PILOT STUDY

The Effects of HSOP on Cognition, Depression, and Activities of Daily Living in Older Adults with Cognitive Issues

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Abstract

Context: Worldwide, large numbers of people have Alzheimer's disease and other forms of dementia, Parkinson's disease, and multiple sclerosis. Unfortunately, approved medications are highly ineffective and have costly, untoward side effects. One alternative for neurodegenerative disorders may be use of plasmalogens, a type of phospholipid.

Objective: The objective of the study was to assess the effectiveness of a unique extract of plasmalogen from scallops for older adults with concerns either about memory and cognition or some form of actual memory loss or cognitive dysfunction.

Design: This pilot study was a 90-day intervention.

Setting: The study took place in the homes of participants.

Participants: Participants were nine older adults from South Florida.

Intervention: Participants were randomly assigned to one of two groups taking different amounts of Hokkaido Scallop Oil Plasmalogen (HSOP) per day: (1) one 0.5-mg capsule—five participants or (2) two 0.5-mg capsules—four participants.

Outcome Measures: The participants completed the assessments at baseline and postintervention. To determine if HSOP would have an effect on cognitive function, participants completed the Mini-Mental State Examination (MMSE). To evaluate issues with activities and depressive symptoms or disorders, participants completed assessments with the Activities of Daily Living (ADL) and Independent Activities of Daily Living (IADL) and the Center for Epidemiological Survey-Depression (CESD). The outcome measures were compared from baseline to postintervention, and the differences were assessed for statistical significance with paired-samples *t* tests. Correlation coefficients were assessed at baseline and postintervention between age and the outcome measures as well.

Results: The average score of the MMSE at baseline was 19.1 (SD = 9.7), the average score at postintervention improved to 21.9 (SD = 10.2), and the difference from baseline to postintervention was statistically significant ($t(6) = -2.7$, $P = .04$). All other changes on the outcome measures were insignificant. For the MMSE, five subjects improved, one subject remained the same, and one subject worsened. For the CESD, one subject worsened, and five subjects improved. For the IADL and ADL, five subjects remained the same, and one subject improved. At baseline and as expected, age was inversely correlated with the MMSE ($r = -0.88$, $P = .002$), and the MMSE was inversely correlated with the ADL ($r = -0.93$, $P = .002$). No other correlations were significant. The correlations at postintervention showed a similar pattern to those at baseline.

Conclusions: The pilot study showed that HSOP is safe to take and may provide some benefits for cognitive function and depressive symptoms, based on the clinically relevant changes in the MMSE and CESD over the 90-day period. Given the lack of efficacy of treatments for people with age-associated memory and cognitive dysfunction, HSOP may provide a natural and safe alternative for those faced with such challenges.

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Today worldwide, approximately 50 million people have Alzheimer's disease and other forms of dementia,[1] about 10 million people have Parkinson's disease,[2] and 2.5 million people have multiple sclerosis,[3] all of which are leading forms of neurodegenerative disease. Alzheimer's disease and related dementias are the sixth leading cause of death of Americans and a primary cause of institutionalization among the elderly.[4]

All of these diseases are marked by cognitive dysfunction and other functional impairments.

Unfortunately, approved medications are highly ineffective and have costly, untoward side effects. Thus, alternative approaches and treatments, such as dietary supplementation and nutrition, are needed to help those affected have a better quality of life.

One alternative approach to addressing the problems inherent with neurodegenerative disorders may be through the consumption of plasmalogens. Plasmalogens are a type of phospholipid present in almost all human tissues and in plasma lipoproteins in the cell membrane.[5] They are thought to be antioxidative due to the presence of a double, vinyl-ether bond. For example, Brosche found that plasmalogens can help to protect cell membranes and lipoproteins from reactive oxygen species.[6] However, their functions are not unequivocally acknowledged by scientists.

Plasmalogens are most abundant in the brain and heart,[7] and these endogenously produced phospholipids can also be obtained from dietary sources, such as in scallop oil. In fact, one recent study in Japan using plasmalogen-rich scallop oil was conducted in people with Alzheimer's disease, mild cognitive impairment, and Parkinson's disease, who showed significant improvement in cognitive function, together with elevations in blood plasmalogen levels.[7]

The objective of the current study was to assess the effectiveness of a unique extract of plasmalogen from scallops in older adults with either (1) age-associated concerns about memory and cognition or (2) some form of actual memory loss or cognitive dysfunction.

Methods

Participants

This pilot study was a 90-day intervention. The baseline and postintervention assessments took place in each participant's home. Participants were nine older adults from South Florida with either (1) age-associated concerns about memory and cognition or (2) some form of actual memory loss or cognitive dysfunction. Potential participants were recruited from a convenience sample of community contacts and referrals of the authors. They were contacted by one or both authors, given the details of the study and expectations for participation, and then were scheduled for the baseline assessment once they agreed to participate.

Participants signed an informed consent prior to starting the study. No institutional review board approved the study protocol, but the study was conducted in accordance with the Helsinki principles for conducting human research.

Procedures

Plasmalogen. The intervention was a unique extract of plasmalogen from scallops, called Hokkaido Scallop Oil Plasmalogen (HSOP), made by Daiwa Pharmaceutical Ltd. (Tokyo, Japan). Scallops from Hokkaido are known for their concentrated amount of plasmalogen relative to other sources and contain more desirable amounts of omega-3 fatty acids than other sources.

Groups. Participants were randomly assigned to take either one 0.5-mg capsule per day (n = 5) or two 0.5-mg capsules per day (n = 4) of HSOP. Participants were randomized according to a simple dichotomous permutation.

Intervention. Participants were provided with enough HSOP for the 90-day study and received instructions about how to take the product, how to complete their intake diary, and what was expected of their participation. Participants taking one capsule per day were advised to take their capsule at a convenient time of the day with other dietary supplements or medications. Those taking two capsules per day were advised to take one in the morning and one in the evening.

Outcome Measures. The participants completed the assessments at baseline and postintervention. To determine if HSOP would have an effect on cognitive function, participants completed the Mini-Mental State Examination (MMSE).[8] The MMSE[8] assesses mental status systematically and thoroughly. It is an 11-question measure that tests five areas of cognitive function: orientation, registration, attention and calculation, recall, and language, with a maximum score of 30. A score of 23 or lower is indicative of cognitive impairment. For the calculation of the changes in participants' scores, a negative score reflected an improvement, a zero reflected no change, and a positive score reflected a decrease.

The Activities of Daily Living (ADL),[9] the Independent Activities of Daily Living (IADL),[9] and the Center for Epidemiological Survey-Depression (CESD)[10] were also assessed, given their relevance to older people who have issues with activities and depressive symptoms or disorders. The ADL[9] score is summed from 0-7, with 0 indicating total independence and 7 complete dependence. The IADL[9] score is summed from 0-8, with 0 indicating total independence and 8 complete dependence. One question on both the IADL and the ADL assesses whether the person had experienced any significant decline in the six months prior to the testing, with possible answers being "no change," "minimal decline," and "significant decline." For the calculation of the changes in participants' scores, a negative score reflected a decrease, a zero reflected no change, and a positive score reflected improvement. The CESD[10] total score is the sum of 20 questions, with a possible range of 0-60, and a score of 16 points or more is considered indicative of depression. For the calculation of the changes in participants' scores, a negative score reflected a decrease, a zero reflected no change, and a positive score reflected improvement.

Statistical Analysis

Frequency and descriptive statistics were calculated on all variables. Paired-samples *t* tests were utilized to

evaluate differences in the outcome variables from baseline to postintervention. To gain some insight into how much participants' age and the outcome measures were related, Pearson correlation coefficients were calculated at baseline and postintervention between age and the MMSE, CESD, IADL, and ADL. IBM SPSS Statistics 27 for Windows (IBM, Inc., Chicago, IL, USA) was used for all statistical analyses, and $\alpha < 0.05$ was considered statistically significant.

Results

Trial Completion

Out of the nine participants who agreed to participate in the study, seven completed the 90-day trial. Those seven participants reported a very high level of compliance with taking their daily dose of HSOP for the 90 days, and no one reported an adverse effect.

Two participants, a husband and wife, dropped out about midway through the study due to an apparent worsening of the Parkinson's condition of the husband, which also caused the wife to move out of their house and in with their daughter. Unfortunately, they refused repeated attempts to reestablish participation in the study.

The oldest participant in the study was 95 years old, had a severe case of Alzheimer's, and could not complete the MMSE or CESD at baseline or postintervention. His score for the MMSE was recorded as zero, and his score for the CESD was missing, but his daughter, the primary caregiver, completed the ADL and the IADL. Additionally, according to his daughter he took two 0.5 mg capsules of HSOP every day of the study, and a couple of times showed awareness of his surroundings.

Participants

Participants had a mean age of 76 years ± 10.1, and of the four men and five women, six were married, and three were widowed. Five participants were white and non-Hispanic, and four were white and Hispanic. Four participants primarily spoke English, and five primarily spoke Spanish. One participant had completed the sixth grade, two had completed high school, one had post-high-school vocational training, two had completed an associate's degree, and three were college graduates.

Clinical History

Five participants had been diagnosed with some form of dementia, including possible Alzheimer's; one had been diagnosed with Parkinson's disease; one had been diagnosed with hydrocephalus; and two had age-associated memory difficulties or concerns. Three participants had also been diagnosed with depression, one with insomnia, one with aneurism, and one with diabetes. As expected, each participant was taking several different medications, and some were also taking several dietary supplements, but no one was taking a plasmalogen product prior to the baseline assessment.

Table 1. Changes in Individual Participants' Scores on the MMSE Between Baseline and Postintervention (N = 7).

Change in Score	n (%)
-6	1 (14.3)
-5	1 (14.3)
-4	2 (28.6)
-1	1 (14.3)
0	1 (14.3)
1	1 (14.3)
Total	7 (100.0)

Note: Negative = improved, 0 = no change, and positive = declined

Abbreviations: MMSE, Mini-Mental State Examination.

MMSE

Seven participants completed the MMSE assessment. The mean score on the MMSE at baseline was 19.1 ± 9.7, and postintervention was 21.9 ± 10.2, which was a statistically significant improvement [$t(6) = -2.7$, $P = .04$]. Table 1 shows the change in individual participants' scores between baseline and postintervention.

Five participants improved; one remained the same; and one worsened. In particular, of the five who improved, two participants went from moderate cognitive impairment to within the lower end of the normal cognitive range. They were a 77-year-old female who had had an aneurism 10 years prior to the study and Alzheimer's a year prior to the study (a six-point improvement) and an 86-year-old female who had cognitive impairment and possible Alzheimer's (a five-point improvement). Another participant, a 73-year-old male, with a history of hydrocephalus and memory-associated problems went from mild cognitive impairment to within the normal cognitive range, a four-point improvement from 23 to 27 points. When splitting the group into those taking one HSOP capsule per day and those taking two HSOP capsules per day, no differences were noted for the change in the MMSE score from baseline to postintervention.

CESD

Six participants completed the CESD assessment. The mean score on the CESD at baseline was 18.7 ± 11.2, and postintervention was 10.0 ± 8.4, which was not a statistically significant difference ($t(5) = 1.6$, $P = .16$). Table 2 shows the changes in individual participants' scores between baseline and postintervention.

One participant worsened, and five improved. In particular, three participants showed impressive improvements in their depressive symptoms. A 73-year-old male with a history of hydrocephalus and memory-associated problems went from mild depressive symptoms

Table 2. Changes in Individual Participants' Scores on the CESD Between Baseline and Postintervention (n = 6).

Change in Score	n (%)
-6	1 (16.7)
1	1 (16.7)
2	1 (16.7)
12	2 (33.3)
31	1 (16.7)
Total	6 (100.0)

Note: Negative = declined, and positive = improved.

Abbreviations: CESD, Center for Epidemiological Survey-Depression.

Table 3. Changes in Individual Participants' Scores on the IADL Between Baseline and Postintervention (n = 6).

Change in Score	n (%)
0	5 (83.3)
3	1 (16.7)
Total	6 (100.0)

Note: Positive = improved, and 0 = no change.

Abbreviations: IADL, Independent Activities of Daily Living

Table 4. Changes in Individual Participants' Scores on the ADL Between Baseline and Postintervention (n = 6).

Change in Score	n (%)
0	5 (83.3)
1	1 (16.7)
Total	6 (100.0)

Note: Positive = improved, and 0 = no change.

Abbreviations: ADL, Activities of Daily Living.

in the upper range to mild depressive symptoms in the lower range, with a 12-point improvement from 16 to 4 points. An 80-year-old male with a recent diagnosis of Alzheimer's went from moderate depressive symptoms to mild depressive symptoms in the lower range, with a 12-point improvement from 21 to 9 points. A 77-year-old female with a long history of depression and associated memory problems showed a dramatic 31-point improvement, from 35 to 4 points, and went from severe depressive symptoms to mild depressive symptoms in the lower range. When splitting the group into those taking one HSOP capsule per day and those taking two HSOP capsules per day, no differences were noted for the change in the CESD score from baseline to postintervention.

IADL

Six participants completed the IADL assessment. The mean score on the IADL at baseline was 4.7 ± 3.8, and postintervention was 4.2 ± 3.9, which was not a statistically significant difference ($t(5) = 1.0$, $P = .36$). Table 3 shows the changes in individual participants' scores between baseline and postintervention on the IADL. Five participants remained the same, and one improved.

ADL

Six participants completed the ADL assessment. The mean score on the ADL at baseline was 1.5 ± 2.5, and postintervention was 1.3 ± 2.2, which was not a statistically significant difference ($t(5) = 1.0$, $P = .36$). Table 4 shows the changes in individual participants' scores between baseline and postintervention on the ADL. Five participants remained the same, and one improved.

Relationship between Age and Outcome Measures

At baseline and as expected, age was significantly inversely correlated with the MMSE ($r = -0.88$, $P = .002$). The MMSE was significantly inversely correlated with the ADL ($r = -0.93$, $P = .002$). No other correlations were significant. The correlations at postintervention showed a similar pattern to those at baseline.

Discussion

HSOP demonstrated a significant improvement in MMSE scores between baseline and postintervention. Changes on the MMSE of at least one point were clinically relevant for several participants, including those who went from mild-to-moderate cognitive impairment into the normal cognitive-function range.

Five participants showed reductions in depressive symptoms according to the CESD, and three participants showed dramatic improvements in their scores. Changes in the IADL and ADL scores mostly demonstrated no differences between baseline and postintervention.

Correlations between age and the outcome measures were typical and not noteworthy of discussion. The two participants who dropped out apparently did so not because of the study's program or use of HSOP but to a worsening of the husband's medical condition (Parkinson's), which caused the wife to drop out as well.

No participants or caregivers reported any adverse effects. According to each daily diary, compliance was particularly good for taking the one or two capsules per day for the 90-day period.

The study's results are limited due to a small sample size that was drawn from a convenience sample in South Florida that may not be representative of the entire population. No comparison condition was utilized, so it is not possible to compare the effects of HSOP against any

other regimen. The study was only conducted for 90 days, so the results are not generalizable beyond this time period.

Conclusions

The pilot study showed that HSOP is safe to take and may provide some benefits for cognitive function and depressive symptoms, based on the clinically relevant changes in the MMSE and CESD over the 90-day period. Given the lack of efficacy of treatments for people with age-associated memory and cognitive dysfunction, HSOP may provide a natural and safe alternative for those faced with such challenges.

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