Twenty weeks of Centella asiatica improved cognitive function of women elderly with dementia

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Abstract. Centella asiatica is known to improve cognitive function, but its influence on several domains of cognitive function in dementia women is still limited. This study aimed to determine the effect of Centella asiatica on cognitive function in women elderly with dementia. Screening for dementia used an MMSE questionnaire (Mini-Mental State Examination) with a cut off of 23. The trial comprised the two groups: Centella Asiatica group (CAG) 1x500 mg/day and placebo control group (PCG) 1x500 mg/day. Thirty-nine women were included in this study with mean age 74 ± 10.05. The results showed that the CAG group was effective in increasing the semantic fluency domain (p<0.001) and visual memory (p<0.001) compared to PCG. Meanwhile, the phonemic fluency domain and the forward-backward digit span did not show a significant difference compared to the placebo control group. In conclusion, administration of Centella asiatica for 20 weeks is effective in increasing semantic fluency and visual memory in women elderly with dementia.

1. Introduction

Dementia is a syndrome of decline in multiple mental domains that persist and affect normal daily life [1]. Dementia is increasingly a focus for policymakers, civic organizations, and multidisciplinary researchers as its prevalence are increasing in low and middle-income countries compared to developed countries which are relatively stable or declining [2]. This is due to an increase in cardiovascular disease. Meanwhile, people in developed countries have seen major changes and trends in their lifestyle, education, and health care that may affect their physical, mental, and cognitive health [3].

Centella asiatica originates from Southeast Asia and has been used traditionally as a brain tonic in ayurvedic medicine [4]. This plant has been shown to improve cognitive function in mild cognitive impairment (MCI) patients [5]. MCI is known to be the beginning of the development of dementia or Alzheimer's disease. According to Alzheimer's disease facts and figures, millions of people worldwide suffer from cognitive impairments. Cognitive impairment causes deficits in cognitive tasks related to awareness, insight, knowledge, memory, and problem-solving skills. Centella asiatica has therapeutic potential because it is neuroprotective [6]. In addition, Centella asiatica is reported to have comprehensive neuroprotection through enzyme inhibition mechanisms, prevention of amyloid plaque formation in Alzheimer's disease, dopamine neurotoxicity in Parkinson's disease, and reduction in oxidative stress [4]. According to data, dementia occurs more in women than men [7]. The purpose of
This study was to determine the effect of Centella asiatica on various cognitive functions in women with dementia.

2. Materials and Methods

2.1 Study participants
This research is a quasi-experiment started in August 2019 for 20 weeks. Observations were completed in December 2019. Subjects in this study were 39 people recruited from three nursing homes in town B. Subjects were divided into 2 groups, namely 20 people in the Centella asiatica group and 19 people in the placebo group.

2.2 Intervention
Centella asiatica (CA) group
Standardized CA extract was prepared by the Laboratory of Natural Product of Pharmacology, School of Pharmacy, Institut Teknologi Bandung. The process of standardization and conformity of the CA extract were strictly done during manufacturing. Quality control was completed until dry extract was produced. Each capsule has an asiaticoside level of 1.41 mg/g is checked by the HPLC method. One hundred-forty capsule inside a sealed bottle was prepared. Each capsule contains 500 mg of CA extract. The dosage was one capsule per day. Each respondent was given a CA capsule by a nurse in charge of the nursing home.

Placebo Control group
The placebo control group took capsules 1x500 mg/day. The placebo content consists of starch that has been tested for safety at the Laboratory of Natural Products of Pharmacology, School of Pharmacy, Institut Teknologi Bandung.

2.3 Data collections
Sociodemographic and clinical data were collected by history taking and physical examination. Data include age, blood pressure, education, and marital status. Education levels were categorized into two groups: low (Elementary School and Junior High School) and high (High School and University). A cognitive test was carried out for 30 minutes. This study was conducted before and after 20 weeks of intervention.

2.4 Measurement of cognitive function
The cognitive function test consists of verbal fluency (semantic and phonemic fluency), digit span (forward and backward), and visual memory. Semantic fluency is by means of the research subject mentioning the names of animals that are known for 1 minute, then the examiner records and adds up the animals mentioned by the subject [8]. Meanwhile, phonemic fluency is done by the research subject mentioning the names of animals from the letter S for 1 minute [9]. This examination functions to test language fluency and executive function [10,11].

The span forward digit is done by the research subject repeating the numbers mentioned by the examiner from front to back sequentially, while the span backward digit of the research subject mentions the numbers mentioned by the examiner from back to front in sequence. Then the examiner records and adds up the numbers that can be correctly stated by the subject [12]. This examination functions to test the working memory [10].

Visual memory test means that the research subjects were asked to read and remember the 10 words given by the examiner for 20 seconds, then asked to mention the words read earlier. Then the subject was asked to read and remember the 10 words that had been randomized for 20 seconds, and then asked again what words were read earlier, so repeated 3 times, and the examiner counted the number of words that could be pronounced correctly [10].
2.5 Statistical methods
Data analysis using SPSS version 25 with a confidence level of \( p < 0.05 \). The data normality test used the Shapiro Wilk test to find out the average sample data with the normal or abnormal distribution. Analysis to determine changes in the effect of CA and placebo on cognitive function using paired t-test analysis for normally distributed data and Wilcoxon test for data not normally distributed.

2.6 Ethical considerations
The research was conducted at the Ethics Committee of Padjadjaran University (No.1266 / UN6.KEP / EC / 2018). All research subjects and/or their guardians have been given an explanation of the objectives, research procedures, and the risks of this study, then the subject or guardian is willing to give an informed consent form prior to the study.

3. Results
Data Table 1 shows that the mean age in the Centella asiatica (CAG) group was 73 ± 9.7 years and the placebo control (PCG) group was 75.6 ± 9.3 years. The MMSE score at CAG was 22.7 ± 3.6 and on PCG was 21.3 ± 3.2. Meanwhile, the blood pressure assessment showed at CAG 136.5 / 80.5 mmHg and on PCG 130.7 / 75.4 mmHg. Low education in the CAG was 47.1% and 52.9% for PCG. Meanwhile, the marital status showed 44.1% for CAG and 55.9% for PCG as widowed/unmarried.

The data in Table 2 shows that there is a significant difference between before and after 20 weeks of administration of Centella asiatica in dementia women compared to the placebo control group. The difference can be seen from the examination of semantic fluency (\( p < 0.001 \)) and visual memory (\( p < 0.001 \)) which were significantly different compared to the placebo control group. Meanwhile, examination of phonemic fluency, forward digit span, and backward digit span did not show a significant difference between the Centella asiatica group and the placebo control group.
Post-test 2.1 (1.5) 0.6 (1.1)
Visual memory
Pre-test 10.5 (6.4) <0.001* 5.6 (4.5) 0.366
Post-test 15.6 (5.4) 4.5 (5.6)

*p<0.05; data are expressed as mean ± SD; p-value were derived from paired t-test or Wilcoxon test

4. Discussion
The results showed that presenting Centella asiatica for 20 weeks showed a significant effect on semantic fluency and visual memory studies in dementia women compared to the control group. This is consistent with studies showing that high doses of plant extracts improve memory and increase the amplitude of the N100 component and treat mood disorders in healthy elderly people [13]. Another study shows no strong evidence to support the use of C. asiatica for the improvement of cognitive function in any cognitive domain, but it can increase alertness and relieve anger [14]. However, studies regarding the effect of Centella asiatica in elderly people with dementia and its effect on fluency have not been found in the other studies.

Centella asiatica L. is traditionally used as a medicinal plant and alternative medicine in the treatment of a wide variety of ailments and its use in food and beverages has been increasing over the years. The potential for antioxidant and neuroprotective activity has been widely claimed in many reports and interviewees are closely related to the nature and action of the bioactive plant constituents namely asiaticosides, asiatic acids, madecassosides, and madecasic acids [15]. Centella asiatica is also known to contain vitamins B and C, protein, essential minerals, and several other phytonutrients such as flavonoids, essential oils, tannins, and polyphenols [16]. The highest phytochemical concentrations were found in leaves compared to petioles and roots, namely asiaticoside (2.56 μg / ml), madecassoside (5.30 μg / ml) and asiatic acid (3421.60 μg / ml) [17].

5. Conclusion
The results of this study indicate that the administration of Centella asiatica for 20 weeks has an effect on increasing semantic fluency and visual memory in elderly women with dementia. Further research can be carried out with a larger number of respondents and their effects on various blood biochemical tests.

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