Effects of Dietary Supplementation with High-Dose Choline Alfoscerate (Cerebrain® Forte) on Cognitive Functioning in Patients with Minor Neurocognitive Disorder (Mind): A Pilot Study

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Abstract

Introduction and aim of the study: Normal and pathological aging have been related to deficits of several neurotransmitters able to account for cognitive, emotional and behavioral disorders associated with mild cognitive decline or overt dementia. Among the neurotransmitter deficits involved in cognitive disorders, with particular reference to those underlying memory and attentional functions, the cholinergic one is certainly the main one [1]. This justified the treatment of these disorders with drugs and supplements capable of enhancing cholinergic transmission by inhibiting the degradation of acetylcholine (acetylcholinesterase inhibitors) or by increasing the production of the neurotransmitter through the exogenous supply of precursors [2,3]. Choline Alfoscerate is at the forefront of these supplements. The effect of the supplements is dose-dependent, and it is therefore likely that a high-dose formulation is associated with effects on cognition of a higher entity than that with medium or medium-low dosages. Aim of this pilot study is to evaluate the effects of dietary supplementation with choline alfoscerate at 1200 mg per day (Cerebrain® Forte) on cognition in patients with Mild Neurocognitive Disorder (MiND).

Design of the study: open label, single group), pilot study of efficacy of Cerebrain® Forte on cognitive functions. Duration of 24 weeks on patients with MiND.

Methods

Patients

Eighteen patients were consecutively enrolled at the Center for Cognitive Disorders and Dementia (CDCD) of the UOC of Neurology - Stroke Unit of the CTO Hospital, Specialized AO “Ospedali dei Colli” in Naples. The recruited sample consisted eight men and ten women, with mean age=74.83 years (SD = 4.55) and mean schooling (years of education) of 7.61 (SD = 4.74). All subjects underwent a diagnostic protocol including cognitive and behavioral history, neurological examination, blood chemistry routine, neuroimaging (brain CT and/or MRI). The diagnosis of MiND was supported by a short neuropsychological evaluation, using the Italian version of the Quick mild cognitive impairment (Qmci) [4]. All patients provided informed consent to the study, which was conducted in accordance with the Declaration of Helsinki.

Inclusion criteria

1. Diagnosis of MinD according to the DSM-5 criteria below [5]:

A. Evidence of a mild cognitive decline from a previous level of performance in one or more domains based on: 1) concern of the individual, a trusted informant or clinician that there has
been a slight decline in cognitive functions; 2) mild impairment of cognitive performance, preferably documented by standardized neuropsychological tests or, in their absence, by another quantified clinical evaluation.

B. Cognitive deficits do not interfere with independence in daily activities.

C. Cognitive deficits do not occur exclusively in the context of a delirium.

D. Cognitive deficits are not best explained by another mental disorder.

2. Age between 55 and 80 years.

3. Education: at least 5 years.

4. Corrected score at MMSE between 21 and 26 and corrected score at Qmci below the cut-off of 49.5.

5. No or minimal impairment of function at the IADL (no more than one point lost at the scale).

**Exclusion criteria**

1. Significant neurological disorders (cognitive impairment; overt dementia of any etiology; epilepsy; major stroke).

2. Major psychiatric disorders (psychosis; major depression; bipolar disorder)

3. Taking cognitive depressants.

4. Alcohol or substance abuse.

5. Significant general medical conditions (active neoplasms, decompensated cardiovascular or metabolic diseases, end-stage renal failure, etc.).

**Procedures**

**Timing**

After the recruitment, three evaluations were conducted: baseline (T0), at 12 weeks (T1) and at the outcome at 24 weeks (T2).

**Assessment**

The Mini Mental State Examination (MMSE) with correction of the scores based on the Italian normative values [6] was administered at all assessment times. Since the MMSE was included among the inclusion criteria, its score was assumed as an evaluation at T0, provided that the distance between recruitment and baseline did not exceed two weeks.

**Data analysis**

Given the non-continuous nature of the measurements, and the small size of the sample, non-parametric statistical methods were applied. The comparison between the MMSE scores at the various observation times was analyzed using the Wilcoxon rank test. Statistical analysis was supported by the statistical packages StatView and Medcalc running on PC.

**Results**

The mean MMSE score at T0 was 23.17 (SD = 2.87). This score was unchanged at T1 (M = 23.26; SD = 3.03), with no statistical significance in the comparison (Z = -0.389; p: ns; Wilcoxon rank test). At T2, the mean MMSE score rose to 24.11 (SD = 3.10) with a difference that was significant in comparison with the previous evaluation (Z = -2.266; p 0.023). Figure 1 illustrates the temporal variations of the MMSE scores.

![Figure 1: Changes in MMSE scores at the three observation times.](image)

**Discussion and Conclusions**

The results of the study highlight the positive effect of high-dose choline alfoscerate on the cognitive performance of patients with MiND, thereby confirming the usefulness of a dietary supplementation with this supplement in the forms of mild cognitive impairment of the elderly. However, it should be emphasized that the effect occurs over reasonably extended times, as in the short term the scores at the MMSE remain substantially unchanged. Several factors could account for this “latency of effect”. A first explanation, which could be labeled as “synaptic”, points to the chronic deficiency of the cholinergic neurotransmitter, with the consequent changes in the density and sensitivity of the post-synaptic receptor, and which require the minimum biological times of reorganization of the receptor regulation, similarly to what happens for all drugs that with different processes (agonism, inhibition of reuptake or degradation) try to compensate for a neurotransmitter deficit. A second explanation, that we call “metabolic”, is based on the evidence that there is a more general lack of choline responsible for a metabolic imbalance leading to
functional and structural changes in the brain related to cognitive impairment. This imbalance would be reflected in a systemic difficulty in synthesis and use of nutrients. This is supported by repeated evidence regarding the low concentration of nutrients in both plasma and brain of patients with mild cognitive impairment or dementia (see Baumel et al., 2021 for a recent review) [7]. Among the nutritional deficiencies that of choline is probably the most difficult to correct with simple dietary aids, as it is known that the cerebral uptake of choline is drastically reduced with age-related mechanisms. It is therefore likely to believe that such a complex metabolic and nutritional rebalancing necessarily requires extended time before appreciable improvement in brain and cognitive function [8]. In conclusion, the results of our study support the usefulness of a dietary supplementation of choline alfoscerate in patients with mild forms of cognitive impairment. In addition, they suggest its use in high dosages and over prolonged times.

References


