH) D range. Additionally, in a large meta-analysis of 16 randomized controlled trials, Cranney *et al.* found a significant association, where serum 25(OH)D concentrations increased by 1–2 nmol/L (or 0.4–0.8 ng/mL) for each additional 100 units of vitamin D3 intake.⁵⁴ If applied to this study, we would expect that the high vitamin D intake group, who consumed 4.59 mcg (183.6 IU) more than the low vitamin D intake group, would have a serum 25 (OH)D concentration of roughly 1.8 nmol/L to 3.7 nmol/L greater than the low vitamin D intake group. We are also unable to account for the amount of sun exposure for each subject. We tried to control for this by choosing participants that had SCI with similar level and severity, by including only those who suffered paraplegic and motor complete injuries with similar mobility deficit. Additionally, dietary recall was used which relies on the participants documenting daily caloric intake and assumes that the documented meals were typical meals for the participants. We have

previously shown that three-day dietary records can provide an accurate account of dietary intake.³⁶ This also does not account for the variability of vitamin D absorption from food, which can range from 55–99% depending on the food source and the presence of calcium.⁵⁴ The calcium intake for the higher vitamin D intake group was within the daily calcium recommendation (700–1300 mg/d),¹ while the calcium intake for the lower vitamin D intake group was significantly lower than that daily recommendation. Since none of the participants met the recommended daily dose of vitamin D, an arbitrary cutoff had to be made to separate the higher intake group from the lower intake group. The cutoff was made at 1.5 µg to split the 20 participants equally into two groups of 10. We also did not measure any inflammatory biomarkers in this study, but a strong correlation has been reported between the total-C/HDL-C ratio and serum levels of high-sensitivity C-reactive protein, an inflammation marker.⁵⁵ In our study, the total-C/HDL-C ratio was slightly lower in the higher vitamin D group compared to the lower vitamin D group suggesting that the higher vitamin D consumption may have decreased inflammation. Given the limiting factors of our study, additional studies with larger sample sizes and calciferol blood sample analysis are needed to confirm that vitamin D intake may favorably impact the lipid profile independent of body composition.

Conclusion

Persons with SCI suffer from hypovitaminosis of vitamin D as highlighted in the current findings. None of the 20 individuals met the recommended guidelines for vitamin D intake. The higher intake group consumed only one third of the daily recommendation. Given such low vitamin D intake, the results demonstrate that even a small increase in vitamin D intake may improve total-C independent of lean mass in the SCI population. Moreover, vitamin D adjusted to total dietary intake was positively correlated to parameters of carbohydrate profile in persons with SCI. Despite the limitations of the current work, the results are an important contribution to research because persons with SCI have a higher risk of developing dyslipidemia, and these results may suggest an easy way for clinicians to potentially improve total-C and carbohydrate profile in persons with SCI.

Supplies

- a) wheelchair scale: Tanita, Arlington Heights, Ill., USA
- b) Lunar Prodigy Advance: Lunar Inc., Madison, WI
- c) MinMod analysis: MinMod Inc., Pasadena, CA, USA

- d) radioimmunoassay kit: Linco Research, St. Charles, Mo., USA
- e) colorimetric assays: Sigma, Wako Chemicals US, Richmond, Va., USA; Thermo DMA, Roche, Minneapolis, Minn., USA
- f) SPSS version 21.0: IBM- SPSS, Chicago, IL

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