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Effect of vitamin D3 supplementation on serum 25 (OH)D Levels, hand gripstrength, blood sugar levels, and cognitive function in the elderly

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ABSTRACT

Background: The aging process in the elderly can be caused by a decrease in vitamin D precursors and reduced Vitamin D levels due to impaired absorption of Vitamin D. Vitamin D plays a role in cognitive function, acts as an immunomodulator affecting blood glucose levels, promotes muscle atrophy, and affects the intranuclear VDR concentration and gene expression of VDR.

Objectives: To determine the effect of vitamin D3 supplementation on Serum 25(OH)D levels, hand grip strength, blood sugar levels, and cognitive function in the elderly.

Materials and Methods: This study used a quasi-experimental pre-posttest control group design with a total of 60 subjects included and divided into two groups. The treatment group received vitamin D3 at a dosage of 1000 IU/day for three months, while the control group was given a placebo. Blood serum levels were used to obtained serum 25(OH)D and blood sugar level. Hand grip strength values were measured by a hand grip dynamometer, and cognitive function was assessed using the Mini-Mental State Examination (MMSE) Questionnaire. The data was analyzed using the Wilcoxon test, and the bivariate analysis was performed using the Mann-Whitney test.

Results: Most subjects were between 60 and 92 years old and had a vitamin D deficiency. Significant (P<0,05) differences were observed in serum 25(OH)D levels, blood sugar levels, and cognitive function following the intervention. The differences in serum 25(OH)D levels were 8,50±6,17, blood sugar levels were -21,68±25,88, and cognitive function was 2,23±3,05. Additionally, hand grip strength increased after the intervention (mean=0,42±4,66) but was not statistically significant (P=0,633).

Conclusion: There is an improvement in cognitive function and a decrease in blood glucose levels, along with an increase in 25(OH)D levels after three months of vitamin D supplementation. However, hand grip strength did not significantly increase after supplementation.

Keywords: Vitamin D3 Supplementation; serum 25(OH)D; hand grip strength; blood sugar level; cognitive function; elderly.

BACKGROUND

According to statistic Indonesia, the number of elderly in 2019 the are more than 27,5 million people, or 10,3% of the total population. This number is predicted to increase to 57 million in 2045, representing 17,9% of the Indonesian population.[1] Central Java has the second-largest elderly population in Indonesia after the Special Region of Yogyakarta. In 2015, the elderly population in Central Java reached 11,7% and increased by 12,6% in 2017.[2] These figures indicate an increase in the global life expectancy of the elderly population, including in Indonesia.[3] Based on the 2010-2035 population projection data, Indonesia is expected to enter an aging period, with 10% of the population being over 60 years old. Between 2004 and 2015, the life expectancy in Indonesia showed an increase from 68,6 to 70,8 years. The projected life expectancy for 2030 to 2035 is estimated to be 72 years.[4] However, an increased life expectancy for older adults does not necessarily imply additional healthy years, although an extended lifespan is a notable achievement. With greater life expectancy, many more people will attain older ages, and because the risk of dementia increases exponentially with increasing age

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According to Government Regulation of the Republic of Indonesia Number 43 of 2004, an elderly person is defined as someone who has reached the age of more than 60 (sixty) years. The elderly population is growing rapidly in both developed and developing countries. The increasing number of elderly population in Indonesia will have both positive and negative consequences in the future. The positive impact will be seen if the elderly population remains healthy, active, and productive. Conversely, suppose health issues lead to heightened healthcare expenditures, reduced income, increased disability, lack of social support, and an inhospitable environment for the elderly. In that case, this demographic situation may present a significant burden.[2] The decline in the tissue's regenerative capacity and ability to maintain normal function due to aging makes the elderly more susceptible to injury or infection.[5,6] The prevalent conditions observed in the elderly include a decrease in muscle strength, alteration in glucose metabolism leading to an increase in blood glucose levels, and cognitive impairment linked to dementia.[7-9] These conditions are often associated with Vitamin-D deficiency in the elderly.[10-12]

Vitamin D is a fat-soluble steroid prohormone that can be produced in the skin through 7-dehydrocholesterol. Vitamin D also comes from food sources such as fish and supplements. Serum 25(OH)D is the most widely used indicator of Vitamin D status, due to its relatively stable and accurate bioavailability.[13]The Endocrine Society states that Vitamin D deficiency occurs when the serum 25(OH)D value is below 20 ng/ml.[14] The aging process in the elderly is associated with a reduction in skin thickness, leading to diminished synthesis of Vitamin D precursor in the skin. This, in combination with insufficient exposure to sunlight, reduced consumption of Vitamin D-rich foods, compromised absorption of Vitamin D in the intestine, and impaired hydroxylation process in the liver and kidneys, contributes to Vitamin-D deficiency in the elderly.[15]

Research shows that administering 800 IU of Vitamin D supplements to elderly individuals for 16 months has demonstrated effectiveness in enhancing the MMSE (Mini-Mental State Examination) scores, an assessment toll utilized for measuring cognitive level.[16] In the elderly, cognitive decline often correlates with the presence of dementia, a syndrome characterized by diminished cognitive function attributed to neurodegenerative and cerebrovascular processes.[17,18] Common signs and symptoms in elderly individuals with dementia include memory loss, difficulty in performing daily tasks, language problems, disorientation with time and place, inability to make decisions, and mood swings.[18] A study involving 74 elderly individuals residing in a nursing home found that 35% of the subjects had a Vitamin D deficiency.

Vitamin D has demonstrated the potential to reduce neurotoxicity and protect brain tissue from free radicals. Nitric oxide synthetase (iNOS) is responsible for producing nitric oxide, which, in elevated concentrations, can induce the formation of free radicals capable of inflicting damage on neurons and oligodendrocytes.[19] The involvement of Vitamin D in cognitive function is also influenced by the interaction of Vitamin D metabolites with the Vitamin D receptor (VDR), a component of the steroid receptor group. Vitamin D-25(OH)D3 and 1,25(OH)D3 metabolites have the ability to penetrate the blood-brain barrier and are involved in various metabolic and neuroprotective functions within the central nervous system. Furthermore, the 1-hydroxylase enzyme is responsible for the synthesis of Vitamin D and VDR, predominantly located in the hippocampus, cortex, and limbic system, which are pivotal regions for cognitive function.[20]

Moreover, the role of Vitamin D as an immunomodulator involves reducing cytokine production and lymphocyte proliferation. These processes have been implicated in the destruction of insulin-secreting β-cells in the pancreas. In addition, the islet β-cells express VDR and respond to 1,25(OH)D by increasing insulin production. The role of Vitamin D in arm muscle grip strength is mediated through the genomic pathway. Vitamin D, in the form of 1α,25(OH)2 D3, bind with VDR. Subsequently, this complex interacts with the heterodimeric partner, Retinoid X Receptor (RXR), forming the 1,25D-VDR-RXR complex. This complex is then transported to the nucleus, where it binds to the Vitamin D response element (VDRE) to initiate the transcription process. As a result of these signals, muscle cell proliferation is induced, leading to the conversion of myoblasts into myosin. This process initiates cell regeneration, increase the cross-sectional area of muscle fibers, and enhances the development of contractile filaments and muscle strength.

Considering the aforementioned background, it is crucial to maintain the adequacy of Vitamin D in the elderly. Studies have demonstrated that Vitamin D supplementation has been able to increase serum 25(OH)D levels in the elderly. Additionally, there is an urgent need for evidence regarding the clinical benefits of Vitamin D supplementation for the elderly, including its impact on quality of life and functional abilities.[21] Research pertaining to the efficacy of Vitamin D supplementation in improving cognitive function in the elderly is currently limited in Indonesia. Therefore, the authors aimed to investigate the advantages of Vitamin

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D supplementation in the elderly, specifically focusing on arm grip muscle strength, blood sugar levels, and cognitive function. This study aims to analyze the effect of Vitamin D3 supplementation on serum 25(OH)D levels, hand grip strength, blood sugar levels, and cognitive function in the elderly.

MATERIALS AND METHODS

This study utilized a quasi-experimental pre-posttest control group design and was performed at "*Panti Wredha Dharma Bakti*" Surakarta, Central Java, from July to September 2020. The samples were collected using the random sampling method. Sampling was conducted using purposive sampling method, according to the inclusion criteria. The sample size of the study was calculated using the sample size test formula for experimental design, so that the minimum sample size was 30 each group. A total of 60 subjects were recruited and divided into two groups. The treatment group received Vitamin D3 1000 IU/day in the morning for 3 months while the control group was given a placebo. Considering previous research by , where giving vitamin D3 supplements can significantly increase serum 25 (OH)D and MMSE scores in elderly people with dementia. The Vitamin D used was Pro-Vitamin D3 (Cholecalciferol) 25 mcg, which was produced by KALBE. Subject adherence was monitored by recording the intake of supplements or placebo every day and assisted by nurse at "*Panti Wredha Dharma Bakti*", using a checklist column.

The sample size for this study was calculated using population proportion estimation. A minimum of 27 subjects was allocated for each group, with an additional 10% added to anticipate subject dropout. Therefore, the total sample size was determined to be 30 subjects for each group. However, during the study, one subject dropped out due to the consumption of other supplements and refused to consume supplements provided by the researcher. As a result, the total number of subject in this study was 59 people. The research subjects were elderly individuals between the ages of 60 and 92 who met specific inclusion criteria: were attended primary school or its equivalent, did not consume Vitamin D supplements, did not smoke, did not drink alcohol, and were willing to participate in the research. Exclusion criteria for this study included experiencing severe side effects that necessitated discontinuation of Vitamin D supplements, refusal to continue the study, or death.

The independent variables of this study comprised blood glucose levels, hand grip strength, and cognitive function, while the dependent variable was Vitamin D3 supplementation. The confounding variables include energy, protein, carbohydrates, fat, Vitamin B6, Vitamin C, Vitamin E, and folate intake, physical activity, and BMI (nutritional status). Serum 25 (OH)D and blood glucose level were derived from venous blood serum samples. Serum 25 (OH)D was measured using VIDAS® 25 OH Vitamin Total (VITD) batch number REF 30 463 with Enzyme Linked Fluorescent Assay (ELFA) technique. Hand grip strength values were measured using a hand grip dynamometer, with the subject held the device with their right and left hands alternately and the largest value was recorded. The cognitive function was assessed using the Mini-Mental State Examination (MMSE) Questionnaire, which included 7 cognitive performance areas and a total of 11 questions, with a maximum score of 30. The cognitive performance areas included place orientation (maximum score 5 points), time orientation (maximum score 5 points), registration (maximum score 3 points), recall (maximum score 3 points), attention (maximum score 5 points), language ability (maximum score 8 points), and visual construction (maximum score 1 points). The total point value of 30 cannot be used as a whole, but it should be adjusted according to the length of the subject's education. For subjects with an education of 7 years old or below, a total score of 22 was considered normal. Subjects with an education of 8 years to senior high school (SMA) score of 24 points was considered normal. Subjects who have completed high school or equivalent and have a score of 25 was considered normal.

Dietary intake before the intervention was assessed using a Food Frequency Questionnaire (FFQ). During the intervention, dietary intake was monitored by visually observing food intake using Comstock three times a week; two times on weekdays and one time on weekends for three months. Data on food intake was then analyzed using NutriSurvey for Windows 2004 software to obtain nutrient analysis data. The energy, protein, fat, carbohydrates, and other micronutrients requirement were calculated based on Recommended Daily Allowance (RDA) 2019 and adjusted for different age groups. Dietary intake was considered 'adequate' if it met 80-110% requirements, 'excessive' if it exceeded ≥110%, and 'inadequate' if it fell below 80%. The body mass index (BMI) was calculated by dividing body weight by the square of height. BMI values were classified based on the Asia Pacific cut-off points where, BMI <18,5 kg/m^2 was categorized as underweight, normal if BMI ranges from 18,5 to 22,9 kg/m^2, overweight if BMI was between 23,0 and 24,9 kg/m^2, obesity

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grade I if BMI fell between 25,0 and 29,9 kg/m^2, and obesity grade II if BMI was ≥30 kg/m^2. The physical activity data was collected using the International Physical Activity Questionnaire (IPAQ) through interviews conducted in the past seven days of exercise. The physical activity scores were calculated following the IPAQ scoring protocol. These scores were categorized as 'low' if <600 MET-minutes/week, 'moderate' if 600-2999 MET-minutes/week, and 'high' if ≥3000 MET-minutes/week.

Data analysis was performed using the computer-based statistic program, SSPSS, which included univariate and bivariate analyses. Univariate analysis was used to describe subject's characteristics and data normality was assessed using the Shapiro-Wilk's test. The differences in Vitamin D levels and MMSE scores were analyzed using the Wilcoxon test. Additionally, the changes in the control and treatment groups were analyzed using the independent t-test. Moreover, comparative analysis of confounding variables between groups was conducted using the Mann-Whitney test. This research was approved by the Health Research Ethics Committee (KEPK) of the Faculty of Medicine, Diponegoro University/Dr. Kariadi General Hospital, under the reference number No.219/EC/KEPK/FK-UNDIP/V/2019.

RESULTS

Characteristics of the Subjects

Characteristics of the subjects include age, nutritional status, physical activity, Vitamin D levels, blood glucose levels, *Mini-Mental State Examination* (MMSE), and hand grip strength (HGS).

Table 1. Characteristics of the Subjects

Characteristic	Treatment (n = 30)			Control (n = 14)			*P-value*
	Mean ± SD	n	%	Mean ± SD	n	%	
Age (60-92 years)	71,97 ± 8,85	30	100	72,48 ± 8,22	29	100	0,818[a]
Nutritional Status (kg/m^2)							
Underweight (<18,5)		4	13,3		5	17,2	
Normal (18,5-22,9)		9	30,0		12	41,4	
Overweight (23,0-24,9)	22,86± 4,05	10	33,3	22,93 ± 4,95	2	6,9	0,957[a]
Obese I (25,0-29,99)		6	30,0		8	27,6	
Obese II (≥30,0)		1	3,3		2	6,9	
Physical Activity (MET)							
Low (<600)		8	26,7		14	48,3	
Moderate (600-2999)	855,00 ± 593,64	21	70,0	847,55±721,60	15	51,7	0,135[b]
High (>3000)		1	3,3		0	0,0	
Vitamin D (ng/mL)							
Deficiency (0-20)		21	70,0		24	82,8	
Insufficiency (21-29)	18,00 ± 8,45	6	20,0	14,49 ± 6,30	3	10,3	0,142[b]
Normal (30-100)		3	10,0		2	6,9	
Toxic (>100)		0			0	0,0	
HGS							
Normal	17,36 ± 7,83	1	3,3	14,30 ± 6,04	0	0,0	0,062[b]
Low		29	96,7		29	100,0	
Blood Glucose (mg/dL)							
Non-DM (<100)		6	20,0		6	20,7	
Uncertain (100-200)	118,60 ± 25,61	24	80,0	126,18 ± 38,73	23	79,3	0,688[b]
DM (>200)		0	0,0		0	0,0	
MMSE							
Severe		2	6,7		1	3,4	
Moderate	22,20 ± 5,90	7	23,3	20,62± 5,77	13	44,8	0,303[a]
Mild		7	23,3		8	27,6	
Normal		14	46,7		7	24,1	

[a]*Independent T-test*

[b]*Paired T-test*

In Table 1, the majority of the elderly subjects were between 60 to 92 years old, with an average age of 71,97 ± 8,85 in the treatment group and 72,48 ± 8,22 in the control group. The average nutritional status in the treatment group was 22,86 ± 4,05 with the highest percentage (33,3%, n=10) being overweight. In the control group, the average nutritional status was 22,93 ± 4,95, with the highest percentage (41,4%, n=12)

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having normal BMI. The majority of the subjects in both the treatment group (70,0%, n=21) and the control group (51,7%, n=15) engaged in moderate physical activity. The average MET score obtained was 855,00 ± 593,64 for the treatment group and 847,55 ± 721,60 for the control group.Most of the elderly subjects were found to be deficient in vitamin D, with the highest percentage at 70,0% (n=21) for the treatment group and 82,8% (n=24) for the control group. Additionally, both the control group (100,0%, n=29) and the treatment group (96,7%, n=28) exhibited low hand grip strength (HGS). Blood glucose levels were normal, and cognitive function was moderate for subjects in both the control and treatment groups.

Effect of Vitamin D3 Supplementation on Serum 25(OH)D Levels, HGS, Blood Glucose Levels, and Cognitive Function

Table 2. The Effect of Vitamin D3 Supplementation on Each Variable

Variable	Before (Mean ± SD)	After (Mean ± SD)	Δ Variable (Mean ± SD)	P-value
Serum 25 (OH)D (ng/mL)				
Treatment	18,00 ± 8,45	26,50 ± 6,80	8,50 ± 6,17	0,000[b]
Control	13,56 ± 3,05	13,49 ± 5,68	-0,07 ± 3,19	0,943[b]
P-value			0,000[a]	
HGS (KgF)				
Treatment	16,50 ± 8,60	16,92 ± 9,22	0,42 ± 4,66	0,633[b]
Control	15,03 ± 5,77	14,01± 7,37	-1,01 ± 4,95	0,288[b]
P-value			0,423[a]	
Blood Glucose (mg/dL)				
Treatment	118,62 ± 25,59	96,95 ± 25,48	-21,68 ± 25,88	0,000[b]
Control	126,85 ± 3,05	90,41± 16,58	-36,44 ± 33,75	0,000[b]
P-value			0,210[a]	
MMSE				
Treatment	22,37 ± 5,96	24,60 ± 6,75	2,233 ± 3,05	0,001[b]
Control	20,96 ± 3,05	21,54 ± 7,32	0,57 ± 3,05	0,316[b]
P-value			0,043[a]	

[a] *Independent T-test* *$p<0,05$
[b] *Wilcoxon test*

In Table 2, the effect of Vitamin D3 supplementation on each variable was presented. The results of the analysis indicated significant (P<0,050) differences in serum 25(OH)D levels, blood sugar levels, and cognitive function following the intervention. Specifically, the differences in serum 25(OH)D levels were 8,50±6,17, blood sugar levels were -21,68±25,88, and cognitive function was 2,23±3,05. Hand grip strength (HGS) increased (mean=0,42±4,66) following the intervention, but was not statistically significant (P=0,633).

Confounding Variable

The confounding variables in this study were energy intake, protein, fat, and carbohydrates, aswell as Vitamin D, folate, Vitamin C, Vitamin E, Vitamin B6, and physical activity.

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Table 3. Confounding Variable

Variable	Treatment Mean ± SD	Control Mean ± SD	P-value*
Energy (kkal)	1623,00 ± 161,38	1566,00 ± 296,99	0,21[a]
Protein (g)	58,50 ± 8,57	56,29 ± 11,93	0,19[a]
Fat (g)	56,31 ± 9,85	57,06 ± 111,16	0,08[a]
Carbohydrates (g)	224,06 ± 42,54	211,13 ± 53,29	0,29[b]
Fiber (gr)	9,78 ± 1,42	9,35 ± 1,54	0,11[b]
Vitamin D (mcg)	1,04 ± 0,63	0,85 ± 0,53	0,74[b]
Folate (µg)	186,71 ± 10,39	182,64 ± 21,48	0,45[a]
Vitamin C (mg)	37,87 ± 22,14	29,83 ± 14,07	0,34[b]
Vitamin E (mg)	4,97 ± 0,87	5,01 ± 0,76	0,91[b]
Vitamin B6	1,05 ± 0,19	1,01 ± 0,27	0,63[b]

[a]*Independent T-test* *$p<0,05$
[b]*Mann-Whitney test*

Table 3 indicates that there were no significant variations in confounding variables such as energy intake, protein, fat, carbohydrates, Vitamin D, folate, Vitamin C, Vitamin E, Vitamin B6, and physical activity.

DISCUSSION

The study involved 59 elderly in "Panti Wredha Dharma Bakti Surakarta" who were 60 to 92 years old. Most elderly subjects had a Vitamin D deficiency, with the highest percentage being 70,0% (n=21) for the treatment group and 82,8% (n=24) for the control group. Additionally, the research indicated that increasing age positively correlates with insulin resistance, reduced insulin synthesis, and inflammation. Insulin resistance in the elderly can be attributed to several factors. These factors include an elevation in body fat composition from 14% to 30%, decreased physical activity leading to a reduction in insulin receptors, changes in dietary patterns characterized by increased carbohydrate consumption, and alterations in neurohormonal function.[22,23]

According to research, 90% of the elderly population in India aged over 50 years have decreased level of vitamin D in their blood.[24] This deficiency is due to various factors such as inadequate intake, increased adiposity, reduced Vitamin D synthesis from the skin, decreased kidney and liver function, and limited exposure to sunlight.[25]

The intervention was conducted for three months period, during which the intervention group received Vitamin D3 cholecalciferol supplements at a dosage of 1000 IU/day, while the control group was administered a placebo. Following the intervention, there was an increase in 25(OH)D levels in the treatment group (mean=8,50±6,17) and a decrease in the control group (mean= -0,07±3,19). This indicates that Vitamin D supplementation can increase 25(OH)D levels in the elderly. This finding is consistent with a study by *Katja et al.* where the administration of 1000 IU Vitamin D for two months significantly increased serum 25(OH)D levels in 235 subjects aged 18-64 years old.[26] It is important to note that serum 25(OH)D levels are the primary biomarker for determining Vitamin D status in humans, as most of the circulating Vitamin D in the human body is in the form of 25(OH)D.[26,27] The control group did not experience an increase in 25(OH)D levels, as they were administered a placebo. In the elderly, Vitamin D deficiency often arises from combination of physiological and pathological factors. One of the most common factors is the reduced production of vitamin D in the skin, which decreases by 75% by the age of 70.[28] Additionally, eating difficulties and decreased appetite in the elderly indirectly lead to reduced food intake, as well as decreased calcium absorption linked to decreased in Vitamin D metabolism and impaired renal function. Pathological factors contributing to decreased Vitamin D levels in the elderly are related to organs involved in the digestion and metabolism of vitamin D.[26]

Moreover, aging leads to a decrease in hand grip strength, which is attributed to the transformation of muscle types, muscle-tight arrangements and the Excitation-Contraction (EC) process, genetic factors, and oxidative stress, such as increased IL-6 and TNF-α proapoptotic cytokines.[29] Type II muscle-tight is essential for anaerobic metabolism, and the decreased function of this muscle is the primary reason for the reduced hand grip strength. Additionally, reductions in neurotrophic factors, including serotonergic, cholinergic, adrenergic, dopaminergic, aminobutyric acid, and glutamatergic, contribute to hypo-excitability in the cortex, impaired

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motoric coordination, and diminished cortical plasticity, further affecting motoric performance.[8]

The study found that the hand grip strength of the treatment group increased (mean=0,42±4,66) after the intervention, but this increase was not statistically significant (P=0,633) with median 18 (2,6 – 34,5) KgF. On the contrary, the mean hand grip strength decreased (mean= -1,01±4,95) in the control group. The treatment group experienced increased hand grip strength due to vitamin D supplementation. This finding aligns with a study by *Pirrota et al.*, which found that providing 2000 IU of Vitamin D for ten weeks to 26 subjects over 65 years resulted in an 8-11% increase in muscle strength, although the increase was not statistically significant. The differences in the health conditions, functional status, and 25(OH)D serum levels of each subject before the intervention may have contributed to these findings.[30]

In another study, *Cavalcante et al.* found that providing postmenopausal subjects with a weekly dose of 6600 IU of Vitamin D for three months, or an average of 942 IU per day for the same duration, resulted in a significant increase in hand grip strength ($p<0.05$).[31] The study suggests that the effect of Vitamin D on hand grip strength is mediated through the genomic pathway, where Vitamin D in the form of 1α,25(OH)2 D3 binds to the Vitamin D Receptor (VDR). The VDR belongs to the steroid receptor group and has been found in the hippocampus, cortex, and limbic system, which are key areas for cognitive function.[32] VDR will interact with its heterodimeric partner, Retinoid X Receptor (RXR), to form the 1,25D-VDR-RXR complex. This complex will then be translocated to the nucleus and bind to the vitamin D response element (VDRE) to activate the transcription process. Signals from the VDR will induce muscle cell proliferation and transform myoblasts into myosin. This process will initiate cell regeneration, increase the cross-sectional area of muscle fibers, and enhance contractile filaments and muscle strength.[33,34]

The analysis results showed significant (P<0,05) differences in blood sugar levels. The blood sugar levels decreased by -21,68±25,88 in the treatment group and -36,44±33,75 in the control group. These findings are consistent with the research of *Fereira et al.*, which demonstrated that the administration of 1000 IU of Vitamin D3 for nine months to 160 post-menopausal women aged 50-65 years can significantly reduce blood glucose and metabolic parameters associated with other syndromes.[35] One possible explanation for the effect of Vitamin D on blood sugar levels involves the active form of vitamin D in the bloodstream, called 1.25(OH)D. This form of vitamin D acts as an immunomodulator by reducing cytokine production and lymphocyte proliferation. These two processes have been linked to the destruction of insulin-secreting β-cells in the pancreas. In addition, the β-cells in the islets of the pancreas express VDR and respond to 1,25(OH) by increasing insulin production.[36] Decreased blood glucose in control group more higher than treatment group, it may be caused by the factor of food intake that controlled and maintained by each individual. Another possible factor is the length of fasting before checking blood glucose levels because in this study the length of fasting for each respondent did not always match the specified time, which was 8-10 hours, some were more or less. Another possibility that affects blood glucose levels is physical activity and exercise. There are several things that cause blood sugar to rise, namely lack of exercise, increased amount of food consumed, increased stress and emotional factors, weight gain and age, and the impact of drug treatment, such as steroids.

Cognitive function involves acquiring, storing, retrieving, and processing knowledge, including speed of thinking, memory, visuo-perceptual, visuospatial, and visuo-constructive skills, language skills, attention, and executive function.[37] According to research by *Van Hooren et al.* (2007), age plays an important role in cognitive decline.[38] Cognitive decline is a common condition resulting from brain aging.

According to the research, following the intervention, there was a notable increase in the MMSE score in both the treatment group (mean= 2,23±3,05) and the control group (mean= 0,57±3,05). This finding indicates that vitamin D supplementation can significantly increase the cognitive function of the elderly. The increase in cognitive function within the treatment group was attributed to vitamin D supplementation, while various factors, such as differences in physical activity levels and the subject's education level, influenced the increase in cognitive function in the control group. The research conducted by *David J. Llewellyn* indicates a correlation between Vitamin D levels and MMSE scores in the elderly. It was found that elderly individuals with a deficiency in serum 25(OH)D were at 60% increased risk of experiencing substantial cognitive decline in MMSE scores. This decline in cognitive function is observed progressively on an annual basis. Moreover, elderly individuals with insufficient 25(OH)D exhibit an annual decrease in MMSE score of 0.7 compared to those maintaining adequate levels of 25(OH)D.[39] Furthermore, inadequate Vitamin D concentrations in the body elevate the susceptibility to cerebrovascular pathology, thereby triggering dementia through heightened occurrence of hypertension, diabetes, cardiovascular disease, and atherosclerosis.[40]

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The confounding variables in this study include energy, protein, fat, carbohydrates, vitamin D, folate, vitamin C, vitamin E, and vitamin B6 intake, as well as physical activity. The data analysis results presented in Table 3 revealed no significant differences in these variables between the control and treatment groups. As a result, the study findings indicated no discernible variance between the two groups. Research About Effect of Vitamin D for Elderly is importance, it is hoped that further research can be conducted on the relationship between vitamin D levels and elderly by considering subject homogeneity, sample calculation, better research design and involving factors that can affect vitamin D levels and handgrip strength.

CONCLUSION

Supplementation of Vitamin D3 increases serum 25(OH)D levels and cognitive function, while blood glucose levels decrease. There are significant differences in serum 25(OH)D levels, blood sugar levels, and cognitive function after the intervention. Hand grip strength experienced an increase after the intervention, but it is not statistically significant.

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