International Journal of Bio-Science and Bio-Technology
Vol.8, No.2 (2016), pp.255-264
http://dx.doi.org/10.14257/ijbsbt.2016.8.2.24

Effects of Orally-taken Vitamins on Blood-Homocysteine Levels and Cognitive Functions: Focusing on Senior Citizens with Mild Cognitive Impairments

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Abstract

This study was conducted on 48 senior citizens with mild cognitive impairments and it aims at examining changes in the blood-homocysteine levels and cognitive functions after taking vitamins orally. For analysis, Chi-Square test, Fisher's Exact test and independent t-test, Repeated Measure ANOVA, Contrast test, Repeated Measure ANCOVA, and Wilks' lambda test were carried out. In result, when senior citizens with mild cognitive impairments took vitamin pills, the blood-homocysteine level continuously reduced in week 4, week 8 and week 12, and cognitive functions continuously increased every week. Such results show that by having senior citizens with mild cognitive impairments orally take vitamin pills, which are relatively cheap and easy to take compared to other methods, it can prevent addition drop in cognitive functions and prevent dementia.

Keywords*: Blood homocysteine level, m\Mild cognitive impairment.*

1. Introduction

The national expected average life of Korean men as of 2010 is 77.2 years and for women is 84.1 years. The Korean society is experiencing rapid aging of the population and the rate of the population over 65 years of age in 2010 is 11% and it is expected that it will enter the aged society in 2018 at 14.3% [1]. With the increase of the senior population, there is also a rapid rise in various chronic diseases related to old age and Alzheimer's disease. Alzheimer's among senior citizens has recently received considerable attention from many people and has become a serious social issue. With the rapid increase in the senior population, Alzheimer's has become a disease receiving high levels of interest in our society and economic and social problems resulting from this are also rising [2]. From the dementia prevalence rate research conducted in 2008, it was found out that 8.4% of elderlies over 65 years old which is population of 42,000 have dementia and 1/4 of elderlies over 65 years old have cognitive impairment which may result dementia [3]. There are Alzheimer disease and vascular dementia and there are around 60 types of causes and progressions such as chemical substance addiction and vitamin deficiency [4]. Moreover, the relations between the increased blood homocysteine level, decreased B12 and folic acid level with dementia have been gradually studied and demonstrated [5]. Mild cognitive impairments, which has recently received a lot of attention, is defined as a clinical state where the damages to cognitive functions deemed normal for the age group exceeds normal ranges, but do meet the standards of Alzheimer's [6]. The diagnosis criteria for mild cognitive impairments according to Peterson (2008) are complaints over memory impairments, damage to objective memory compared to the age, and a clinical state that is not Alzheimer's where overall cognitive functions and daily life are preserved. Furthermore, mild cognitive impairments are the middle stage between normal and Alzheimer's and it is the starting point for early diagnosis and treatment important for slowing down the onset of Alzheimer's [7]. In

ISSN: 2233-7849 IJBSBT

particular, there is a high rate of people with mild cognitive impairments later having Alzheimer's disease [8]. Therefore, accurately diagnosis Alzheimer's and beginning treatment in a timely manner is crucial for preventing the progression of the disease. The percentage of mild cognitive impairments developing into Alzheimer's is approximately 5-10%. Therefore, those with mild cognitive impairments are in the risk group for Alzheimer's and thus, the early discovery and treatment is significant for preventing neurodegenerative damages [9]. The factors that are most persuasive among other risk factors related to the impairment of cognitive functions are deficient folic acid level and vitamin B group such as vitamin B6 and vitamin B12 which can cause the increase of blood homocysteine level [10]. Therefore, in this study, the changes of blood homocysteine and cognitive functions were observed in elderlies with mild cognitive impairment after they took the vitamin supplements such as folic acid, vitamin B6, and vitamin B12.

1.1. Purpose

The purpose of this study is to analyze the effects of vitamin therapy on blood-homocysteine levels and cognitive functions for senior citizens with mild cognitive impairments. In detail, the first goal is to check the general features of the subjects. Secondly, it aims at measuring the blood homocysteine levels and cognitive functions of subjects by period to examine the effects of vitamin therapy.

2. Study Method

2.1. Study Design

For study design, nonequivalent untreated control group, intermittent time series design was used with elderlies who have mild cognitive impairment<Table 1>.

Table 1. Research Design of this Study

Group	Pre-test	Treatment	Post-test
Experiment	Ye1	X	Ye2 Ye3 Ye4
Control Group	Yc1		Yc2 Yc3 Yc4

Ye1 & Yc1 : Collection of materials in advance (general features, homocysteine, cognitive functions)
X : Test group testing (taking of vitamins)
Ye2 Ye3 Ye4 & Yc2 Yc3 Yc4 : Post- (week 4, week 8, week 12) data collection (homocysteine, cognitive functions)

2.2. Study Subjects

This study subjects were 48 elderlies with mild cognitive impairment who reside in a elderly welfare facility in city of K.
Persons over the age of 65 with mild cognitive impairments who can communicate were included in the selection criteria. Persons who showed hypersensitivity against vitamins in the past or persons currently receiving treatment after being diagnosed with gastroenterological diseases or kidney diseases were excluded pursuant to the instructions of vitamin pills and advice from vitamin society doctors. Considering the ethical aspect, persons who understood the purpose of this study and provided written consent for participation in this study were chosen as the subjects.

2.3. Study Tools

2.3.1. Homocysteine: Homocysteine blood test was added during the regular blood test period. This was conducted a total of 4 times and the regular normal blood homocysteine level is 9.75±3.80μmol/L.

2.3.2. Cognitive Function (MMSE-K): MMSE-K was used as a test tool to diagnose the possibility of dementia. Below 19 score out of 30 score was considered as dementia and 20~23 score as mild cognitive impairment and above 24 score was considered as normal.

2.4. Study Procedures and Data Analysis Method

The data used in this study went through the validation process with K University (KHU IRB2010-009). For preliminary studies, counsel was received from one doctor at a senior citizen's hospital located in K City and one doctor at a vitamin society and assistance was received from two nurses. A total of thirteen senior citizens with vascular dementia, Alzheimer's and mild cognitive impairments were selected. They took vitamin pills orally for four weeks and their blood homocysteine level was measured. The average and standard deviation of the blood homocysteine level before taking vitamins were 14.41±4.62 and after taking vitamins, the average and standard deviation was 10.63±3.93, thus confirming that blood homocysteine levels dropped after taking vitamins. The data collection period to verify the effects of this study was for six months from February 2012 to July 2012. The actual research procedure was first, sending a letter to the senior citizen's medical facility director in K City to select research subjects and receive approval. Second, the researcher visited the facility and explained the purpose of this study to subjects and received a written consent form for participation in this study. Third, for the preliminary studies, a questionnaire was used prior to testing on the test group to measure the general features and cognitive functions, and blood was drawn to measure the blood homocysteine level. Preliminary studies were conducted on the control group as well. Fourth, for the testing, the test group took vitamin pills and participated for 12 weeks. In order to help the subjects to continuously take the vitamins, the facility was visited at least once a week so that questions on taking the vitamins or counseling on health could be provided for the nurses and subjects. Fifth, for follow-up examinations, the blood homocysteine level and cognitive functions were measured using the same time and method as the preliminary studies at week 4, week 8 and week 12. Follow-up examinations were conducted on the control group using the same method as the test group. The reason why follow-up studies were conducted on weeks 4, 8 and 12 were because of the research results that claimed that taking vitamins containing folate, vitamin B12 and vitamin B6 displayed normalization of blood homocysteine levels usually four to six weeks after treatment [11]. There were also studies that showed improved cognitive functions by injecting vitamins containing folate and vitamin B at week 4, 8 and 12 [12], studies that showed improved cognitive functions after nine weeks [13], and studies that showed that upon injecting vitamins containing folate and vitamin B for 18 weeks, the blood-homocysteine level dropped [14].

As a preliminary research, blood homocysteine level and cognitive function test were conducted with 13 subjects in collaboration with one medical staff, one professional from a vitamin society, and two nurses. SPSS Window21.0 was used for collected data to conduct Chi-Square test, Fisher's Exact test, independent t-test, Repeated Measure ANOVA, Contrast test, Repeated Measure ANCOVA with Covariate, and Wilks' lambda test.

2.5. Data Analysis Method

The collected data analyzed according to the research purpose and features of the data using SPSS Window 21.0. First, homogeneity test between groups was conducted with Chi-Square test, Fisher's Exact test and independent t test. Second, homogeneity test for the pre-measured values was conducted with independent t test, and when the significance level of the homogeneity test bigger than .10, it was judged to be the same. Third, repeated measured ANOVA was carried out for the time period of the test group and control group, and when there was a significant difference, contrast test was carried out to analyze differences by period. Fourth, effect verification was conducted using repeated measure ANCOVA by adjusting items that were not the same with covariates. Effect verification was assessed with significance of the interaction effect, and when the interaction effect was significant, contrast test was carried out to verify the interaction effects. Fifth, in order to carry out the repeated measure ANOVA, Mauchly's test of sphericity was carried out and if the sphericity assumption was not satisfied, Wilks' lambda test was carried out in the multivariate test.

3. Study Results

3.1. Homogeneity Test for General Features

Upon analyzing the test group and control groups' gender, age, education, religion, spouse, economic level, smoker or non-smoker, diabetes, high blood pressure, and heart diseases for the general features of subjects, it was found that religion (p=.099<.10), economic level (p<.001), and high blood pressure (p=.066<.10) were not homogenous <Table 2>

Table 2. Homogeneity Test for General Features of Test Group and Control Group

		Test Group n (%)	Control Group n(%)	χ^2or t	p
Gender	M	9(37.5)	11(45.8)	.343	.558
	F	15(62.5)	13(54.2)		
Age		76.08±5.15	78.33±4.98	-1.539	.131
Education	Elementary school or less	11(45.8)	12(50.0)	.358	>.999†
	High school	12(50.0)	11(45.8)		
	College or higher	1(4.2)	1(4.2)		
Religion	Protestant	10(41.7)	10(41.7)	6.326	.099†
	Buddhist	2(8.3)	8(33.3)		
	Catholic	7(29.2)	2(8.3)		
	No religion	5(20.8)	4(16.7)		
Spouse	Yes	0(0.0)	3(12.5)		.234†
	No	24(100.0)	21(87.5)		
Economic level	High	0(0.0)	5(20.8)	51.021	<.001†
	Mid	0(0.0)	18(75.0)		
	Low	24(100.0)	1(4.2)		

Current smoker	Yes	0(0.0)	4(16.7)		.109†
	No	24(100.0)	20(83.3)		
Diabetes	Yes	15(62.5)	14(58.3)	.087	.768
	No	9(37.5)	10(41.7)		
High blood pressure	Yes	13(54.2)	19(79.2)	3.375	.066
	No	11(45.8)	5(20.8)		
Heart disease	Yes	4(16.7)	3(12.5)		>.999†
	No	20(83.3)	21(87.5)		

3.2. Preliminary Homogeneity Validation for Dependant Variables

Homogeneity of untreated dependant variables such as homocysteine and cognitive functions were validated by means of t-test and it was found out that there are no significant statistical differences (p>.10) and therefore the preliminary measurements between the experimental group and controlled group were demonstrated as homogeneous<Table 3>.

Table 3. Preliminary Homogeneity Validation Between Experimental Group & Controlled Group

Depentant Variables	Experimental Group (n=24)	Controlled Group (n=24)	t	p
	Mean±SD	Mean±SD		
Homocysteine	19.29±7.09	17.57±5.40	.967	.338
Cognitive Functions	21.04±0.98	20.76±0.78	1.120	.268

3.3. Validation of Effects

3.3.1. Homocysteine: Homocysteine level was significantly decreased from 19.29 to 10.92 in experimental group and significantly increased from 17.57 to 19.08 in controlled group(p<.05) <Table 4>.

Table 4. Validation of Effect on Blood Homocysteine Level

Group	Before taking the vitamins (Mean±SD)	After taking the vitamins for 12 weeks (Mean±SD)	Differences before and after taking the vitamins (Mean±SD)	t	*p*
Experimental Group (n=24)	19.29±7.09	10.92±1.67	-8.45±7.21	6.383	<.001*
Controlled Group (n=24)	17.57±5.40	19.08±5.57	1.45±2.41		

*p<.05

3.3.2. Cognitive Functions: Cognitive functions were significantly increased from 21.04 to 21.79 in experimental group and significantly decreased from 20.76 to 20.21 in controlled group (p<.05) <Table 5>.

Table 5. Validation of Effect on Cognitive Function

Group	Before taking the vitamins (Mean±SD)	After taking the vitamins for 12 weeks (Mean±SD)	Differences before and after taking the vitamins (Mean±SD)	t	*p*
Experimental Group (n=24)	21.04±0.98	21.79±1.14	0.71±0.81	-5.661	<.001*
Controlled Group(n=24)	20.76±0.78	20.21±0.83	-0.54±0.72		

*p<.05

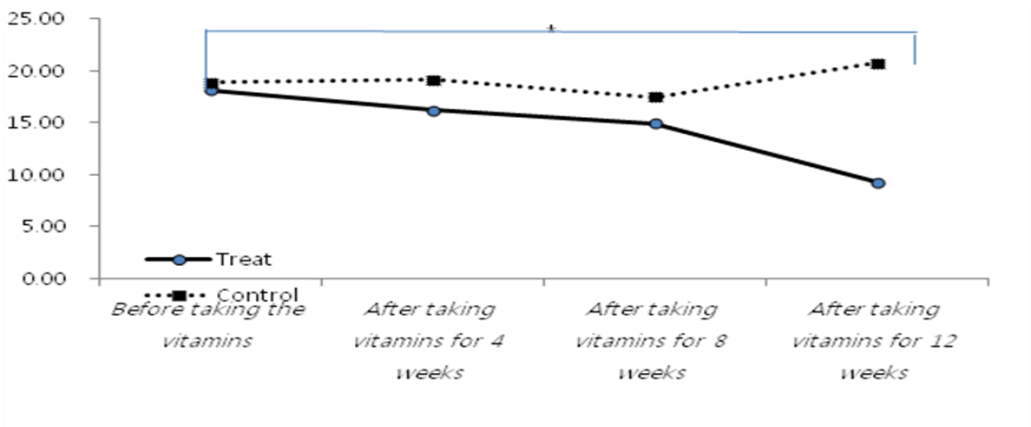
3.4. Validation of Effect by Time Period

3.4.1. Homocysteine: In the result of validating the effects by the time period, it was found out that homocysteine was decreased from 19.29, which was before the treatment, to 16.21 (±1.92) after 4 weeks of treatment, to 14.94 (±1.46) after 8 weeks, and to 10.92 (±1.67) after 12 weeks. Meanwhile, in the controlled group, it was increased from 17.57 which was before the treatment, to 19.10 (±1.92) after 4 weeks of treatment, decreased to 17.47 (±1.46) after 8 weeks and increased to 19.08(±5.57) after 12 weeks. In the result of repeated measure ANOVA, there were no significant differences between the experimental and controlled group (F=2.224, *p*=.142) and no significant differences between time periods (F=1.620, *p*=.200), however, significant interactions between the time period and groups were found (F=6.975, *P*=.001). In the result of conducting the comparative validation study on the effect of decreased blood homocysteine level, the effect of vitamin supplements was significantly found in the controlled group at week 12. <Table 6> <Figures 1>

Table 6. Validation of Effect on Blood Homocysteine by Time Period

Group	Before taking the vitamins	After taking vitamins for 4 weeks	After taking vitamins for 8 weeks	After taking vitamins for 12 weeks		F	*p*
	Mean±SE	Mean±SE	Mean±SE	Mean±SE	Source		
Experimental Group (n=24)	19.29±7.09	16.21±1.92	14.94±1.46	10.92±1.67	Group	2.244	.142
					Week	1.620	.200
Controlled Group (n=24)	17.57±5.40	19.10±1.92	17.47±1.46	19.08±5.57	G * W	6.975	.001*

*p<.05



Figures 1. Validation of Effect on Blood Homocysteine by Time Period

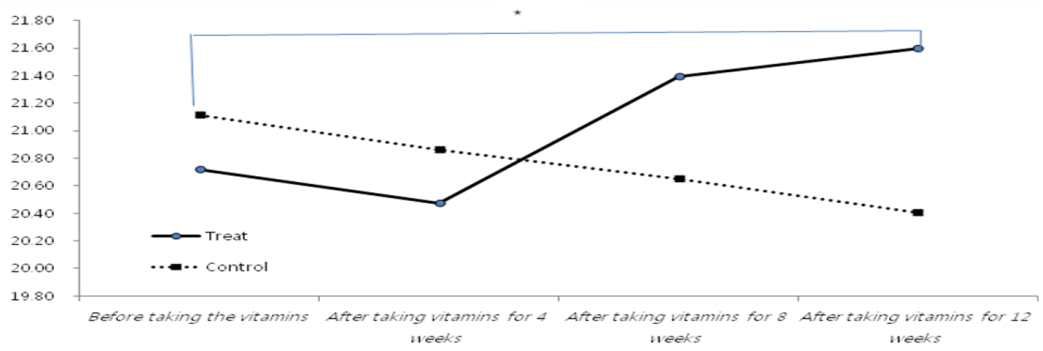
3.4.2. Cognitive Functions: In the result of validating the effects by the time period, in experimental group, cognitive function level was decreased from 21.04, which was before the treatment, to 20.47 (±0.32) after 4 weeks of treatment, increased to 21.39 (±1.14) after 8 weeks, and increased to 21.79 (±1.14) after 12 weeks. Meanwhile, in the controlled group, it was decreased from 20.76, which was before the treatment, to 20.86（±0.32) after 4 weeks of treatment, decreased to 20.65 (±0.39) after 8 weeks and decreased to 20.21 (±0.83) after 12 weeks. In the result of repeated measure ANOVA, there were no significant differences between the experimental and controlled group (F=.385, *p*=.539) and no significant differences between time periods (F=2.608, *p*=.065), however, significant interactions between the time period and groups were found (F=3.625, *P*=.021). In the result of conducting the comparative validation study on the effect of increased cognitive functions, the effect of vitamin supplements was significantly found at week 12 <Table 7> <Figures 2>.

Table 7. Validation of Effect on Cognitive Functions by Time Period

Group	Before taking the vitamins	After taking vitamins for 4 weeks	After taking vitamins for 8 weeks	After taking vitamins for 12 weeks		F	*p*
	Mean±SE	Mean±SE	Mean±SE	Mean±SE	Source		
Experimental Group (n=24)	21.04±0.98	20.47±0.32	21.39±0.39	21.79±1.14	Group	.385	.539
					Week	2.608	.065
Control Group(n=24)	20.76±0.78	20.86±0.32	20.65 ±0.39	20.21±0.83	G * W	3.625	.021*

*p<.05

Figures 2. Validation of Effect on Cognitive Functions by Time Period



4. Discussion

In this study, the effect of taking vitamin supplements on the blood homocysteine level and cognitive functions in elderlies with mild cognitive impairment was researched. The experimental group that took vitamin supplements showed the decrease of blood homocysteine level and increase of cognitive functions compared to the controlled group, of which is similar to the results from previously conducted studies [15].

This study was on senior citizens with mild cognitive impairments and it was found that the cognitive functions of test groups that took vitamin pills orally were significantly higher than the cognitive functions of the control group that did not take the pills. Like studies on the correlation of blood-homocysteine levels and cognitive functions for vitamin B groups that senior citizens with mild cognitive impairments were low in compared to the blood-homocysteine levels, it was consistent with studies that showed that vitamin B was related to improving cognitive functions [16]. There were also studies that revealed that the rise in homocysteine concentration was relevant to the drop in cognitive functions [17].

5. Conclusions and Suggestions

This study was conducted by designing intermittent time-sires of unequal, untreated control groups to examine the effects of vitamin pills taken orally on blood-homocysteine levels and cognitive functions for senior citizens with mild cognitive impairments. In order to verify the effects of orally-taken vitamins, 48 senior citizens diagnosed with mild cognitive impairments were selected from a senior welfare facility in K City, where 24 were placed in the test group and 24 in the control group. The test group took vitamin pills orally for 12 weeks and the dependent variables of blood-homocysteine levels and cognitive functions were measured. Control groups were not given any kind of treatment, but only carried out basic health counseling. Like the test group, the dependent variables of blood-homocysteine levels and cognitive functions were measured at week 4, 8, and 12.

The blood homocysteine level of both experimental group, which took the vitamin supplements, and controlled group, which didn't take the vitamin supplements got continuously decreased every week and the cognitive function score got increased. In the validation of effect of vitamin supplements for both experimental group and controlled group, experimental group showed lower blood homocysteine level and higher cognitive functions at week 12 compared to the controlled group. From this results, taking the vitamin supplements may be an inexpensive and easier way to prevent the dementia and decrease in cognitive functions which is suggested to elderly hospitals and facilities to implement to the elderlies.

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