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⁹⁹ᵐTC- ECD SPECT

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Regional Cerebral Blood Flow Changes in Alzheimer's Disease Patients Treated with Cholinesterase Inhibitors: A Preliminary Study using ⁹⁹ᵐTC-ECD SPECT

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Background: This study aimed to evaluate regional cerebral blood flow (rCBF) changes using ⁹⁹ᵐTC-ECD SPECT (Ethylene Cysteine Diethylester Single Photon Emission Computed Tomography) and contemporary clinical responses such as cognitive and psychiatric symptoms and activities of daily living (ADL) after cholinesterase inhibitors (ChEI) treatment. **Methods**: The subjects were eight probable Alzheimer's disease (AD) patients (four males and four females, mean age 69.63 years) who were recruited from the department of Neurology, at Yeungnam University Medical Center, between August 2000 and April 2002. The clinical diagnosis of AD was based on the DSM- and NINCDS-ADRDA criteria. Hachinski ischemic scores of all the patients were below 1. The mean treatment duration was 30.38 weeks which ranged from 24 to 44 weeks. Four patients received Rivastigmine (Exelon) 12 mg after titration, and three patients received Donepezil (Aricept) 10 mg during the whole period and only one patient had Donepezil 10 mg after the initial 5 mg for three weeks. The base line and follow up ⁹⁹ᵐTC-ECD SPECT studies were done on an average 6 days before the ChEI treatment and 4 days after finishing the study. **Results**: The most significant increase in blood flow occurred in the bilateral parietal lobes ($p < 0.05$). Reduction in the rCBF is more profound on the left hemisphere in the base line ($p < 0.05$) and it achieved significant increase of rCBF after ChEI treatment compared with the right hemisphere ($p < 0.05$). **Conclusions**: Treatment with ChEI for 30.38 weeks increased rCBF and overall increased in global cognitive functions including K-MMSE, ADAS-cog, CDR, CDR-SB, GDS, and NPI and ADCS-ADL scores.
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Key Words: Alzheimer's disease, Cholinesterase inhibitors, Regional cerebral blood flow, ECD-SPECT

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acethylcholine (Ach)

(AD)   .[1] Ach   acethylcholine transferase (CAT)

acethylcholinesterase (AchE)

(Cholinesterase inhibitor: ChEI)   Ach

Ach

.[2]

Brain MRI

Brain SPECT

'

.[3]

.

.[4]

.

ChEI   AD

,[5-8]

(modify)

.   AD   ChEI   1.

[9]

[10]   ,   2000 8   2002 4

(rCBF: regional Cerebral Blood

Flow)   .[11]   DSM   dementia crite-

ChEI   ria   NINCDS/ADRDA (National Institute for

Neurological and Communicative disorders and

.   Stroke/Alzheimer`s Disease and Related Disorders

AD   Donepezil   99mTC- HMPAO   Association) criteria   probable AD 8 (·

SPECT   4)   . MRI

,[12] orbital   dorsolateral frontal

rCBF   AD   ,   ChEI

(irritability)   Hachinski   4

(euphoria)   .   Hachinski   1

ChEI   .[13]   .   61   78   69.63

rCBF   ± 5.60   . CHEI   rivastigmine (Exelon)   4

,   donepezil (Aricept)   4

ChEI   AD   . Rivastigmine   3 mg 4
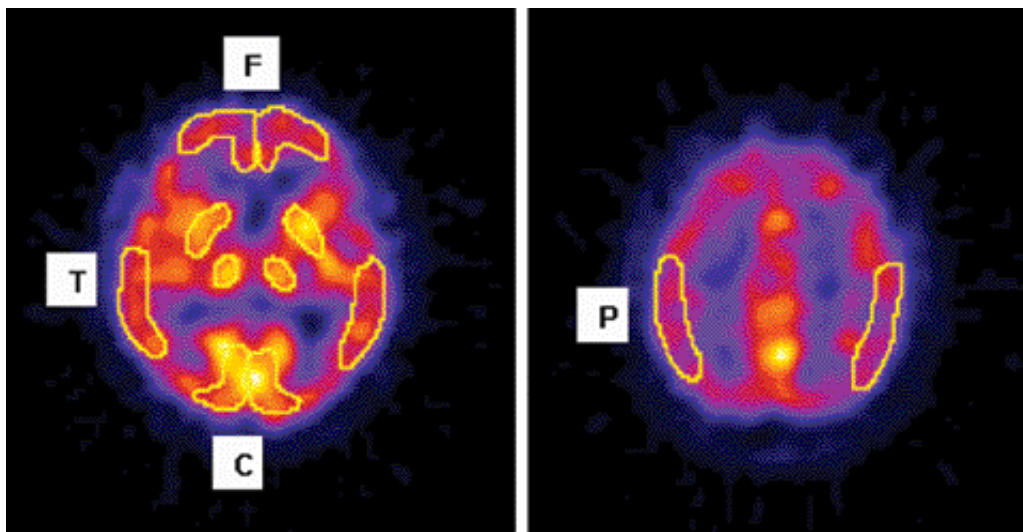
AD   6 mg, 9 mg   4

.[9-11]   12 mg   . Donepezil   1

AD   3   5 mg   4   10 mg   3

ChEI   10 mg   .

SPECT   ChEI   ChEI   24   44

AD   30.38± 7.82   .

Fig. 1. Regions of interest
F; frontal, T; temporal, P; parietal, C; cerebellum

2. SPECT

^{99m}TC- Ethylene Cysteine Diethylester(ECD)
SPECT ChEI 6 (0~7)
4 (1~7) rCBF
. SPECT

(E- cam, Siemens, Germany) .

10 740 MBq ^{99m}Tc- ECD
1 20 , 128× 128 3
120 .
Butterworth
Chang
. (ROIs: regions of interest)
, , 8
ROI (count)
(RCR: region to cerebellar ratio)
(Fig. 1).

AD ,

RCR .

$$RCR = \frac{\text{Mean Count of ROI}}{\text{Mean count of cerebellar hemispheres ROIs}}$$

ChEI ROI RCR
Wilcoxon matched- pairs
signed- ranks test .

3.

ChEI
, ChEI 6 (0~7)
3 (0~7)
K- MMSE (Korean Version Mini
Mental State Examination), ADAS- cog (Alzheimer`s
Disease Assessment Scale- cognitive subscale)
GDS (Global Deterioration
Scale) CDR (Clinical Dementia Rating) CDR

SB (Clinical Dementia Rating Sum of Box)
. NPI
(Neuropsychiatric Inventory)[14]
ADCS- ADL
(Alzheime`rs Disease Cooperative Study- Activities of
Daily Living) . ,
Wilcoxon matched- pairs signed- ranks test
.

ChEI rCBF
. , RCR 0.06
ChEI rCBF
(p<0.05). RCR
ChEI 0.03
(Table 1). , rCBF
0.84± 0.09, 0.87±
0.09
(p<0.05)(Table 2), rCBF ,
0.88± 0.08 0.89± 0.09 rCBF ChEI

(p<0.05)(Table 3).
ADAS- cog, K-
MMSE, CDR, CDR SB, GDS, NPI, ADCS- ADL
,
. ChEI ADAS-
cog 28.50± 18.12 8 52 ChEI
23.25± 8.96 5.25
. K- MMSE ChEI 1 25
1 1 7 10
14.63± 8.73 0.62
15.25± 7.22 . CDR ChEI
0.5 3 1.44± 0.94 0.13
1.31± 0.92 . CDR SB ChEI
3.5 16 8.25± 4.42 0.44
7.81± 4.46 . GDS ChEI
3 6 4.63± 1.41 0.25

Table 1. RCRs in each lobes (mean±s)

ROIs	Frontal lobe		Temporal lobe		Parietal lobe	
RCR	Rt	Lt	Rt	Lt	Rt	Lt
Pre-CHEI	0.86±0.10	0.85±0.11	0.87±0.11	0.82±0.10	0.87±0.08	0.85±0.06
Post-CHEI	0.89±0.11	0.88±0.10	0.87±0.09	0.85±0.09	0.93±0.07*	0.91±0.04*

*P<0.05, ROIs; regions of interest, RCR; region to cerebellar ratio, CHEI; cholinesterase inhibitor, Lt; left, Rt; right

Table 2. Base line RCRs in each hemispheres (mean±s)

RCR \ ROIs	Rt. hemishere (F+T+P)	Lt. hemishere (F+T+P)
Pre-CHEI	0.87±0.09	0.84±0.09*

*P<0.05, F: frontal lobe, T: temporal lobe, P: parietal lobe, ROIs: regions of interest, RCR: region to cerebellar ratio, CHEI: cholinesterase inhibitor

Table 3. Changes of RCRs in each hemispheres (mean±s)

RCR \ ROIs	Rt. hemishere (F+T+P)	Lt. hemishere (F+T+P)
Pre-CHEI	0.87±0.09	0.84±0.09
Post-CHEI	0.89±0.09	0.88±0.08*

*P<0.05, F; frontal lobe, T; temporal lobe, P; parietal lobe, CHEI; cholinesterase inhibitor, ROIs; regions of interest, RCR; region to cerebellar ratio

Table 4. Changes in neuropsychological test scores (mean±s)

Scores \ Scales	ADAS-cog	K-MMSE	CDR	CDR SB	GDS	NPI	ADL
Pre-AchEI	28.50 (±18.12)	14.63 (±8.73)	1.44 (±0.94)	8.25 (±4.42)	4.63 (±1.41)	18.00 (±21.59)	53.50 (±10.85)
Post-AchEI	23.25 (±8.96)	15.25 (±7.22)	1.31 (±0.92)	7.81 (±4.46)	4.38 (±1.19)	16.88 (±18.08)	58.00 (±9.76)
Difference	-5.25	0.62	-0.13	-0.44	-0.25	-1.12	4.5

Positive and negative, both values stand for improvements, K-MMSE; Korean-Version Mini Mental State Examination, ADAS-cog; Alzheimer's Disease Assessment Scale-cognitive subscale, ADCS-ADL; Alzheimer's Disease Cooperative Study-Activities of Daily Living, CDR; Clinical Dementia Rating, CDR SB; Clinical Dementia Rating Sum of Box, GDS; Global Deterioration Scale, NPI; Neuropsychiatric Inventory, CHEI; cholinesterase inhibitor

4.38± 1.19 . (NPI)
(ADCS- ADL) rCBF .
, rCBF
NPI ChEI AD
1 59 18.00± 21.59 1.12
16.88± 18.08 . ADCS- ADL ChEI rCBF
ChEI 41 64 53.50± 10.85 .
4.50 58.00± 9.76
(Table 4).

ROI

rCBF .
, rCBF ChEI
Probable AD 30 (7.5) ChEI (p<0.05),
rCBF . ChEI rCBF
(p<0.05).
. AD
[15-17]
, ChEI .
[3,18] 30
ChEI 1 K-

MMSE 3 . AD ChEI [20] ChEI

, ,

NPI ChEI ,

AD (heterogenous) ,

.

NPI ADCS- ADL .

ChEI

. . AD ChEI

AD 35 Donepezil rCBF . ChEI

rCBF AD AD

rCBF [11]

. ChEI ChEI

(ischemic core)

rCBF [21] .

SPECT AD

50 (17~99)

.

AD

ChEI

ChEI .

AD .

rCBF

. ADAS- cog, K- MMSE, CDR, CDR SB, GDS

ChEI AD ChEI NPI, ADCS- ADL

AD rCBF . ADAS- cog

. Donepezil 12 AD ^{99m}TC- [22] 5.25

ECD SPECT Donepezil AD MMSE CDR SB

rCBF 2.8 [23-24] 2.4 [25]

rCBF ChEI K- MMSE 0.62

CDR SB 0.44

.

[9] Rivastigmine 6~9 mg 6 AD 8 (: = 4:4) ChEI

16 12 24 44 ^{99m}TC- ECD SPECT

4 Rivastigmine rCBF

.

,

[10] 1. rCBF ($p < 0.05$).

2. ChEI rCBF

($p < 0.05$), ChEI rCBF

rCBF rCBF ($p < 0.05$).

masking ChEI 3. ADAS- cog 5.25 , K- MMSE

. 0.62 , CDR 0.13 , CDR SB 0.44 , GDS 0.25 ,

ChEI rCBF NPI 1.12 .

ChEI 4. ADCS- ADL 4.50 .

rCBF [19] (postsy-

naptic)

ChEI   AD

rCBF   ,

      . ChEI

.

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