Plasma Fibrinogen and C-reactive Protein levels in Alzheimer's Disease and Mild Cognitive Impairment

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OBJECTIVES

Alzheimer's disease (AD) is the most common form of dementia and is characterized clinically by a gradual decline in cognitive function, an increasingly neuropsychiatric and behavioral disturbances. Until recently, the treatment targeting neurodegenerative chain reaction has not shown clear results. And cholinesterase inhibitors have improved some cognitive function, it was not a satisfactory result. In this situation, studies have shown that inflammation of the brain can be the cause of AD.

The aim of this study was to measure and compare the levels of CRP and fibrinogen in patients with AD, Mild cognitive impairment (MCI), normal control (NC) groups and to investigate the correlations between blood-based inflammatory factors and cognitive functions.

METHODS

The study population was recruited from the Department of Psychiatric Medicine and Dementia Clinic of Inje University Ilsan Paik Hospital in the South Korea from 2 August 2018 to 13 December 2018. Based on the clinical judgements of psychiatrist, we classified AD, MCI and normal control group. The study protocol was approved by the Ilsan Paik Hospital Ethics Committee.

Seventy one subjects participated in this study (AD: 28, MCI: 23, NC: 20). The overall cognitive function of the subjects and the severity of the disease stage were assessed using Mini-Mental State Examination (MMSE-K), Clinical Dementia Rating (CDR), Global Deterioration Scale (GDS), Korean neuropsychiatric inventory (K-NPI) and Geriatric Depression Scale-Korean (GDS-K). Serum CRP and fibrinogen were also measured in AD, MCI, and normal control groups.

Blood sampling were taken in the morning after overnight fasting. Blood tests were conducted at Seoul Clinical Laboratories. Inflammatory factors such as IL-1 β , TGF- β and CRP were examined.

One-way ANOVA was performed to analyze differences in concentrations of fibrinogen and CRP among the three groups of AD, MCI and NC. Pearson correlation analysis was performed to analyze the correlation between inflammatory factors (fibrinogen, CRP) and neurocognitive functions (MMSE-KC, CDR, GDS), K-NPI and GDS-K. The collected data were analyzed using Statistical Package for the Social Science (SPSS) ver. 20.0. P <0.05 was the level used to determine statistical significance.

RESULTS

The demographic characteristics and cognitive function of the subjects participating in this study are shown in Table 1. The total number of subjects was 71, of which 22 were males and 49 were females. The number of subjects was 28 in the AD group, 23 in the MCI group, and 20 in the NC group, and the mean age was 78.27, 78.61 and 79.95, respectively. The score of the MMSE-KC, GDS and CDR was significantly different among three groups. Fibrinogen level in AD, MCI and NC was 347.50, 341.87 and 332.80 respectively and CRP level was 0.36, 0.15 and 0.13 respectively. Inflammatory factors tended to increase with cognitive decline, but not statistically significant. K-NPI tended to increase with NC, MCI, and AD, respectively, but there was no statistically significant difference. There was no statistically significant difference in GDS-K between AD, MCI, and NC. These results are shown in Table 1.

Pearson correlation analysis was performed to determine the relationship between inflammatory factors and neurocognitive test. Both fibrinogen and CRP were negatively correlated with MMSE-KC, GDS, CDR, and K-NPI, but not statistically significant. These results are shown in Table 2).

CONCLUSION

Fibrinogen and CRP have not been identified as risk factors for dementia in this study. And this study has some limitations. First, the number of samples is not large, so that the reliability and validity of the study may be degraded. Second, not all of the factors that might be related to fibrinogen and CRP levels were controlled, such as sleep apnea and rheumatoid arthritis. Third, because this study was cross-sectional study, it was difficult to consider all the circumstances of the patient, which may have affected the outcome of the study. Fourth, the blood collection time was not constant. But this study was the first meaningful study in Republic of Korea about the relationship between cognitive impairment and peripheral fibrinogen and CRP levels. It is necessary to conduct prospective studies on more patients in the future.

Table 1. Demographic and clinical variables of patients (n=71)

	AD (n=28)	MCI (n=23)	NC (n=20)	p-value
Age(years)	78.27 (6.29)	78.61 (4.83)	79.95 (7.14)	0.125
Female - n (%)	23 (82.14%)	14 (60.87%)	12 (60.00%)	0.160
MMSE-KC	15.00 (2.99)	22.17 (1.95)	26 (2.25)	0.000**
GDS	3.71 (0.81)	2.96 (0.64)	2.50 (0.61)	0.000**
CDR	1.00 (0.41)	0.63 (0.22)	0.48 (0.20)	0.000**
Fibrinogen (mg/dL)	347.50 (98.75)	341.87 (60.47)	332.80 (50.70)	0.804
CRP (mg/dL)	0.36 (0.71)	0.15 (0.12)	0.13 (0.72)	0.146
K-NPI	18.32 (20.09)	14.78 (24.40)	4.55 (8.68)	0.053
GDS-K	13.64 (8.17)	13.04 (6.78)	13.10 (7.09)	0.951

**Significant at p<0.01, *Significant at p<0.05, MMSE-KC: Mini-Mental state Examination in the Korean version of CERAD assessment packet, CDR: Clinical Dementia Rating, GDS: Global Deterioration Scale, K-NPI: Korean neuropsychiatric inventory, GDS-K: Geriatric depression scale-Korean

Table 2. Correlation between inflammatory factor and Neuropsychiatric factor.

		MMSE-KC	GDS	CDR	K-NPI	GDS-K
Fibrinogen	r	-0.053	-0.195	-0.167	-0.036	0.092
	p	0.662	0.103	0.165	0.764	0.445
CRP	r	-.126	-0.102	-0.084	-0.050	-0.061
	p	.294	0.396	0.485	0.676	0.615

**Significant at p<0.01, *Significant at p<0.05, r: coefficient of correlation, MMSE-KC : Mini-Mental state Examination in the Korean version of CERAD assessment packet, CDR: Clinical Dementia Rating, GDS: Global Deterioration Scale, K-NPI: Korean neuropsychiatric inventory, GDS-K: Geriatric depression scale-Korean.

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