

Is the Response of Patients with Alzheimer's Disease to Cholinesterase Inhibitors different with Presence / Absence of Vascular Risk Factors ?

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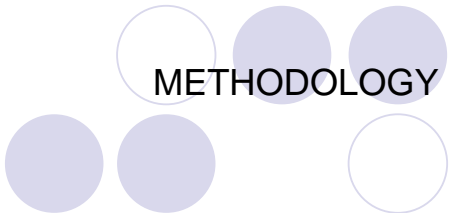
BACKGROUND

- Cholinesterase Inhibitor (ChEI) is beneficial to patients with Alzheimer's Disease (AD)
- vascular risk factors are recognised as risk factors for developing AD (*Kivipelto M et al, BMJ 2001; Forette F et al, Lancet 1998; Otta A et al, Neurology 1999*)
- vascular changes may often coexist with AD
- cerebrovascular changes may play an important role in the clinical expression of AD (*Snowdon DA et al, The Nun Study, JAMA 1997*)


- since not all patients will benefit from ChEI, it raises the question of whether there is a difference in response to ChEI in AD patients with and without vascular risk factors
- answer to this question may help to identify a group of patients that are likely to benefit from treatment with ChEI

OBJECTIVE

To evaluate whether there is a response difference to ChEI in AD patients with and without vascular risk factors



# METHODOLOGY




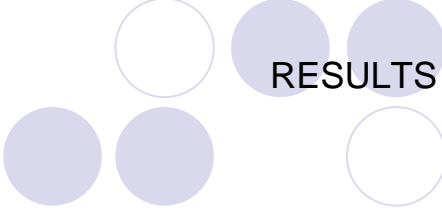
## Designs / Methods

Retrospective cohort study of 90 AD patients

## Setting

Cognitive / Gerontology clinic in Tai Po Hospital from 12.1998 to 10.2002

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- ## Measurement
- Demographic characteristics
  - Presence of vascular risk factors (HT, DM, hyperlipidaemia, smoking, Hx of IHD, MI and CVA)
  - Use of ChEI (only Donepezil available as PCI)
  - Score of Mini-Mental State Examination (MMSE) at baseline and 6 months
- ## Statistical Analysis
- Student's t-test, ANOVA
  - significant level is set at  $p < 0.05$



# RESULTS




Table 1. Distribution of patients had or had no ChEI intake, and with or without vascular risk factors

	ChEI intake group	Non-ChEI intake group	Total
AD with vascular risk factors	29	14	43
AD without vascular risk factors	32	15	47
<b>Total</b>	<b>61</b>	<b>29</b>	<b>90</b>

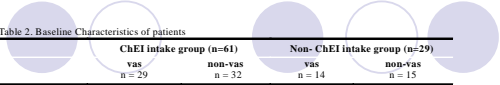


Table 2. Baseline Characteristics of patients

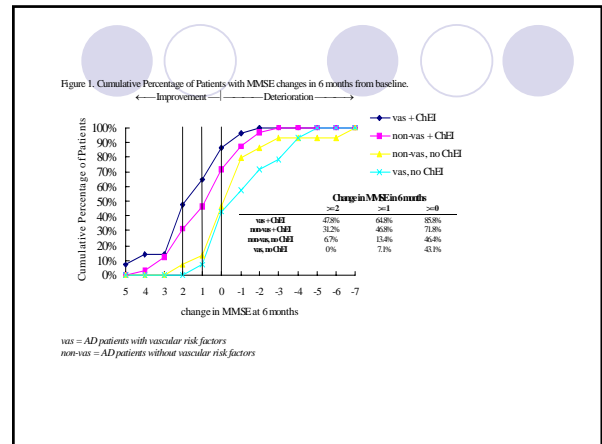
	ChEI intake group (n=61)		Non-ChEI intake group (n=29)	
	vas n = 29	non-vas n = 32	vas n = 14	non-vas n = 15
Age (years), mean ±SD	80.1 ± 7.0	80.5 ± 8.2	80.9 ± 5.2	77.8 ± 5.4
Gender (%)				
Male	12 (41)	8 (25)	6 (43)	6 (40)
Female	17 (59)	24 (75)	8 (57)	9 (60)
Education (%)				
literate	9 (31)	9 (28)	5 (36)	4 (26)
illiterate	20 (69)	23 (72)	9 (64)	11 (74)
Dementia Duration (years) Mean ± SD	1.55 ± 0.59	1.77 ± 0.81	1.82 ± 0.54	1.7 ± 0.68
Living status (%)				
Family	19 (66)	23 (72)	10 (71)	10 (67)
Alone	2 (7)	2 (6)	0 (0)	1 (7)
OAH	8 (27)	7 (22)	4 (29)	4 (26)
Plasma dose of Donepezil (mg/day)	5	5	-	-
MMSE at baseline Mean ± SD	15.28 ± 3.53	15.34 ± 3.73	15.86 ± 3.66	15.93 ± 3.61

vas = AD patients with vascular risk factors  
non-vas = AD patients without vascular risk factors  
OAH = old age home

**Table 4. Comparison of MMSE change at 6 months between groups**

	Mean MMSE change from baseline at 6 months ± SEM	Mean Groups Difference (95% Confidence Interval)	p-value
All patients with ChEI intake n = 61	0.89 ± 0.22	2.09 (1.28 to 2.91)	0.000*
All patients without ChEI intake n = 29	-1.21 ± 0.36		
Vascular risk group with ChEI intake n = 29	1.31 ± 0.32	2.81 (1.64 to 3.98)	0.000*
Vascular risk group without ChEI intake n = 14	-1.50 ± 0.50		
Non-vascular risk group with ChEI intake n = 32	0.50 ± 0.30	1.43 (0.29 to 2.58)	0.015*
Non-vascular risk group without ChEI intake n = 15	-0.93 ± 0.53		
Vascular risk group with ChEI intake n = 29	1.31 ± 0.32	0.81 (-0.07 to 1.69)	0.071
Non-vascular risk group with ChEI intake n = 32	0.50 ± 0.30		
Vascular risk group without ChEI intake n = 14	-1.50 ± 0.50	-0.57 (-2.07 to 0.93)	0.445
Non-vascular risk group without ChEI intake n = 15	-0.93 ± 0.53		

\*denote statistically significant (p<0.05)



## DISCUSSION

### Efficacy of ChEI in AD patient

- this study, like previous placebo-controlled trials, demonstrated ChEI had beneficial effect in mild to moderate AD

### Treatment effect of ChEI in AD patient with vascular and without vascular risk factors

- treatment effect was generally greater in AD patients with vascular risk factors
- greater difference in MMSE change between ChEI and non-ChEI intake in vascular group as compared to non-vascular risk group (2.81 in vascular risk group vs 1.43 in non-vascular risk group)

- within the ChEI taking group, there was no significant difference in MMSE change over 6 months between vascular and non-vascular risk groups
- insignificant difference in MMSE change could be due to the small sample size or the difference in natural course between 2 groups

### **Percentage of patients had response to ChEI**

- patients in both treatment and non-treatment group had a wide range of response
- ChEI intake patients were more likely to show greater improvement as indicated by a higher proportion showing a good response than those without ChEI intake
- among the ChEI intake patients, those with vascular risk factors showed a better response

### **MMSE deterioration in AD patients without treatment**

- illustrate the difference in the natural progression of disease between vascular and non-vascular groups
- did not show significant difference in this study
- it may relate to inadequate sample size

### **LIMITATIONS**

- retrospective
- limited sample size, incomplete data in medical record and attrition of patient
- may not be generalised to other patient groups
- bias : observers were not blinded to patient groups; patient who took ChEI could have more social support and better financial status
- MMSE was the only outcome measure, it is better to use several outcome measures e.g ADAS-cog and CIBC-plus
- cannot differentiate which vascular risk factors had greater effect on AD progression

### **CONCLUSION**

- ChEIs have beneficial effect to AD patients in terms of slight improvement of MMSE scores over 6 months
- use of ChEI in AD patient with vascular risk factors resulted in more treatment benefit and may regard as a good outcome predictor
- AD patients with vascular risk factors may have a more rapid decline in MMSE as c/w those without vascular risk factors
- further studies, especially well-designed randomized placebo-controlled trials, may give further convincing evidence in these aspects

