Caffeine enhances memory function after cholinergic blockade

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group were withdrawn from the study due to rash, 16 FEs or adverse events. No serious adverse events were observed. One patient in the placebo group and two patients in the tacrine group died from causes which were considered unrelated to the treatment.

Conclusion: Tacrine produced an improvement that was detected by a physician and the patient's carer. Overall psychometric scores did not change, but more patients did better on tacrine than placebo. The clinical relevance of these findings varied considerably among patients.

- Doses over 8 mg tacrine per day may be more effective in patients who were considered to be responders. Doses up to 60 mg per day were well tolerated and safe even after prolonged treatment.

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perceptual and psychomotor speed, information processing, primary and secondary memory, memory scanning and focused and divided attention, at 1 hour before and 2, 4 and 6 hours after scopolamine administration. The first analysis of the performance data shows that scopolamine produced severely disturbing memory as well as psychomotor dysfunction. Caffeine significantly diminished the impairing effect of scopolamine in the memory tasks. Especially secondary memory and delayed recognition parameters were improved after caffeine relative to scopolamine alone. This led to the conclusion that (disturbed) memory storage, but not retrieval, was positively affected by caffeine. Psychomotor performance was not affected by caffeine. The effects of nicotine were minor and were less than expected on the basis of previously reported studies. Analysis of blood levels can possibly lead to an explanation.

As far as we know, this is the first demonstration of caffeine's potential to selectively enhance memory functioning in subjects who suffer from scopolamine-induced cholinergic dysfunction. Taking into account that caffeine also attenuates many other effects of benzodiazepines and that cholinergic dysfunction is one of the manifestations of Alzheimer's Disease, it can be concluded that caffeine consumption might be helpful in preventing or postponing the symptoms of Alzheimer's Disease.

414 THERAPY WITH A COMBINATION OF IRON, VITAMIN B6 AND COENZYME Q10 IN THE LONG TERM FOR SPORADIC ALZHEIMER'S DISEASE. Masaki Imagawa MD. Department of Neuropsychiatry, Hyogo Prefectural Amagasaki Hospital, Hyogo, Japan.

Of the therapy with combination of coenzyme Q10 (CoQ10), vitamin B6 and iron, two in the same family were found to have mis sense mutation of amyloid β-protein precursor gene. This therapy have been tried in 20 patients with the sporadic Alzheimer's disease (AD) in the long term (one year). It is suggested that this therapy may be effective for AD. SUBJECTS AND METHODS This clinical study included 20 AD, mean ± SD age, males 61.8 ± 6.8 y.o.; females 61.8 ± 6.8 y.o.; 20 patients have been suffered from AD from 1 year to 7 years. Diagnosis was based on DSM-III-R. Mental stage and daily activity were evaluated with mini-mental state examination score (MMSE) and functional assessment staging (FAST) and so the clinical course was followed by the two methods. These numbers have changed according to the severity of the patient's symptoms and signs. Thesoo scales were marked on the time scale (0, 2 weeks, 3, 6 months, one year). The dose of the drugs taken by the patients was iron 50-150 mg, B6 90-180 mg, CoQ10 60-180 mg, daily. RESULTS In this therapy, each points have significantly different from zero in scores. In MMSE, 0: 14.6 ± 7.0 (11~20), 2W: 22.5 ± 5.4 (n=16)*, 1M: 20.3 ± 5.4 (n=18)*, 3M: 21.5 ± 5.4 (n=20)*, 6M: 20.3 ± 7.1 (n=20)*, 1Y: 21.8 ± 5.5 (n=11)*. * paired t-test, p<0.01. In FAST, the stage have changed from 3 stage (zero point) to 3 stage. DISCUSSION Why dose this therapy effect in AD? In general, iron, particularly the action of Fe²⁺ have a intoxication in vivo because of free radicals. But iron is essential mineral on the body, especially, brain. Adding to CoQ10, iron dependent free radicals may be disappeared. In this therapy it is focus on the production of the neurotransmitters through the dehydroxylation (B6,B8-enzyme) with ATP. B6 is an energy synthesis of GABA. Neuronal cell's death said to be the hypothesis of glutama induced cell's death. Therefore, it is important that the neurotransmitters relate to GABA should be increased.


This drug is currently under study in many clinical trials in Europe, according to results obtained in preliminary studies in patients suffering from dementia, either of Alzheimer type or vascular origin.

The double-blind, randomized, short-term clinical trial was carried out in order to evaluate the safety profile of Posatirelin on both cardiovascular and hormonal parameters.

24 h post invasive ambulatory blood pressure, cardiac frequency monitoring and EKG recording (for 5 minutes) in 20 patients with dementia (mild to moderate degree) were determined before and after treatments. 10 patients underwent Posatirelin (10 mg daily i.m., 8 days) and 10 placebo treatment according to a randomization code. GH release T₃, T₄, TSH and PRL levels and routine laboratory parameters were determined at baseline and at the end of treatment. 9 males and 11 females (65-80 yrs, mean ± SD: 75.10 ± 3.7, MMSE score 12-21, mean ± SD: 16.35 ± 2.5) entered and completed the study.

Behaviour of cardiovascular parameters did not show significant difference comparing to Posatirelin to placebo. Similarly, no changes in the EKG were recorded. No significant changes (out of normal biological variability) in haematological, serum chemistry or urinalysis were observed. GH concentration, GH secretion, T₃, T₄, TSH, and PRL levels changes were statistically not significant and unrelated to treatment.

At the end of the treatment (60 minutes after injection) higher values of TSH and PRL in Posatirelin group than in placebo group were observed. This finding was not verified in further studies, but it is necessary to take into consideration that variability was within normal range of values.

The results of this study suggest that Posatirelin may be proposed as a safe drug for the treatment of demented elderly patients.

417 CENTRAL SEROTONERGIC HYPERRESPONSIVITY IN ALZHEIMER'S DISEASE. D.M. McLoughlin, J.V. Lucey and T.G. Dinan. Institute of Psychiatry, London S.E.5 B.A.F. and Dept. of Psychiatry, Trinity College Medical School, Dublin 8, Ireland.

A wide range of neuroanatomical and biochemical deficits have been identified in the central serotonergic (5-HTR) system in Alzheimer's disease (AD). In order to investigate the functional significance of these abnormalities the prolactin (PRL) response to the 5-HT specific neuroendocrine probe d-fenfluramine (d-FEN) was measured in 9 patients with late onset probable AD (NINCDS-ADRDA criteria) and in an elderly healthy comparison group. PRL levels were measured hourly for 5 hours following an oral dose of 30mg of d-FEN. The PRL response to d-FEN (Δ PRL) was Calculated by subtracting the baseline PRL from the maximum PRL level post ingestion of d-FEN. There was no significant difference in baseline PRL levels between the two groups and the peak PRL response occurred in all subjects within 300 mins. The mean ΔPRL in the AD group was 209.6(SD=116.9) μ/ml and 95.8(μ/ml±13.4) μ/ml in the comparison group, the PRL response was significantly greater in the AD group (Z=2.04, df=16, p=0.04; Mann-Whitney U test).

This preliminary study is the first to report an enhanced 5-HT neuroendocrine responsivity in late-onset AD. 5-HT abnormalities have been implicated in depression, anxiety and impulsive, aggressive behaviour. 5-HT has also been recognised as having an influence, possibly inhibitory, on learning and memory. The finding of a functionally hyperresponsive 5-HT system in AD could provide a rationale for the use of 5-HT antagonists for the management of behavioural and cognitive symptoms in AD.

418 MANAGING PROBLEM BEHAVIORS ASSOCIATED WITH ALZHEIMER'S DISEASE: A PIAGETIAN APPROACH. M.A. Matteson, A. Limon, M.J. Lichtenstein, B. Cleary. University of Texas Health Science