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Effect of Oral Nutrition Supplementation (ONS) contains phosphatidylserine, choline, and uridine on cognitive function and quantitative electroencephalography in elderly patients with mild and moderate dementia

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Abstract

Objectives: Cognitive function gradually deteriorating over time is a symptom of dementia. Increased delta and theta slow wave activity is associated with decreased cognitive function. The study aimed to determine the effect of oral nutritional supplementation containing phosphatidylserine, choline, and uridine on improving cognitive function and quantitative electroencephalographic features in older people with mild-moderate dementia.

Method: A pre-experimental study with the design of one groups pretest-posttest at Dr. Radjiman Wediodiningrat Malang's psychogeriatric clinic from January to March 2020. A total research subjects were 19. Oral nutritional supplementation containing phosphatidylserine, choline, and uridine in milk is given for four weeks. Laboratory and cognitive function tests using MMSE and MoCA-Ina scores and QEEG examinations were performed before and after supplementation.

Results: The MMSE and MoCA-Ina scores showed improved cognitive function after four weeks of supplementation with $p<0.000$ and $p<0.000$, respectively. The QEEG picture before supplementation showed that from 19 subjects, hyperactivity was obtained from the slow wave type, namely Delta waves (0.1-4 Hz) and theta (4-8 Hz), namely 63.16% and 89.47% of subjects. After supplementation, there was a decrease in hyperactivity to 31.58% and 47.37% with a significance of 0.006 and 0.003 ($p<0.05$), so it was concluded that there was a significant difference in the appearance of delta and theta waves on QEEG examination.

Conclusion: Oral nutritional supplementation containing phosphatidylserine, choline, and uridine showed improvement in cognitive function, and quantitative electroencephalograph showed a significant difference in changes in delta and theta wave hyperactivity that affected attention improvement in cognitive domains of dementia subjects.

Keywords: Phosphatidylserine Supplementation; Choline; Uridine; Cognitive Function; Dementia; QEEG

1. Introduction

Many age-related neurochemical changes can be traced to structural and functional changes in neuronal membranes. Specific macronutrients and micronutrients have been linked to lowered cognitive performance and an increased risk of Alzheimer's disease, according to epidemiological research. Decreased phospholipids, especially phosphatidylserine

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in neuronal membranes, are associated with impaired memory and mental cognitive decline. Phosphatidylserine is known to reduce oxidative stress in the brain, trigger the release of neurotransmitters, and increase glucose metabolism in the brain [1]. Acetylcholine, betaine, methyl group donors, and phospholipids are all made from choline, a crucial human food. A complicated necessary nutrient, choline is involved in many bodily processes. Endogenous synthesis is insufficient to supply the body's needs for choline. Hence it must be supplied through diet [2].

The Mini-Mental State Examination (MMSE), which evaluates orientation, attention registration, computation, memory, language, and visuospatial skills, is the most commonly utilized test to gauge cognitive function on a global scale [3]. Conventional EEG methods support dividing frequency data into four major bands: delta (1-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), and beta (13-30 Hz). Although conventional EEG is ineffective in differentiating dementias with a different pathophysiological course, QEEG is becoming a more sensitive tool for evaluating dementia subtypes. Increased Delta and Theta slow wave activity is generally associated with decreased cognitive decline [4]. In numerous years of research, the spectral analyses' sensitivity varied from 71% to 81%, which could prove helpful in dementia follow-up and complement clinical examination and an independent assessment of treatment response [5,6].

2. Material and methods

Pre-experimental research with open label groups pretest-posttest design at the Psychogeriatrics Clinic of Dr. Radjiman Wediodiningrat Hospital, Malang, from January to March 2020. According to the protection of human rights and welfare in health, the experiment received approval from the ethical approval committee in the Faculty of Medicine at Universitas Brawijaya with number 04/EC/KEPK/01/2020. The study complied with all applicable international ethical norms on informed consent, secrecy, privacy, and anonymity. Oral nutritional supplementation containing phosphatidylserine, choline, and uridine in milk was given for four weeks. Laboratory and cognitive function tests using MMSE and MoCA-Ina scores and QEEG examinations were performed before and after supplementation.

The study population was older patients at the Mental Hospital of Dr. Radjiman Wediodiningrat, with the target population being older dementia patients. The affordable population in this study were older patients with mild to moderate dementia who were willing to participate in the study. Inclusion criteria were age > 60 years, DSM-IV criteria for mild to moderate dementia, willingness to drink milk, willingness to provide informed consent and participation in the study. Exclusion criteria were a history of malignancy, stroke, severe cognitive impairment, heart failure, chronic kidney disease, chronic liver disease, and subjects who had previously drank milk.

The subject's size is determined according to the formula according to M. Sopiyudin Dahlan, with a minimum number of subjects being 15, plus 10%, assuming that if you drop out, the minimum number of subjects is 17. Of the 20 research subjects, one subject dropped out due to being constrained by the caregiver's busy work, and the subject refused to continue the research, so they could only follow the research at the end. So the number of research subjects until the end amounted to 19 people.

The data on the characteristics of the research subjects are given as a frequency distribution table. Statistical analysis to assess cognitive function, nutritional status, and depression status before and after one month of treatment was performed using paired t-test, assuming the distribution was normal, and the data was not normally distributed using the Wilcoxon test. If the p-value is less than 0.05, the difference is significant. Bivariate analysis was conducted to test differences in cognitive function, nutritional status, and depression status before and after one month of treatment. If the distribution was normal, the paired t-test was employed; otherwise, the Mann-Whitney U test was used. The difference was significant if the p-value < 0.05.

3. Results

Based on the data (Table 1) on the characteristics of the research subjects, the individuals' average age was discovered to be 76.5 years (B±6.02 years). For gender, there were almost the same number of 10 male subjects and nine female subjects. The results of the MMSE and MoCA-Ina examinations were the same: mild dementia in 11 (63.20%) subjects and moderate dementia in 8 (36.80%) subjects. MNA nutritional status showed that 5 (26.30%) were malnourished and 11 (57.90%). Most of the subjects were high school graduates. Subjects continued to take their medication which was routinely taken during the study. The medication taken by mouth for dementia is mostly donepezil.

Table 1 Characteristic of Study Subjects

Characteristics	**n**	**%**
Age (years)		
60-69	4	21.10
70-79	8	42.10
80-89	7	36.80
Gender		
Man	10	52.60
Woman	9	47.40
MMSE *		
Mild Dementia	11	57.89
Moderate Dementia	8	42.11
MoCA-Ina*		
Mild	11	57.89
Moderate	8	42.11
ADL*		
Independent	1	5.26
Minimal Assist	14	73.68
Moderate Assist	2	10.53
Maximal Assist	2	10.53
GDS*		
Normal	4	21.05
Mild Depression	13	68.42
Moderate Depression	2	10.53
Nutritional Status (MNA)*		
Normal	3	15.80
Risk of Malnutrition	11	57.90
Malnourish	5	26.30
BMI Classification*		
Underweight (<18.5)	3	15.79
Normal weight (18.5-22.9)	9	47.37
Overweight (23-24.9)	3	15.79
Pre-obesity (25-29.9)	2	10.53
Obesitas I (≥ 30)	2	10.53
Education		
Junior School	4	21.05
High School	10	52.63

Characteristics	n	%
University	5	26.31
Drugs		
Donepezil	13	68.42
Ativan	11	57.89
Haloperidol	9	47.36
Clozapine	5	26.31
Lorazepam	4	10.52
Seroquel	2	5.26
Sifrol ER	1	5.26
Risperidon	1	5.26
Stalevo	1	68.42

Table 2 showed the examination of cognitive function using the MMSE score and the MoCA-Ina score between before and after supplementation showed a significant improvement with 0.000 (p>0.05) as the significance level. BMI showed a significant difference with a significance value of 0.015 (p<0.05), where the subject's BMI score after supplementation increased. The MNA score also showed a significant difference with a significance value 0.000 (p<0.05).

Table 2 Differences in Research Results Before and After Adding Phosphatidylserine, Choline, and Uridine Supplementation for 4 Weeks

Variable	Before (Average±SD) n, %	After (Average±SD) n, %	p
MMSE[t]	21.53±4.69	22.11±4.94	0.000
MoCA-Ina[t]	18.84±5.45	19.79±5.62	0.000
BP Systolic (mmHg)[t]	128.24±15.81	131.76±14.11	0.354
BP Dyastolic (mmHg)[t]	71.82±12.75	72.88±12.07	0.674
Berat Badan (kg)[t]	51.05±11.28	51.61±11.77	0.020
BMI (kg/m^2)[t]	21.72±4.11	21.96±4.34	0.015
TUG (second)[w]	22.37±4.83	22.00±4.58	0.833
Handgrip (kg)[w]	8.81±6.79	8.78±5.14	0.893
ADL[w]	15.16±4.06	15.26±4.05	0.916
GDS[w]	5.42±2.73	5.11±2.85	0.180
MNA[t]	19.92±4.35	20.21±4.33	0.000
BMI(WHO)[c]			
Underweight (<18.5)	3 (15.79)	3 (15.79)	0.995
Normalweight (18.5-22.9)	9 (47.37)	8 (42.11)	
Overweight (23-24.9)	3 (15.79)	4 (21.05)	
Pre-obesity (25-29.9)	2 (10.53)	2 (10.53)	
Obesity I (≥ 30)	2 (10.53)	2 (10.53)	

*Analysis with paired t-test; [w] = Wilcoxon's test ; [c] = Chi Square; SD=Standard Deviation

Protein intake was 38.98 g before supplementation and 53.36 g after, with a significance value of 0.000 (p <0.05), so it can be concluded that there was a significant difference where the patient's protein intake increased.

Table 3 Differences in Energy and Protein Intake Before and After Adding Phosphatidylserine, Choline, and Uridine Supplementation for 4 Weeks

Variable	Before (Average±SD)	After (Average±SD)	p
Energy Intake (kcal)	1514.92±2296.40	1056.23±417.49	0.002
Protein Intake (g)	38.98±15.60	53.36±15.59	0.000

Analysis with Wilcoxon test

Table 4 showed that the laboratory results of Hb, SGOT, SGPT, creatinine, urea, glucose, total cholesterol, and LDL before and after supplementation were not significantly different. HDL cholesterol and triglycerides showed significant differences before and after supplementation, with a significance value of 0.018 (p<0.05).

Table 4 Differences in Laboratory Results Before and After Supplementation Phosphatidylserine, Choline, and Uridine for 4 Weeks

Laboratory Results	Before (Average±SD)	After (Average±SD)	p
Hb (g/dl)[t]	12.48±1.43	12.75±1.34	0.078
SGOT (U/L)[t]	21.84±6.85	23.47±9.34	0.381
SGPT (U/L)[w]	17.53±7.14	18.84±6.95	0.981
Creatinin (mg/dl)[w]	1.11±0.57	1.01±0.49	0.257
Ureum (mg/dl)[w]	3527±14.33	36.24±17.25	0.494
Random Glucose (mg/dl)[t]	112.16±23.54	114.16±18.93	0.654
Total Cholesterol (mg/dl)[t]	170.79±37.46	174.95±34.85	0.392
HDL (mg/dl)[w]	38.37±11.61	42.58±10.99	0.018
LDL (mg/dl)[t]	105.00±39.29	111.16±34.73	0.078
Triglycerides (mg/dl)[w]	130.42±52.60	145.05±52.49	0.018

Analysis with paired t-test; [w] = Wilcoxon's test

Table 5 showed a significant difference in the QEEG of Delta and Theta waves, where the waves before supplementation tended to be more hyperactive, whereas after supplementation was more typical.

Table 5 Differences in QEEG Figures in Men and Women Before and After Phosphatidylserine, Choline, and Uridine Supplementation for 4 Weeks

Brain mapping	Before		After		p
	n	%	n	%	
Brain mapping on Delta Waves					0.006
Hypoactivity	6	31.58	3	15.79	
Normal	1	5.26	10	52.63	
Hyperactivity	12	63.16	6	31.58	
Brain mapping on Theta Waves					0.003
Hypoactivity	2	10.53	1	5.26	
Normal	0	0	9	47.37	

Hyperactivity	17	89.47	9	47.37	
Brain Mapping on Alfa Waves					0.001
Hypoactivity	1	5.26	0	0	
Normal	0	0	10	52.63	
Hyperactivity	18	94.74	9	47.37	
Brain mapping on Beta Waves					0.000
Hypoactivity	4	21.05	1	5.26	
Normal	0	0	15	78.95	
Hyperactivity	15	78.95	3	15.79	

Analysis with Chi-Square Test

Table 6 showed that the QEEG images on Delta, Theta, Alpha, and Beta waves before and after supplementation in 10 male subjects showed significant differences, as more hyperactivity waves became normal after supplementation.

Table 6 Differences in QEEG Description Before and After Supplementation of Phosphatidylserine, Choline, and Uridine for 4 Weeks in Men

Brain mapping	**Before (n=10)**		**After (n=10)**		**p**
	n	**%**	**n**	**%**	
Brain mapping on Delta Waves					0.026
Hypoactivity	2	20	2	20	
Normal	0	0	5	50	
Hyperactivity	8	80	3	30	
Brain mapping on Theta Waves					0.011
Hypoactivity	1	10.0	1	10	
Normal	0	0	6	60	
Hyperactivity	9	90	3	30	
Brain Mapping on Alfa Waves					0.010
Hypoactivity	0	0	0	0	
Normal	10	100	5	50	
Hyperactivity	0	0	5	50	
Brain mapping on Beta Waves					0.005
Hypoactivity	3	30	1	10	
Normal	0	0	7	70	
Hyperactivity	7	70	2	20	

Analysis with Chi-Square Test

Table 7 shows that the QEEG images of Delta, Theta, Alpha, and Beta waves in women before supplementation mostly showed hyperactivity, and after supplementation, many showed usual or reduced hyperactivity.

Table 7 Differences in QEEG Overview Before and After Supplementation Phosphatidylserine, Choline, and Uridine for 4 Weeks in Women

Brain mapping	Before (n=9)		After (n=9)		p
	n	%	n	%	
Brain mapping on Delta Waves					0.100
Hypoactivity	4	44.4	1	11.1	
Normal	1	11.1	5	55.6	
Hyperactivity	4	44.4	3	33.3	
Brain mapping on Theta Waves					0.117
Hypoactivity	1	11.1	0	0	
Normal	0	0	3	33.3	
Hyperactivity	8	88.9	6	66.7	
Brain Mapping on Alfa Waves					0.026
Hypoactivity	1	11.1	0	0	
Normal	0	0	5	55.6	
Hyperactivity	8	88.9	4	44.4	
Brain mapping on Beta Waves					0.001
Hypoactivity	1	11.1	0	0	
Normal	0	0	8	88.9	
Hyperactivity	8	88.9	1	11.1	

Analysis with Chi-Square Test

The QEEG categories of Delta, Theta, Alpha, and Beta waves between males and females before supplementation cannot be deduced from Table 8 that there are appreciable variations.

Table 8 Differences in QEEG Figures between Men and Women before Adding Phosphatidylserine, Choline, and Uridine Supplementation for 4 Weeks

Brain mapping	Men (n=10)		Women (n=9)		p
	n	%	n	%	
Brain mapping on Delta Waves					0.228
Hypoactivity	2	20	4	44.4	
Normal	0	0	1	11.1	
Hyperactivity	8	80	4	44.4	
Brain mapping on Theta Waves					0.937
Hypoactivity	1	10	1	11.1	
Normal	0	0	0	0	
Hyperactivity	9	90	8	88.9	
Brain Mapping on Alfa Waves					0.279
Hypoactivity	0	0	1	11.1	
Normal	0	0	0	0	

Hyperactivity	10	100	8	88.9	
Brain mapping on Beta Waves					0.313
Hypoactivity	3	30	1	11.1	
Normal	0	0	0	0	
Hyperactivity	7	70	8	88.9	

Analysis with Chi-Square Test

Table 9 shows no appreciable changes between males and females in the QEEG categories of Delta, Theta, Alpha, and Beta waves following supplementation.

Table 9 Differences in QEEG Figures between Men and Women After Adding Phosphatidylserine, Choline, and Uridine Supplementation for 4 Weeks

Brain mapping	**Men (n=10)**		**Women (n=9)**		**p**
	n	**%**	**n**	**%**	
Brain mapping on Delta Waves					0.869
Hypoactivity	2	20	1	11.1	
Normal	5	50	5	55.6	
Hyperactivity	3	30	3	33.3	
Brain mapping on Theta Waves					0.228
Hypoactivity	1	10	0	0	
Normal	6	60	3	33.3	
Hyperactivity	3	30	6	66.7	
Brain Mapping on Alfa Waves					0.809
Hypoactivity	0	0	0	0	
Normal	5	50	5	55.6	
Hyperactivity	5	50	4	44.4	
Brain mapping on Beta Waves					0.509
Hypoactivity	1	10	0	0	
Normal	7	70	8	88.9	
Hyperactivity	2	20	1	11.1	

Analysis with Chi-Square Test

Table 10 shows no significant differences in the Delta, Theta, Alpha, and Beta wave QEEG categories between subjects with a duration of dementia of less than one year and subjects with a duration of dementia of more than one year before supplementation.

Table 10 Differences in QEEG Overview on Duration of Dementia Before Adding Phosphatidylserine, Choline, and Uridine Supplementation for 4 Weeks

Brain mapping	Duration of Dementia				p
	< 1 year (n=14)		>1 year (n=5)		
	n	%	n	%	
Brain mapping on Delta Waves					0.622
Hypoactivity	5	35.7	1	20	
Normal	1	7.1	0	0	
Hyperactivity	8	57.1	4	80	
Brain mapping on Theta Waves					0.372
Hypoactivity	2	14.3	0	0	
Normal	0	0	0	0	
Hyperactivity	12	85.7	5	100	
Brain Mapping on Alfa Waves					0.539
Hypoactivity	1	7.1	0	0	
Normal	0	0	0	0	
Hyperactivity	13	92.9	5	100	
Brain mapping on Beta Waves					0.179
Hypoactivity	4	28.6	0	0	
Normal	0	0	0	0	
Hyperactivity	10	71.4	5	100	

Analysis with Chi-Square Test

Table 11 shows no significant differences in the Delta, Theta, Alpha, and Beta wave QEEG categories between subjects with a duration of dementia of less than one year and subjects with a duration of dementia of more than one year after supplementation.

Table 11 Differences in QEEG Figure on the Length of Suffering from Dementia After Adding Phosphatidylserine, Choline, and Uridine Supplementation for 4 Weeks

Brain mapping	Duration of Dementia				p
	<1 year (n=14)		>1 year (n=5)		
	n	%	n	%	
Brain mapping on Delta Waves					0.132
Hypoactivity	1	7.1	2	40	
Normal	9	64.3	1	20	
Hyperactivity	4	28.6	2	40	
Brain mapping on Theta Waves					0.718
Hypoactivity	1	7.1	0	0	
Normal	6	42.9	3	60	
Hyperactivity	7	50	2	40	

Brain Mapping on Alfa Waves					0.701
Hypoactivity	0	0	0	0	
Normal	7	50	3	60	
Hyperactivity	7	50	2	40	
Brain mapping on Beta Waves					0.805
Hypoactivity	1	7.1	0	0	
Normal	11	78.6	4	80	
Hyperactivity	2	14.3	1	20	

Analysis with Chi-Square Test

Table 12 shows the QEEG picture in Delta and Theta waves before supplementation; there were no significant differences between subjects without drug therapy, with donepezil therapy alone, with donepezil therapy and other drug combinations, and without donepezil therapy, and significant in Alpha and Beta waves.

Table 12 Differences in QEEG Figure on Types of Drug Therapy Before Adding Phosphatidylserine, Choline, and Uridine Supplementation for 4 Weeks

Brain mapping	**No therapy (n=2)**		**Donepezil (n=1)**		**Donepezil+ other drugs combination (n=12)**		**Without Donepezil (n=4)**		**p**
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	
Brain mapping on Delta Waves									0.168
Hypoactivity	1	5.3	1	5.3	1	5.3	3	15.8	
Normal	0	0	0	0	1	5.3	0	0	
Hyperactivity	1	5.3	0	0	10	52.6	1	5.3	
Brain mapping on Theta Waves									0.126
Hypoactivity	1	5.3	0	0	0	0	1	5.3	
Normal	0	0	0	0	0	0	0	0	
Hyperactivity	1	5.3	1	5.3	12	63.2	3	15.8	
Brain mapping on Alfa Waves									0.030
Hypoactivity	1	5.3	0	0	0	0	0	0	
Normal	0	0	0	0	0	0	0	0	
Hyperactivity	1	5.3	1	5.3	12	63.2	4	21.1	
Brain mapping on Beta Waves									0.005
Hypoactivity	2	10.5	0	0	8	42.1	2	10.5	
Normal	0	0	0	0	2	10.5	0	0	
Hyperactivity	0	0	1	5.3	2	10.5	2	10.5	

Analysis with Chi-Square Tes

Table 13 shows the non-significant difference in QEEG images in Alpha, Beta, Delta, and Theta waves after supplementation in subjects without drug therapy, with donepezil therapy alone, with donepezil therapy and other drug combinations, and without donepezil therapy.

Table 13 Differences in QEEG Figure on Types of Drug Therapy After Adding Phosphatidylserine, Choline, and Uridine Supplementation for 4 Weeks

Brain mapping	No therapy (n=2)		Donepezil (n=1)		Donepezil+ other drugs combination (n=12)		Without Donepezil (n=4)		p
	n	%	n	%	n	%	n	%	
Brain mapping on Delta Waves									0.309
Hypoactivity	0	0	0	0	1	5.3	2	10.5	
Normal	2	10.5	1	5.3	6	31.6	1	5.3	
Hyperactivity	0	0	0	0	5	26.3	1	5.3	
Brain mapping on Theta Waves									0.258
Hypoactivity	0	0	0	0	0	0	1	5.3	
Normal	2	10.5	1	5.3	5	26.3	1	5.3	
Hyperactivity	0	0	0	0	7	36.8	2	10.5	
Brain mapping on Alfa Waves									0.515
Hypoactivity	0	0	0	0	0	0	0	0	
Normal	1	5.3	1	5.3	7	36.8	1	5.3	
Hyperactivity	1	5.3	0	0	5	26.3	3	15.8	
Brain mapping on Beta Waves									0.961
Hypoactivity	0	0	0	0	1	5.3	0	0	
Normal	2	10.5	1	5.3	9	47.4	1	5.3	
Hyperactivity	0	0	0	0	2	10.5	3	15.8	

Analysis with Chi-Square Test

4. Discussion

In the basic characteristics of the subjects of this study, the most senior citizen was over 70 years old (76.50±6.02) and balanced between the male and female sexes. Most of the subjects showed mild dependence on daily activities and mild depression. The characteristics of this age are almost the same as the research at a social institution in East Jakarta, where out of 87 respondents from the cognitive examination study on older adults, it was found that most were >75 years old [7]. In 1910, the life expectancy rate for men was 48 years and for women 52 years, and men's and women's average ages grew to 76 and 81, respectively, in 2010. The elder adults who survive, the number of age-associated neurodegenerative dementia is also expected to increase [8]. This supplementation showed an increase in HDL cholesterol as a positive effect in reducing blood vessel damage by preventing plaque build-up but as an adverse effect, increasing triglycerides which could lead to the thickening of blood vessel walls. It requires further monitoring and research. Based on nutritional status, most subjects had a risk of malnutrition (57.90%) and were already malnourished (26.30%). Previous studies have shown the same results, where the older people with dementia had the lowest MNA and BMI scores compared to the elderly group with mild cognitive impairment and normal cognitive function [9]. According to a different study, older people with mild cognitive impairment were more likely to be malnourished than seniors with adequate cognitive function [10]. yCognitive function is positively related to nutritional status [11].

Energy intake in subjects is smaller than the energy intake of older people in previous studies that have been conducted in Indonesia, namely 1266.7 ± 336.5 kcal [12]. Energy is needed for all activities carried out by the body, including maintaining processes carried out by internal organs, carrying out external activities, growing, and keeping the body warm. The need for calories decreases with age because whole-cell metabolism and muscle activity decrease. Energy requirements in older people per day are determined by basal energy requirements, physical activity, a small part of thermogenesis related to food eaten, and heat produced in response to the environment. Basal energy requirements are also determined by age and sex, meaning this need decreases [13]. Previous research has demonstrated that BMR is higher in people with Alzheimer's disease than in people with normal cognitive function, where several factors can

increase BMR in patients with dementia, including increased protein intake, changes in thyroid function, increased sympathetic nervous system activity in the basal ganglia, and proton leakage leading to mitochondrial damage [14]. In this study, decreased energy intake after supplementation could be due to the feeling of satiety arising from the intake of protein in the form of milk, which was given between meals, thereby reducing the amount of energy that the subjects usually get from other foods, but on the other hand showed that this supplementation increased mean weight, BMI score, and nutritional status significantly. This study did not adjust the number of calories of food intake needed each day for each subject and only calculated the average number of calories from food recalls for each subject each day. Recall that nutrition officers who do food on some subjects with dementia encounter difficulties if a caregiver does not assist them. Supplementation in the form of milk by research subjects can be processed through food or drinks such as pudding, porridge, or ice cream. Counseling from nutrition officers with a doctor's assistance will make it easier for subjects to understand proper food intake.

Protein intake in this study showed a significance value of 0.000 ($p<0.05$), so it could be concluded that there was a difference in protein intake in numerical scores between before and after phosphatidylserine, choline, and uridine supplementation, where the patient's protein intake increased. Various studies have shown the relationship and effect of macronutrient intake on dementia. These macronutrients, when consumed in specific amounts, can prevent dementia by increasing cognitive function; on the other hand, they can also accelerate the occurrence of dementia by worsening cognitive function. Certain combinations of nutrients are required in synaptogenesis. Researchers at the Massachusetts Institute of Technology undertook a lengthy 12-year development program for the Souvenaid® oral nutritional supplement product, which contains a particular patented nutritional combination (FortasynTM Connect) that includes choline, uridine (as uridine monophosphate), and omega-3 polyunsaturated fatty acids (docosahexaenoic acid and eicosapentaenoic acid), which are precursors of nutrients required for synth. Phospholipids and other cofactors that boost the bioavailability of precursors are also included in the souvenir. Despite consuming a healthy diet, patients with Alzheimer's disease have relatively low levels of these precursors, whose availability is known to decline with age [15].

Another cross-sectional investigation revealed that, compared to control participants, those with mild cognitive impairment and dementia had reduced levels of uridine, folate, and choline in their blood and CSF fluid, three nutrients crucial for the production of membranes [16]. The results of this study are also supported by research. Another, where during a 6-month study Soybean-Derived Phosphatidylserine was known to improve cognitive function in older people [17]. Other studies have also shown that combined phosphatidylserine and phosphatidic acid supplementation can improve memory and cognitive function in older people, especially those with cognitive function deficiencies [1]. In an area that is difficult to get milk or supplementation containing phosphatidylserine, choline, and uridine can be obtained from various foods available in the area, such as salmon, tuna, eggs, lean chicken breast, beef liver, shrimp, edamame, and peanuts. Greens, blueberries, broccoli, soybean oil, chocolate.

In this study, cognitive function examination using MMSE and MoCA-Ina showed improved cognitive function after four weeks of supplementation with significant values, namely $p < 0.000$ and $p < 0.000$. After administering phosphatidylserine, choline, and uridine supplementation, the results showed a significant improvement in Delta and Theta wave hyperactivity, indicating a cognitive improvement, especially in attention. It aligns with the improvement of the MMSE as the most widely used test to assess cognitive function globally, which assesses orientation, attention registration, calculation, memory, language, and visuospatial abilities [3]. The results of this study support previous research, the LipiDiDiet, a 24 trial Monthly randomized, parallel-group, controlled, double-masked, multicenter (11 locations in Sweden, Germany, the Netherlands, and Finland) for the active substance (125 mL once-daily beverage with Fortasyn Connect, which has choline as an essential nutrient) reported MMSE scores were also found as a highly effective predictor of the outcome variable, which makes it potentially predictive. Two distinct populations have been researched concerning phosphatidylserine, a component of cell membranes: people with moderate cognitive decline reported cognitive gains. However, research examining phosphatidylserine combined with cognitive training in people with mild to moderate Alzheimer's dementia found only transient cognitive improvement. Other than Alzheimer's disease and moderate cognitive impairment, there is very little research on nutritional therapy for neurodegenerative illnesses [18].

Improvements in cognitive function can also be seen more clearly from the QEEG picture, namely with an improvement in brain waves, where hypoactive brain waves become better or normal and hyperactive waves become less hyperactive. Previous studies have shown that using a computerized QEEG technique can statistically foresee the transition from MCI to Alzheimer's and early stages, and during treatment, monitoring for Alzheimer's dementia can be used for prognostic purposes. Dementia shows an increase in slow wave activity frequency and a reduction in how often there are larger waves [3].

In this study, 19 subjects had slow wave hyperactivity before supplementation, namely Delta waves (0.1-4 Hz) and theta (4-8 Hz), where there were 63.16% subjects with Delta wave hyperactivity and 89,47% subjects with Theta hyperactivity wave. After supplementation, Delta waves showed a change in the direction of improvement, where the hyperactivity of Delta waves was reduced, from 63.16% of subjects reduced to 31.58% of subjects, with the test results showing a significant change with a significance value of 0.006 ($p>0.05$). These outcomes are constant, with several earlier studies demonstrating that Delta wave hyperactivity is common in dementia patients, especially in severe and advanced dementia [3].

Theta wave hyperactivity also improved after supplementation, dropping from 89.47 percent of patients to 47.37 % with a significance value of 0.003 ($p<0.05$), indicating a substantial change in the QEEG image. Theta waves between before and after supplementation. Patients with dementia show a more significant amount of Theta wave activity than ordinary aging people [19]. In terms of QEEG examination in dementia patients, this study also showed hyperactivity of Delta waves and Theta waves and hypoactivity of Alpha and Beta waves in dementia patients [19].

QEEG images on fast-type waves, namely Alpha waves (8-15 Hz) and Beta waves (15-30 Hz) before supplementation, showed that from 19 subjects, 94.74% of subjects had alpha wave hyperactivity and 78.95% of subjects with hyperactivity Beta wave. It was determined that there was a significant difference in the QEEG images of the alpha and beta waves between before and after supplementation because after supplementation, the percentage of subjects with alpha wave hyperactivity decreased from 94.74 % to 47.37 %, and the percentage of subjects with beta wave hyperactivity decreased from 78.95 % to 15.79 %. Previous studies also observed that patients with dementia showed hypoactivity or decreased total alpha and beta activity [19]. The outcomes of this investigation are diverse from previous studies where the QEEG picture showed that before supplementation, subjects with mild and moderate dementia showed alpha and beta wave hyperactivity. Alpha and Beta wave hyperactivity in research subjects was found mainly in the posterior lobe of the brain, leading to anxiety and insomnia symptoms. In contrast, Beta wave hyperactivity leads to anxiety symptoms in the form of hyperactivity and anxiety. Both of these can be seen in the psychological and behavioral symptoms of dementia patients. In addition, it is possible that this hyperactivity of Alpha and Beta waves can be found because the subjects of this study are subjects with mild or moderate dementia and not subjects with severe or advanced dementia. In Surmeli's study, hypoactivity of alpha and beta waves was seen in severe dementia [3]. The weakness of this study was that it did not examine anxiety scores on study subjects and did not include subjects with anxiety disorders in the study exclusion criteria.

This investigation's findings suggest that providing nutritional supplementation containing phosphatidylserine, choline, and uridine significantly reduces the hyperactivity of Alpha and Beta waves, especially in the posterior lobe of brain dementia. Improvements in anxiety, anxiety, and insomnia also impact cognition, especially attention in dementia patients.

QEEG images on Delta, Theta, Alpha, and Beta waves before and after supplementation in 14 subjects with a duration of dementia of less than one year and five subjects with a duration of dementia of more than one year showed that the comparative test results were not significant. This result may be due to the unequal number of subjects in the two groups with long-standing dementia and not subjects with severe dementia. The duration of dementia was seen from the medical record data when the subject was first diagnosed with dementia. Examination using the AD8 Dementia Screening Interview can be used to determine the duration of dementia with sensitivity >84% and specificity >80%, but this study was not carried out. Several studies have shown that Delta wave hyperactivity is more common in patients with severe and advanced dementia, and in dementia patients, there is a high correlation between the severity of cognitive impairment and the amount of QEEG slowing [3]. The most common EEG findings are changes in Delta and Theta frequencies and a decrease in central frequency Alpha, which usually occurs in moderate and advanced disease stages.

This study had a small sample size and the duration of the intervention needed to be longer. The rate of neurodegeneration is relatively slow. Thus, research with larger sample sizes can be anticipated to have higher treatment outcomes, adequate follow-up, and better research methods are needed to verify clinically significant and statistically significant differences.

A tremendous diagnostic technique that may be helpful for dementia follow-up is the QEEG. With its independent evaluation of therapy response, QEEG can supplement clinical examination. Alpha spectral peak analysis measures the therapeutic response to cholinergic medications. Extensive sample research is needed for the procedure's final validation. Previous research has demonstrated that low-cost computerized EEG techniques can statistically predict the development of Alzheimer's dementia in MCI patients and can be used for prognostic purposes early in treatment. Future research with a greater sample size could eliminate this restriction. QEEG has also been created for use in

neurofeedback therapy. An example of conditioning is neurofeedback therapy, which inhibits undesirable brain activity while increasing desired brain activity.

5. Conclusion

Early cognitive function tests and interventions prevent older people with minimal cognitive impairment or MCI from developing dementia. In some areas where it is difficult to carry out an examination using the QEEG tool, the Mini-Cog examination, which combines the Three Words Recall and Clock Drawing Test, MoCA-Ina, or MMSE, can be used which is easier to use for screening cognitive function in several health facilities.

This preliminary study describes an improvement or improvement in cognitive function after supplementation containing phosphatidylserine, choline, and uridine. Also, it describes an improvement in the QEEG of Delta, Theta, Alpha, and Beta waves so that further research is expected to increase knowledge. On cognitive function and nutritional interventions to improve services for older people.

Compliance with ethical standards

Disclosure of conflict of interest

There is no conflict of interest to declare.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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