Original Article

Impact of Vitamin D Replacement on Liver Enzymes in Non-Alcoholic Fatty Liver Disease Patients: A Randomized, Double-blind, Placebo-controlled Trial

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Objective: To demonstrate the effect of vitamin D replacement on liver enzymes and inflammatory markers in non-alcoholic fatty liver disease (NAFLD) patients.

Materials and Methods: A randomized, double-blind, placebo-controlled trial was conducted at liver clinic at Vajira Hospital. Sixty eligible NAFLD participants, who have alanine transaminase (ALT) elevation with vitamin D insufficiency, were randomly enrolled into 2 groups and assigned to receive either a 40,000 IU per week of vitamin D replacement or a placebo for 20 weeks. Serum ALT, inflammatory markers, and transient elastography (TE) were compared before and after the 20-week vitamin D replacement period to evaluate the anti-inflammatory effect of vitamin D.

Results: At the beginning of the study, there were no statistical differences between the 2 groups of patients on the baseline characteristics, including gender, age, body mass index (BMI), ALT, inflammatory markers, transient elastogram and bioelectrical impedance analysis except diabetes and metformin use. At the end of the present study, ALT (-27.4±24.6 U/L, $p<0.001$), IL-6 (-0.5±1.1 pg/mL, $p = 0.036$) and ferritin (-52.8±96.3 ng/mL, $p = 0.006$) decreased significantly in the vitamin D group, while CAP (-4.8±26.1 dB/m), hsCRP (-0.4±1.7 mg/L) were non-significantly decreased. In addition, the decrease of serum ALT in the vitamin D group was significantly greater than in the placebo group (-27.4±24.6 U/L vs. -12.7±25.5 U/L, respectively, $p = 0.026$). Furthermore, all patients in the vitamin D group did not experience any side effects from hypervitaminosis D or hypercalcemia.

Conclusion: Oral vitamin D replacement could significantly reduce ALT in vitamin D insufficiency NAFLD patients with previous ALT elevation, which may mediate via alleviation of inflammatory mechanisms, without evidence of short-term adverse effects.

Keywords: NAFLD, Vitamin D, Replacement

J Med Assoc Thai 2020;103(Suppl.8): S105-12
Website: http://www.jmatonline.com

Non-alcoholic fatty liver disease (NAFLD) is common disease, about 10 to 35% of population depending on nationality and race[1,2] and may progress to cirrhosis or hepatocellular carcinoma[3]. NAFLD is currently considered as a results from a "multiple-hits hypothesis" which originated with simple steatosis and subsequently inflammation of the hepatocytes by variety of mechanisms[4]. There are evidences of relationship between the stage of lacking vitamin D and insulin resistance, diabetes, and metabolic syndrome[5]. These studies lead to question about relationship of vitamin D and NAFLD.

Vitamin D is important factor for various systems, especially to keep balancing calcium level in blood and bone. Vitamin D receptors are found not only in skeleton, kidney and intestine but also in other organs including immune system, endocrine gland, muscle, brain, and liver. Thus, Vitamin D is proposed to has other roles besides skeletal system[6]. Furthermore, vitamin D controls over 200 genes both direct and indirect methods which are responsible for apoptosis, cell proliferation, differentiation, and inflammatory response[7]. Declination in vitamin D level found significantly in NAFLD patients compared with normal people, which associated with severity of steatosis, inflammation, and fibrosis of the liver[8]. Although the relationship and mechanism between vitamin D and NAFLD are uncertain, recent animal study showed that vitamin D has significant role on controlling oxidative stress and pro-inflammatory cytokine production[9] which are alleviated by vitamin D supplementation[10]. Nakano et al showed that sunlight therapy could improve insulin resistance and fatty liver, considering from liver pathology of necrosis, inflammation, and fibrosis[11]. Recently, Sharifi et al demonstrated that the increasing of vitamin D level from supplementation improved inflammatory biomarkers in adults with NAFLD but benefit on liver enzymes remained unclear[12]. Therefore, we aim demonstrate benefit of vitamin D replacement on liver enzyme reduction and

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How to cite this article:

Boonyagard S, Techathuvanan K. Impact of Vitamin D Replacement on Liver Enzymes in Non-Alcoholic Fatty Liver Disease Patients; A Randomized, Double-blind, Placebo-controlled Trial. J Med Assoc Thai 2020;103 (Suppl.8): S105-12.

doi.org/10.35755/jmedassocthai.2020.S08.12052

inflammatory markers in non-alcoholic fatty liver disease patients with vitamin D insufficiency.

Materials and Methods

Study designs

The present study was a randomized, double-blind, placebo-controlled trial with parallel design that was conducted in Faculty of Medicine Vajira Hospital, Navamindradhiraj University from January 2015 to December 2018 and approved by Institute Review Board (IRB No. 086/57).

Study population

Patients aged between 18 and 70 years who were diagnosed with NAFLD by ultrasonography and increased levels of alanine transaminase (ALT) were recruited from the outpatient clinic of Faculty of Medicine Vajira Hospital, Navamindradhiraj University. Serum levels of ALT higher than 1.5 times of upper normal limit for two episodes in 3 months with serum vitamin D level <30 ng/ml were indications as inclusion criteria. Exclusion criteria were (1) alcohol consumption greater than 14 drink/week in women and 21 drink/week for men; (2) pregnancy and nursing; (3) known hepatic diseases such as hereditary hemochromatosis, Wilson's disease, and a1-antitrypsin deficiency; (4) history of jejunoileal bypass surgery or gastroplasty; (5) using total parenteral nutrition in the past 6 months; (6) taking potential hepatotoxic drugs such as high doses of synthetic estrogens, methotrexate, amiodarone, and chloroquine; and (7) history of hypothyroidism, Cushing's syndrome, renal failure, and kidney stones. Serum calcium levels >10.6 mg/dl and using of vitamin D, vitamin E, and calcium supplements during the last 6 months were also excluded. All subjects signed the written informed consent to participate in the present study.

Sample size calculation

We calculated sample size by using data from previous vitamin D supplement study[12]. Totally, 28 subjects were selected for each arm of our trial to detect a change of 30% in the ALT level with 90% power and 5% significance. In order to cover possible dropouts, 10% more subjects were added to sample size.

Methods

Participants were randomly assigned to intervention or control groups by computer random number generator. Randomization and allocation were concealed from the researchers and participants until the statistical analysis was completed. Participants either received 40,000 IU vitamin D2 (Calciferol®, the British Dispensary (LP), Thailand) or a similar capsule of placebo every 7 days for 5 months. Compliance was assessed by unused pill count. Height, weight, waist and hip ratio, and body component of each participant were measured at baseline and at the end of study. Body component was calculated using bioelectrical impedance analysis (BIA) (InBody370®, InBody Co, Ltd; Seoul, Korea). At the beginning, demographic data and history of diseases, medications, and supplements were obtained from the patients. Subjects were advised not to take any vitamin D, calcium, and other supplements during the present study. Lifestyle modifications regarding restriction of high carbohydrate-high fat diet and increasing physical activity level were recommended to all study participants as a standard care of NAFLD for 3 months before recruitment. Transient elastography (Echosens FibroScan® 502 Touch, Valor Health Thailand) was performed at baseline and after finishing the present study by the same examiner blinded to the groups to evaluate steatosis and fibrosis of the liver. Steatosis of the liver was graded as S0 to S4 based on Controlled Attenuation Parameter (CAP) score and fibrosis was graded from F0 to F4 based on liver stiffness.

Outcome measurements

Primary outcome is changes in serum ALT levels. Secondary outcome measures included HOMA-IR, inflammatory biomarkers, steatosis, and liver stiffness grading.

Biochemical analysis

Complete blood count, liver function test, glomerular filtration rate, lipid profile, fasting blood glucose levels, fasting insulin concentrations were measured. The HOMA-IR was calculated using the formula HOMA-IR = fasting glucose (mg/dl) x fasting insulin (μU/ml)/405. Serum 25(OH)D3 levels were used to determine vitamin D status defined on the basis of serum concentrations of 25(OH)D3 as sufficient (≥30 ng/ml), insufficient (20 to 30 ng/ml), and deficient (<20 ng/ml) in our study the authors included only insufficient and deficient of vitamin D. Serum calcium was measured to monitor for vitamin D intoxication. High-sensitive C-reactive protein (hs-CRP), Interleukin-6 (IL-6), ferritin and gamma-glutamyl transferase (GGT) were measured for using as the inflammatory markers.

Statistical analysis

Distribution of data related to normality was assessed by Kolmogorov-Smirnov test. Data with normal or non-normal distribution are reported as mean (standard deviation) or median (25^{th}, 75^{th} percentile), respectively. Comparisons of changes (endpoint minus baseline) after 5 months of intervention between groups were done by independent t-test or Mann-Whitney U test. Paired t-test or Wilcoxon Paired rank test was used for within-group comparisons (pre-and post-intervention values in each group). To control confounding variables, analysis of covariance (ANCOVA) test was used to determine the differences between the two groups post-intervention, while adjusting for baseline measurements and covariates. Differences in proportions were evaluated by χ^2 or Fisher's exact tests. Additionally, to compare differences in proportions of ordinal variables between two related groups, we used the non-parametric sign test. Analysis was conducted using SPSS version 17 statistical software (SPSS Inc, Chicago, Ill). Two-sided p-values ≤ 0.05 were considered

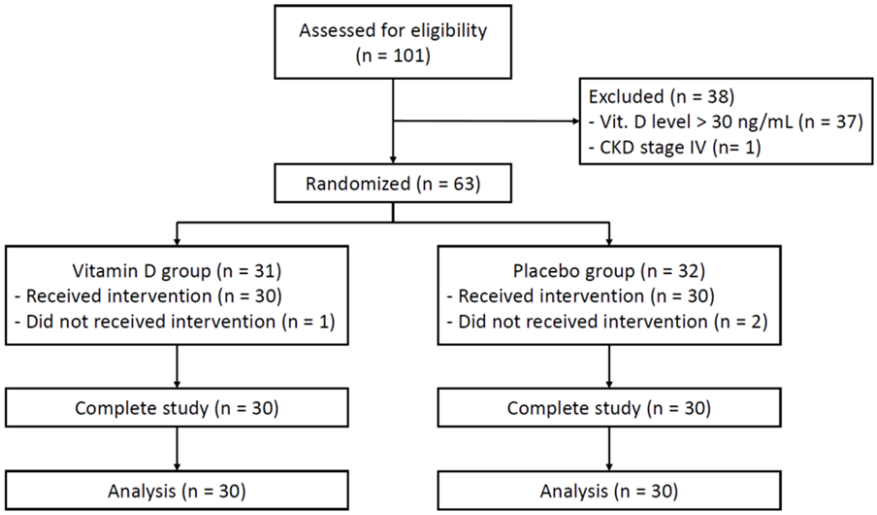

Figure 1. Participant flowchart of the present study.

statistically significant.

Results

We enrolled 63 patients who fulfilled the selection criteria and consented. They were randomized to receive vitamin D (n = 31) or placebo (n = 32), 3 patients were not received any intervention (1 in vitamin D and 2 in placebo groups) (Figure 1). Baseline demographic, laboratory, anthropometric features, steatosis and liver stiffness of these 60 patients were similar in both groups, except for higher of diabetes (17 vs. 7, $p = 0.017$) and metformin use (16 vs. 6; $p = 0.007$) in vitamin D group (Table 1). The 60 patients for analysis included 29 male (48.2%), mean age was 53.7±9.6 years and mean body weight was 75.9±15.4 kg. Fifty-seven percent of patients has diabetes and 78% has dyslipidemia. Baseline serum ALT was 76±24 U/L, vitamin D level was 20.4±5.6 ng/mL. Initial CAP and liver stiffness were 320±44 dB/m and 10.4±6.7 kPa.

At 20 weeks following vitamin D replacement, there were a statistically significant increase in 25(OH)D concentration in the vitamin D group, whereas placebo group was not (16.3±5.7 ng/mL vs. 0.1±3.9 ng/mL, $p<0.001$). There were neither change in the body weight, waist-hip ratio and body composition except for the skeletal muscle mass which increased in patients with vitamin D group (0.5±1.1 kg vs. -0.2±0.9 kg; $p = 0.009$) (Table 2).

Laboratory evaluation showed ALT was significantly decrease in vitamin D group (74.8±19.2 U/L vs. 47.3±17.6 U/L; $p<0.001$) and also significantly different between both groups (-27.4±24.6 U/L vs. -12.7±25.5 U/L; $p = 0.026$) (Figure 2) as same as decline of ferritin (-52.8±96.3 ng/mL vs. 0.7±72.5 ng/mL; $p = 0.018$). An analysis of changes in IL-6 over the 20 weeks showed a statistically significant decrease in vitamin D group, but between-group non-significant (-0.5±1.1 pg/mL vs. -0.1±1.5 pg/mL; $p = 0.365$). Even though, a comparison of HOMA-IR, CAP, steatosis grade over a period of 20 weeks from the time of the initiation of vitamin D replacement showed no significant different in both within- and between-group. CAP tended to decrease after vitamin D replacement and increase in the placebo group (-4.8±26.2 dB/m vs. 2.7±30.9 dB/m; $p = 0.316$), as well as HOMA-IR (-0.3±2.3 vs. 0±2.3; $p = 0.532$). Whereas hsCRP was significantly increase in the placebo group and decrease from baseline in patients with vitamin D replacement but no different between group (0.7±1.5 mg/L vs. -0.4±1.7 mg/L, $p = 0.234$).

Comparison of liver stiffness at the end of this study showed significant decrease from baseline (11.15±6.65 kPa to 10.06±6.53 kPa; $p = 0.002$) in the vitamin D group while no change in placebo group (Figure 3). However, vitamin D replacement did not make any change in GGT after 20 weeks intervening in NAFLD patients. At the end of this study, there was no any adverse effects including hypervitaminosis D or hypercalcemia.

Discussion

The present study demonstrates that vitamin replacement with 40,000 IU of vitamin D2 once a week for 20 weeks in non-alcoholic fatty liver disease patients with ALT elevation and vitamin D insufficiency had significantly effects on reduction of serum ALT and ferritin levels. Moreover, it also contributes to decrease IL-6 and liver stiffness measurement on transient elastography. The changes in these parameters were not associated with significant changes in the dose of any medication and lifestyle, which might be implicated from no change of body fat compositions. However, it did not change on CAP or grades of hepatic steatosis and fibrosis.

Table 1. Baseline demographic data

	Vitamin D group (n = 30)	Placebo group (n = 30)	*p*-value
Male gender, n (%)	11 (36.7)	18 (60)	0.071
Age (years)	55.5 (8.2)	52 (10.9)	0.166
Body weight (kg)	75.3 (16.6)	76.4 (14.7)	0.786
Body mass index (kg/m^2)	28 (6.8)	28.3 (3.9)	0.812
Underlying diseases, n (%)			
Diabetes mellitus	17 (56.7)	7 (23.3)	0.017*
Hypertension	15 (50)	14 (46.7)	0.796
Dyslipidemia	25 (83.3)	22 (73.3)	0.347
Medications, n (%)			
Fenofibrate	6 (20)	4 (13.3)	0.488
Statin	16 (53.3)	10 (33.3)	0.118
Metformin	16 (53.3)	6 (20)	0.007*
Thiazolidinedione	2 (6.7)	0	0.15
Vitamin D (ng/ml)	19.6 (5.8)	21.3 (5.5)	0.235
Transient elastography			
CAP (dB/m)	316.8 (44.2)	323.2 (45.9)	0.584
Steatosis grade	3.5 (0.8)	3.5 (0.9)	0.881
Liver stiffness (kPa)	11.2 (6.7)	9.8 (6.9)	0.435
Fibrosis stage	2.3 (1.6)	2 (1.6)	0.367
Body component			
Waist-hip ratio	1 (0.1)	0.9 (0.1)	0.152
Body fat (%)	35.5 (6.2)	34 (5.8)	0.339
Body fat mass (kg)	27.7 (6.5)	26.9 (7.4)	0.656
Skeletal muscle mass (kg)	24.4 (6.2)	27.1 (6.3)	0.092
GFR (ml/min)	89.5 (13.2)	93.9 (16.6)	0.268
Fasting blood glucose (mg/dl)	119.7 (32.6)	108 (18)	0.092
HOMA-IR	5.9 (3.4)	4.9 (3.4)	0.216
HbA1C (%)	6.5 (1)	6.2 (0.6)	0.169
Liver function test			
AST (U/L)	54 (17)	53 (21)	0.791
ALT (U/L)	75 (19)	79 (29)	0.551
ALP (U/L)	86 (30)	78 (19)	0.217
Albumin (g/dl)	4.5 (0.2)	4.6 (0.2)	0.668
Lipid profile			
Cholesterol (mg/dl)	194 (52)	193 (39)	0.971
HDL (mg/dl)	51 (9)	48 (10)	0.161
LDL (mg/dl)	122 (38)	132 (38)	0.333
Triglyceride (mg/dl)	188 (201)	157 (73)	0.431
IL-6 (pg/ml)	3.8 (1.8)	3.8 (2.5)	0.951
Ferritin (ng/ml)	242 (184)	349 (298)	0.099
hsCRP (mg/l)	3.1 (3)	2.4 (3)	0.374
GGT (U/L)	84 (67)	86 (102)	0.959

Data are expressed as mean (SD) unless specified

Table 2. Comparisons of the changes from baseline to end point measures for parameters variables in vitamin D and placebo groups

Variable	Vitamin D group (n = 30)		Placebo group (n = 30)		*p*-value[a]
	Mean (SD)	Mean change	Mean (SD)	Mean change	
Body weight (kg)					
Baseline	75.3 (16.6)	-0.7 (1.5)	76.4 (14.7)	-0.5 (1.7)	0.807
20 weeks	73.4 (15.9)		74.6 (16.6)		
p-value[b]	0.075		0.285		
ALT (U/L)					
Baseline	74.8 (19.2)	-27.4 (24.6)	78.5 (28.5)	-12.7 (25.5)	0.026*
20 weeks	47.3 (17.6)		65.8 (35.5)		
p-value[b]	<0.001*		0.059		
Vitamin D (ng/ml)					
Baseline	19.6 (5.8)	16.3 (5.7)	21.3 (5.5)	0.1 (3.9)	<0.001*
20 weeks	35.9 (7.3)		21.4 (4.9)		
p-value[b]	<0.001*		0.788		
HOMA-IR					
Baseline	5.9 (3.4)	-0.3 (2.3)	4.9 (3.4)	0 (2.3)	0.532
20 weeks	5.6 (3.1)		4.9 (3.2)		
p-value[b]	0.080		0.284		
IL-6 (pg/ml)					
Baseline	3.8 (1.8)	-0.5 (1.1)	3.8 (2.5)	-0.1 (1.5)	0.365
20 weeks	3.4 (1.8)		3.7 (1.9)		
p-value[b]	0.036*		0.636		
Ferritin (ng/ml)					
Baseline	242.2 (183.7)	-52.8 (96.3)	349.3 (298)	0.7 (72.5)	0.018*
20 weeks	189.5 (112.1)		349.9 (333.4)		
p-value[b]	0.006*		0.959		
hsCRP (mg/l)					
Baseline	3.1 (3.1)	-0.4 (1.7)	2.4 (3)	0.1 (1.5)	0.234
20 weeks	2.7 (2.5)		2.5 (2.2)		
p-value[b]	0.173		<0.001*		
GGT (IU/L)					
Baseline	84 (67)	-9 (37)	86 (102).3	-8 (26)	0.926
20 weeks	76 (73)		78 (99)		
p-value[b]	0.217		0.119		
CAP (dB/m)					
Baseline	316.8 (44.2)	-4.8 (26)	323.2 (45.9)	2.7 (30.9)	0.316
20 weeks	312 (44.4)		325.9 (40.9)		
p-value[b]	0.323		0.64		
Steatosis grade					
Baseline	3.5 (0.8)	0 (0.5)	3.5 (0.9)	0.1 (0.6)	0.351
20 weeks	3.5 (0.9)		3.7 (0.6)		
p-value[b]	1.000		0.211		

Data are presented as mean (SD)
[a] t-test of difference between group, [b] Pair t-test of difference between baseline and 20 weeks; * indicated statistically significant; *p*-value <0.05

Table 2. Cont.

Variable	Vitamin D group (n = 30)		Placebo group (n = 30)		*p*-value[a]
	Mean (SD)	Mean change	Mean (SD)	Mean change	
Liver stiffness (kPa)					
Baseline	11.2 (6.7)	-0.3 (3.5)	9.8 (6.9)	0 (2.2)	0.743
20 weeks	10.1 (6.5)		10.6 (6.7)		
p-value[b]	0.002*		0.37		
Fibrosis stage					
Baseline	2.3 (1.6)	-0.1 (0.9)	2 (1.6)	-0.2 (0.9)	0.649
20 weeks	2.2 (1.6)		2.3 (1.5)		
p-value[b]	0.153		0.101		
Waist-Hip ratio					
Baseline	1 (0)	0	0.9 (0)	0	0.113
20 weeks	1 (0.1)		0.9 (0)		
p-value[b]	0.407		0.126		
Percent body fat (%)					
Baseline	35.5 (6.2)	-0.1 (1.8)	34 (5.8)	0.2 (1.1)	0.328
20 weeks	35.4 (6)		34.3 (5.6)		
p-value[b]	0.666		0.253		
Skeletal muscle mass (kg)					
Baseline	24.4 (6.2)	0.5 (1.1)	27.1 (6.3)	-0.2 (0.9)	0.009*
20 weeks	24.8 (5.9)		26.9 (6.1)		
p-value[b]	0.023*		0.193		

Data are presented as mean (SD)
[a] t-test of difference between group, [b] Pair t-test of difference between baseline and 20 weeks; * indicated statistically significant; *p*-value <0.05

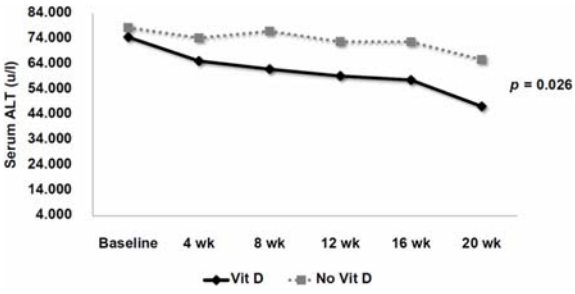

Figure 2. Serum ALT level during follow-up period.

Development of steatohepatitis from simple steatosis is mediated by multiple mechanisms, including lipotoxicity, inflammatory cascades, and hepatic stellate cell activation[13]. Multiple inflammatory markers were identified as biochemical mechanisms of NAFLD such as TNF-alpha, IL-6, adiponectin and IL-10[14]. In our study, vitamin D replacement in NAFLD patients resulted in significantly decreases in not only serum ALT levels but also ferritin and trend to decline of IL-6 level which may support mechanisms of inflammatory modulation. Previous studies that assessed the effect of vitamin D supplementation on systemic inflammation among patients with NAFLD, revealed inconclusive results[12,15,16]. Sharifi et al found no different in AST or ALT level between vitamin D supplement and placebo groups, however hs-CRP level trend to decrease on vitamin D group[12]. Dabbaghmanesh et al also revealed no significant different between vitamin D and placebo groups in terms of serum aminotransferase, ALP, and GGT[15]. The divergence of results may be from the differences in populations, type, dosage and duration of vitamin D supplementation on vitamin D level and metabolic effect[17]. Recent systematic review assessing the effect of vitamin D on serum metabolic profile among NAFLD patients revealed no significant reduction on liver enzymes[18]. The difference may be resulted from elevation of baseline ALT in our study compare to most normal baseline ALT in included trials of meta-analysis. The other possible pathogenesis is insulin resistance. Many trials demonstrated benefit of vitamin D supplement on insulin

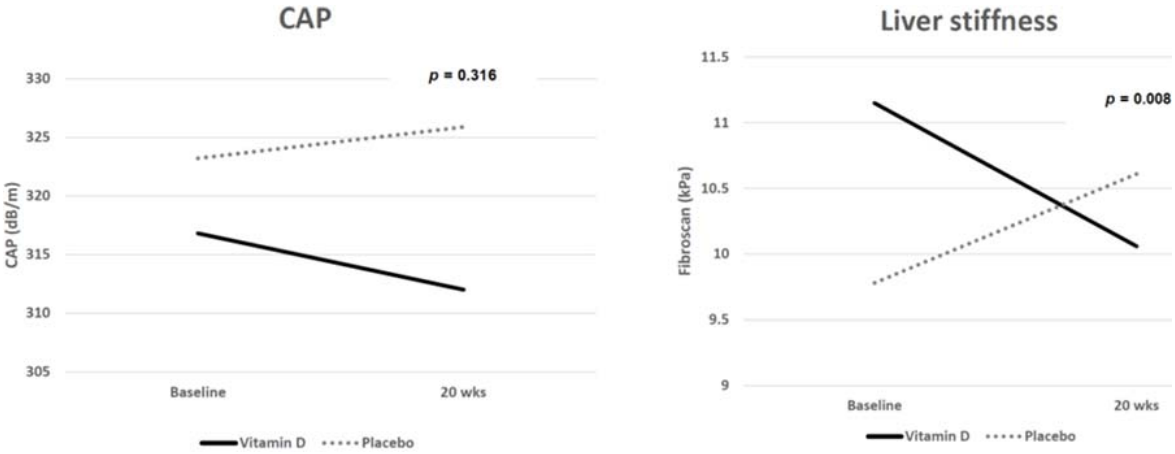

Figure 3. CAP and liver stiffness measurement by transient elastography at baseline and end of study.

sensitivity indices[19,20]. Anyway, the result of randomized controlled trail did not show these effects[21] which similar with our result that no significant decrease of HOMA-IR. Our study has more diabetic patients and higher metformin use in vitamin D group may confound the results due to alleviation effect of metformin on liver enzymes[22]. The decline of fibrosis measurement by transient elastography was significant lower in vitamin D group than placebo group in our study which likewise Taghvaei et al study revealed significant reduction of fibrosis in vitamin D group[16]. Though liver stiffness by transient elastography reflect fibrosis, elevation of aminotransferase may interfere the result by increase liver stiffness score[23]. The reduction of fibrosis in vitamin D group might be a result of ALT decline. Skeletal muscle showed expression of vitamin D receptor and considered mechanism of vitamin D-associated changes in morphology and function[24]. The elevation of skeletal muscle mass in vitamin D group may be another potential benefit of vitamin D replacement to metabolic health and fatty liver.

Our study tried to elucidate important of vitamin D replacement for deficiency or insufficiency ones with NAFLD which evaluate and adjust possible confounding factors such as medications, metabolic diseases, and lifestyle modification parameters. Limitation of the study are lack of histologic evaluation, specific inflammatory markers for vitamin D pathways and finally ALT may not the best marker for evaluate inflammation of the liver in NAFLD patients.

Conclusion

Oral vitamin D replacement could significantly reduce ALT in vitamin D insufficiency NAFLD patients with previous ALT elevation, which may mediate via alleviation of inflammatory mechanisms, without evidence of short-term adverse effects.

What is already known on this topic?

NAFLD is considered as multiple-hits mechanisms including hepatic steatosis, inflammatory response and fibrogenesis. Vitamin D is not only involved in skeletal system or calcium metabolism but also immune system, endocrine gland, and liver. Lifestyle modification is mainstay treatment of NAFLD treatment. Medical treatments are still question.

What this study adds?

Vitamin D replacement in vitamin insufficient NAFLD patients with ALT elevation may benefit for liver enzyme reduction.

Acknowledgement

We would like to thank Faculty of Medicine and Vajira Hospital, Navamindradhiraj University Research Fund for the funding support.

Conflicts of interest

The author declare no conflict of interest.

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ผลของการชดเชยวิตามินดีต่อเอนไซม์ตับในผู้ป่วยไขมันพอกตับที่ไม่ได้เกิดจากการดื่มแอลกอฮอล์

ศุภฤดี บุญญกาศ, กาจพงศ์ เตชธุวานันท์

วัตถุประสงค์: เพื่อศึกษาผลของการชดเชยวิตามินดีต่อเอนไซม์ตับและผลเลือดที่บ่งชี้การอักเสบในผู้ป่วยไขมันพอกตับ

วัสดุและวิธีการ: การศึกษาทดลองแบบสุ่มโดยมีกลุ่มควบคุมที่คลินิกโรคตับ คณะแพทยศาสตร์วชิรพยาบาล อาสาสมัครที่เป็นไขมันเกาะตับ ซึ่งมีเอนไซม์ตับสูงและระดับวิตามินดีในเลือดต่ำกว่าปกติ 60 ราย แบ่งออกเป็นสองกลุ่ม (30 รายต่อกลุ่ม) โดยให้วิตามินดีชดเชย 40,000 ยูนิต/สัปดาห์เป็นระยะเวลา 20 สัปดาห์ หรือยาหลอก ระหว่างการวิจัยอาสาสมัครจะได้รับการตรวจระดับเอนไซม์ตับ ผลเลือดที่บ่งชี้การอักเสบ ความยืดหยุ่นเนื้อตับ เปรียบเทียบก่อนและหลังรับยา

ผลการศึกษา: ลักษณะพื้นฐานของทั้งสองกลุ่มไม่แตกต่างกันได้แก่เพศ อายุ ดัชนีมวลกาย ระดับเอนไซม์ตับ ผลเลือดที่บ่งชี้การอักเสบ ความยืดหยุ่นของเนื้อตับ รวมทั้งการวิเคราะห์ความต้านทานร่างกายยกเว้นเบาหวานและการใช้ยา metformin หลังการวิจัย 20 สัปดาห์พบว่ามีการลดลงของระดับเอนไซม์ตับ ALT (-27.4±24.6 ยูนิต/ลิตร, ค่าพี น้อยกว่า 0.001), IL-6 (-0.5±1.1 พิโคกรัม/มล., ค่าพีเท่ากับ 0.036) และ ferritin (-52.8±96.3 นาโนกรัม/มล., ค่าพีเท่ากับ 0.006) อย่างมีนัยสำคัญในกลุ่มที่ได้รับการชดเชยวิตามินดี ส่วน CAP (-4.8±26.2 เดซิเบล/เมตร), hsCRP (-0.4±1.7 มก./ลิตร) ลดลงอย่างไม่มีนัยสำคัญ นอกจากนั้นยังพบว่าการลดลงของ ALT ในกลุ่มที่ได้วิตามินดีชดเชยมากกว่ากลุ่มยาหลอก (-27.4±24.6 ยูนิต/ลิตรเทียบกับ -12.7±25.5 ยูนิต/ลิตรตามลำดับ, ค่าพีเท่ากับ 0.026) ไม่พบผลข้างเคียงจากวิตามินดีเกินหรือภาวะแคลเซียมสูง

สรุป: การชดเชยวิตามินดีสามารถลดระดับเอนไซม์ตับ ALT ได้อย่างมีนัยสำคัญในผู้ป่วยไขมันพอกตับที่มีระดับเอนไซม์ตับสูงอยู่เดิม ซึ่งอาจเป็นผลจากการลดการอักเสบโดยไม่พบผลข้างเคียงระยะสั้น