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Correlative Study of Folic Acid and Vitamin B_{12} Levels on Senile Dementia of Alzheimers Type.

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ABSTRACT

Alzheimer disease is the most common neurodegenerative disorder in elderly people worldwide. Folic acid and vitamin B_{12} metabolism is interconnected and deficiency of either of these may produce severe neurological consequences. Significant deficiency of folic acid and vitamin B_{12} are common in elderly. Therefore, this study was conducted to evaluate folic acid and vitamin B_{12} levels in elderly patients and its role on cognitive status of patients suffering from senile dementia of Alzheimers type. In addition, the effect of folic acid and vitamin B_{12} supplementation on improvement in clinical dementia rating scale was also observed. This study included 55 blood samples from individuals taken as control and 110 blood samples from patients of senile dementia of Alzheimer Type. Folic acid and vitamin B_{12} was estimated by sandwitch ELISA method in all subjects. Folic acid level was significantly lower in patients of dementia of Alzheimers type as compared to control subjects but vitamin B_{12} levels were not significantly different. Further, no significant improvement in clinical dementia rating scale was observed after supplementation of folic acid/vitamin B_{12}. Thus, this study indicates that low folic acid level is a risk factor for senile dementia of Alzheimer Type and folic acid supplementation is not helpful after the onset of disease.

Keywords: Alzheimer disease, Senile dementia, Folic acid, Vitamin B_{12}

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INTRODUCTION

Alzheimer disease (AD) is a progressive neurodegenerative disorder which causes memory loss and cognitive decline. AD is the most common cause of dementia in elderly constituting 60-70% cases of dementia [1, 2]. Approximately 10% of all persons over the age of 70 have significant memory loss and more than half of them have Alzheimer disease. Dementia resulted in about 486000 deaths in 2010 [3]. Scientists believe that most cases of Alzheimer disease are caused by combination of lifestyle, genetic and environmental factors that affect the brain over time [4]. Age is the most common unavoidable risk factor. It is more likely to develop in older people. A greater proportion of people affected by AD are over 65 years of age [5]. The possibility that folic acid and vitamin B_{12} deficiency may be associated with memory impairment in the aged has long been suggested in literature. A study by Levitt et al., show the relationship between folate, B_{12} and other metabolites, and the severity of cognitive impairment in patients with Alzheimer's disease [6]. Low folate and vitamin B_{12} levels were found to be associated with dementia in some but not all cases. The role of serum folic acid and vitamin B_{12} in the cognitive status of the patients suffering from senile dementia of Alzheimer type has not been evaluated so far in northern India. Hence, in the present study an attempt was made to assess the correlation between serum folic acid and vitamin B_{12} levels and the cognitive status of patients of senile dementia of Alzheimer type.

MATERIALS AND METHODS

Selection of patients and control

The present study included elderly patients aged 60-75 years with confirmed diagnosis of senile dementia of Alzheimer type on the basis of CDR scale by the consultant of Psychiatry department of Sir Sunderlal Hospital in collaboration of department of Biochemistry, Institute of Medical Sciences, Banaras Hindu University, Varanasi. In this study, 55 blood samples from individuals taken as control and 110 blood samples from patients of senile dementia of Alzheimer type was examined. Approval from the ethical clearance committee of the Institute of Medical Sciences, Banaras Hindu University, Varanasi, India, was obtained before the commencement of the study and informed consent was taken before collection of blood samples in every cases and control.

Study Design

The patients of senile dementia of Alzheimer type were divided into two groups. Group I included cases of senile dementia of Alzheimer type aged between 60-75 years, receiving treatment as usual and supplementation with folic acid and vitamin B_{12}. Group II included cases of senile dementia of Alzheimer type aged between 60-75 years receiving treatment as usual without any supplementation.

Collection of samples

Blood samples were collected from patients and controls taking all aseptic precautions. About 5 ml of venous blood was drawn with a disposable syringe. The blood sample thus collected, was kept in a clean dry glass tube and allowed to stand for 20 minutes at room temperature for retraction of the clot. This was now centrifuged at 3000 r.p.m. for 10 min to separate the serum. The serum sample was stored at -20ºC in the refrigerator for analysis. Care was taken to avoid hemolysis of the sample.

Quantitative measurement of serum folic acid and vitamin B_{12}

Serum folic acid and vitamin B_{12} was estimated by enzyme linked immunoassay method using sandwitch ELISA kit. The procedures for insulin estimation were as per instructions provided by the manufacturer (Elabscience, sandwitch ELISA Kit, Hubei Province, China)

Statistical Analysis

Statistical Analysis was done between patients of senile dementia of Alzheimer type (SDAT) and age matched controls using SPSS-20 and R studio software. The data were expressed as mean ± SD, $P < 0.05$ is considered significant and $P < 0.0001$ is highly significant.

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RESULTS

The present study was carried out to examine the effect of folic acid and vitamin B_{12} on the cognitive status of patients suffering from senile dementia of Alzheimer type (SDAT). In the present study, 110 patients of senile dementia of Alzheimer type have been compared with 55 normal healthy individuals.

Serum Folic acid was estimated by ELISA method. Estimation was done in all patients (n=110) and control subjects (n=55). The final result was expressed as ng\ml.

The mean serum folic acid level in patients (17.59 ± 22.74) was significantly lower as compared to controls (26.65 ± 27.26) subjects (Table 1, Fig 1; $p < 0.05$).

Table 1: Folic Acid levels in controls and patients with Alzheimers disease (mean ± S.D)

GROUPS	NO OF CASES	FOLIC ACID (ng/ml)
PATIENTS	110	(17.59±22.74)
CONTROLS	55	(26.65±27.26)

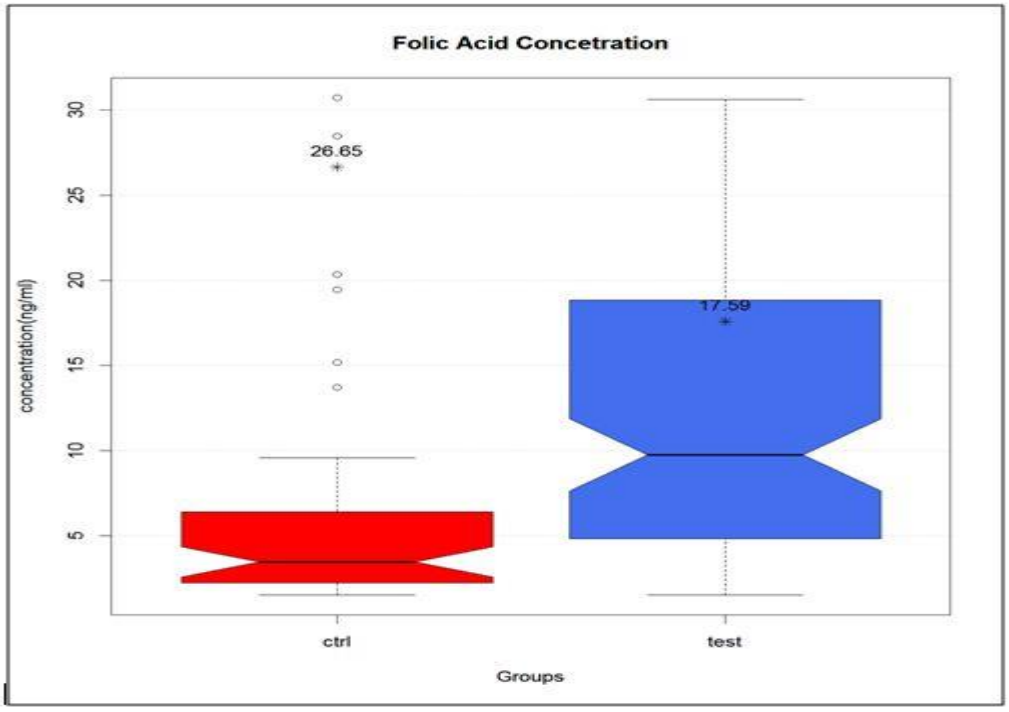

Fig 1: Showing comparison between serum folic acid levels in patients with Alzheimers disease and controls. Serum folic acid level in patients of senile dementia of Alzheimers type was significantly lower as compared to control subjects ($p < 0.05$).

Serum vitamin B_{12} was estimated by ELISA method. Estimation was done in all patients (n=110) and control subjects (n=55). The final result was expressed as ng\ml.

The mean serum vitamin B_{12} level in patients (1.27 ± 1.61) was lower as compared to controls (1.44 ± 0.75) group but the levels were not significantly different (Table 2, Fig 2; $p > 0.05$).

Table 2: Vitamin B_{12} levels in controls and patients with Alzheimers disease (mean ± S.D)

GROUPS	NO OF CASES	VITAMIN B12(ng/ml)
PATIENTS	110	(1.27±1.61)
CONTROLS	55	(1.44± 0.75)

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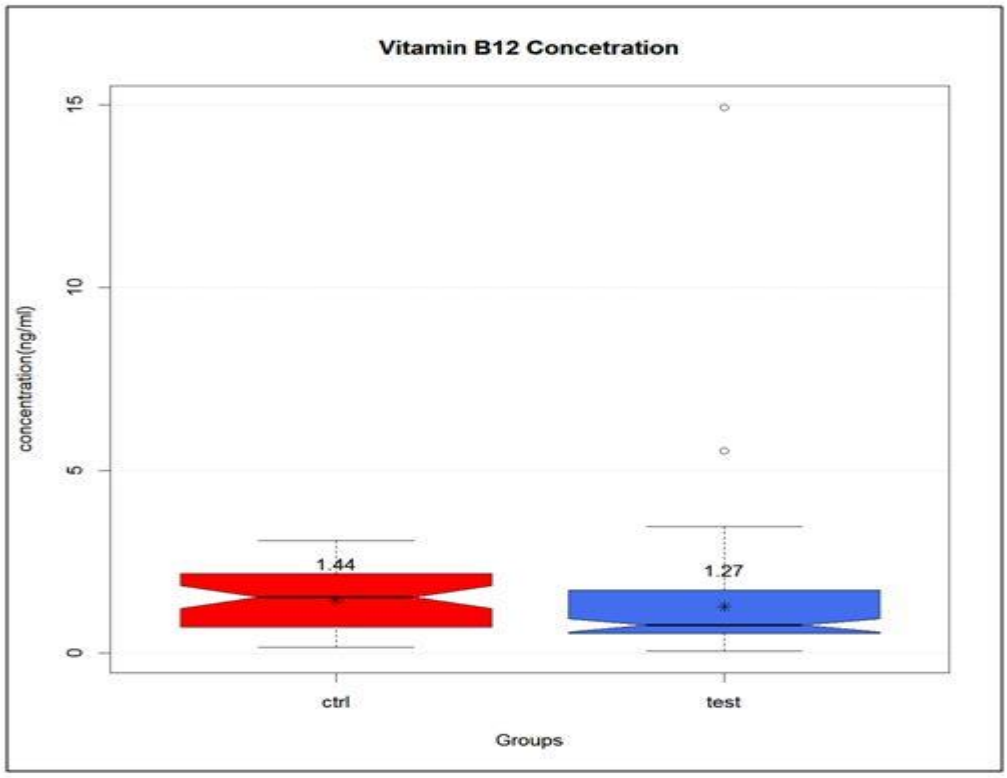

Fig 2: Showing comparison between serum vitamin B_{12} levels in patients with Alzheimers disease and controls. There was no significant difference in serum B_{12} level in patients of senile dementia of Alzheimers type and control subjects ($p > 0.05$).

Clinical Dementia Rating (CDR) scales of the patients without intervention were compared with CDR scales after the intervention with vitamin B_{12} and folic acid (with supplementation of 1.55 mg vitaminB_{12} & 1.10 mg Folic acid) and it was observed that CDR scales of the 110 patients do not show any improvement with vitamin B_{12} and folic acid supplementation for one month. Out of 110 patients 17 patients shown lower CDR scale in the due course of time and rest of 93 patients with same levels of CDR scale.

DISCUSSION

There are many risk factors for the Alzheimer's disease which includes genetic factor, increase in homocysteine levels in blood, aluminum metal exposure from pots, pans and beverage cans, age, smoking etc. An extensive study is needed to determine the etiological factors.

In our study, we estimated the serum levels of folic acid and vitaminB_{12} in all (165) participants. Out of 165 subjects, 110 were patients of senile dementia of Alzheimer type and 55 were age matched controls. A correlation between these parameters was also studied. Further, after intervention with vitamin B_{12} and folic acid supplementation, CDR scale was used to measure the effect of these interventions on the cognitive function of patients of senile dementia of Alzheimer type.

Folic acid and vitamin B12 are important nutrients we obtain from our diets in order to perform a number of cellular processes related to methylation and DNA synthesis. Vitamin B_{12} and folic acid deficiency (often caused by inadequate dietary intake) are associated with well known hematological consequences and neurological symptoms.

Folic acid is a water-soluble vitamin that plays a central role in the synthesis of DNA along with its repair and methylation [7]. Folic acid helps in the development of the body through the reactions such as histidine, serine, methionine, thymidylate and purine cycle [8]. Vitamin B_{12} and folic acid both are required for

DNA synthesis. In the absence of sufficient vitamin B_{12} and folic acid, synthesis of DNA is affected, thus reducing cell proliferation.

While it has been known for decades that severely low vitamin B_{12} levels can cause dementia, the first report of vitamin B_{12} deficiency in Alzheimer's patients emerged in the mid-80s. Cole *et al.,* found lower serum vitamin B_{12} levels in Alzheimer patients as compared to those with non-Alzheimer's type dementia [9]. They concluded with some tentative hypotheses the association of low vitamin B_{12} with AD. In 1959, Droller and Dosset reported that aged individuals with senile dementia have a significantly lower serum vitamin B_{12} levels than normal persons of a similar age [10, 11, 12]. Most of the studies carried out concerning cognition support that vitamin B_{12} levels are positively associated with cognitive function, either global function or specific domains of cognition [13, 14].

In the present study, lower levels of serum folic acid in patients of senile dementia of Alzheimer's type as compared to control subjects suggest that folic acid deficiency may be one of the risk factor for this disorder. Serum B_{12} level was not significantly different in patients and control subjects in our study.

Further, no improvement in the CDR scales of the patients of dementia of Alzheimer's type after the intervention with vitamin B_{12} and folic acid (with supplementation of 1.55 mg vitaminB_{12} & 1.10 mg folic acid) in this study, indicate that vitamin B_{12} and folic acid supplementations have no role in the improvement of the memory of patients with Alzheimer's disease after the onset of the disease process. Further study is needed to delineate the mechanism which may prevent progress of the disease.

CONCLUSION

Folic acid deficiency is found to be one of the important risk factor for the senile dementia of Alzheimers type in our study. Further, it is concluded that vitamin B_{12} and folic acid supplementations do not improve the cognitive status of patients with Alzheimer's disease after the onset of the disease process.

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