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Antioxidant Intake and Mild Cognitive Impairment Among Elderly People in Klang Valley: A Pilot Study

(Kajian Perintis: Pengambilan Antioksidan dan Kegagalan Kognitif Ringan di Kalangan Warga Tua Lembah Klang)

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ABSTRACT

Mild cognitive impairment (MCI) is associated with significant morbidity, especially in the development of Alzheimer's disease and also related to nutritional factors. A pilot study was carried out to determine antioxidant intake and its relation with MCI among elderly people aged between 60 and 74 years in Klang Valley. Subjects were interviewed to obtain socio-demography data and functional status was evaluated using the Instrumental Activities of Daily Living (IADL). Data on food intake was assessed using the diet history questionnaire and food frequency questionnaire, whilst the Geriatric Depression Scale (GDS) was used to assess depression level. A combination of tests was used to assess cognitive decline, which are Mini-mental State Examination (MMSE), Clock Drawing Test (CDT), and Dementia Rating Scale (DRS). Out of 84 elderly recruited, 70 completed all parts of the study (response rate 83.3%). Mean vitamin E intake was less than the Malaysian RNI (50.0% of RNI for men and 43.0% for women). The incidence of amnestic-MCI (aMCI) was 15.7% among the respondents, while 32.8% were depressed. After adjustment for educational background, beta-carotene intake was found to be significantly (β = 0.325, $p<0.05$) correlated to cognitive impairment based on CDT scores. The intake levels of antioxidants among subjects were unsatisfactory and beta-carotene intake was related to poor cognitive status based on CDT.

Keywords: Antioxidants; cognitive impairment; elderly; oxidative stress

ABSTRAK

Kegagalan kognitif ringan sering dikaitkan dengan morbiditi yang signifikan, terutamanya perkembangan penyakit Alzheimer, dan berhubungkait dengan faktor pemakanan. Suatu kajian awal telah dijalankan untuk menentukan pengambilan antioksidan dan hubungkaitnya dengan kegagalan kognitif ringan di kalangan warga tua berumur 60 hingga 74 tahun di Lembah Klang. Subjek ditemuduga untuk memperoleh data sosiodemografi dan status kefungsian diuji dengan menggunakan penilaian Aktiviti Hidup Harian Instrumental (IADL). Data pengambilan diet ditentukan dengan menggunakan soal-selidik sejarah diet dan soal-selidik kekerapan makanan, manakala Skala Kemurungan Geriatrik (GDS) pula digunakan untuk menentukan tahap kemurungan. Satu kombinasi ujian digunakan untuk menentukan kemerosotan kognitif, iaitu Mini-mental State Examination (MMSE), Ujian Pelukisan Jam (CDT), dan Dementia Rating Scale (DRS). Daripada 84 peserta, 70 orang telah melengkapkan kesemua bahagian kajian tersebut (kadar respons 83.3%). Purata pengambilan vitamin E didapati kurang daripada saranan RNI Malaysia (50.0% RNI untuk lelaki dan 43.0% untuk perempuan). Insiden kegagalan kognitif ringan jenis amnestik adalah 15.7% di kalangan responden, manakala 32.8% subjek menghadapi kemurungan. Setelah mengambil kira faktor pendidikan, pengambilan beta-karoten didapati berhubungkait secara signifikan (β = 0.325, $p<0.05$) dengan kegagalan kognitif berdasarkan skor CDT. Tahap pengambilan antioksidan di kalangan subjek adalah tidak memuaskan dan pengambilan beta-karoten didapati berhubungkait dengan status kognitif yang lemah berdasarkan ujian CDT.

Kata kunci: Antioksidan; kegagalan kognitif; tekanan oksidatif; warga tua

INTRODUCTION

Aging of a population is a matter of great concern for the health sector. Generally, the elderly are less healthy than the non-elderly. An increasing in age is associated with higher morbidity and higher use of health services such as more frequent visits to doctors and hospitalization (Joshi et al. 2003; Karim 1997; Woo et al. 2007). The official definition for elderly people in Malaysia includes those 60 years and above (United Nations 1994), and was approximated to be 1 million in 1997. After three years, this particular group had increased to 1.5 million and will further increase to 4 million by 2025 (Arokiasamy 1997).

Mild cognitive impairment (MCI) patients have a significantly higher rate (12 to 15 % per year) of progression to Alzheimer's disease compared to cognitively normal elderly people (1 to 2% per year) (Smith et al. 1996). Mild cognitive impairment (MCI) can be divided into two broad subtypes: amnestic MCI (a-MCI) characterized by reduced memory, and non-amnestic MCI (na-MCI) in which other cognitive functions rather than memory are mostly impaired (Petersen et al. 1999).

Typically, the onset of MCI is marked by a measurable memory loss that is abnormal for an individual's age and education, and is corroborated by an informant. a-MCI seems to represent the earliest point at which treatments for dementia, particularly Alzheimer's disease, can be attempted (Petersen 2000). It is a stage which leads to dementia, but has not yet happened. The criteria for a-MCI include: 1) memory complaint, 2) objective memory impairment for age, 3) normal general cognitive status, 4) normal daily functioning, and 5) absence of dementia (Petersen et al. 2001).

Many factors contribute to a cascade of events at the molecular level that lead to degenerative processes and aging is said to be the predominant risk, a process which produces free radical damage, oxidative stress, alterations in calcium homeostasis and endothelial damage (Hardy & Higgins 1992). It has been found that large amounts of unsaturated lipids and catecholamines in the brain are particularly susceptible to free radical damage. A consistent body of evidence clearly indicates that oxidative stress is increased in brains of patients with Alzheimer's disease, as well as in living patients with probable Alzheimer's disease (Perry et al. 1998; Delanty & Ditchter 2000). Therefore, there are suggestions that intake of antioxidants may help in reducing cognitive decline. However, epidemiology data on antioxidants and cognitive function were inconsistent (Grodstein et al. 2003; Masaki et al. 2000; Mendelsohn et al. 1998; Perkins et al. 1999). There is a paucity of literature concerning such studies in Malaysia. Thus, the main aim of the present study was to investigate the association between antioxidant intake and cognitive impairment in the elderly population of Malaysia.

Materials and Method

This cross-sectional study was carried out from mid-October 2008 to mid-November 2008 in six different locations around Klang Valley, Malaysia. The locations were selected on the basis of convenience sampling and only community-dwelling subjects aged between 60-74 years were included. The subjects consisted of elderly people who were members of the Cheras Elderly Day Care Centre, members of the Hulu Langat Senior Citizen Association, and elderly people living around Keramat, Sentul, Bangi and Cheras. Other inclusion criteria were not terminally ill, no known mental illness, and able to communicate well. All questionnaires were translated into Malay and pre-tested before the actual data collection. Subjects were interviewed based on the questionnaire to obtain the required information.

Part A of the questionnaire consists of questions on socio-demography and functional status. Data such as age, gender, marital status, living arrangement and education level were obtained, whereas functional status was assessed using the Instrumental Activities of Daily Living (IADL) (Lawton & Brody 1969). The 14-point IADL was used and the subjects who were unable or needed help with two or more activities indicated some limitation in daily function.

Part B consisted of neuropsychology tests to measure cognitive status, where a combination of three tests was used: Mini-mental State Examination (MMSE) (Folstein et al. 1975), Clock Drawing Test (CDT) (Sunderland et al. 1989) and Dementia Rating Scale (DRS) (Mattis 1976; Mattis 1988). The Malay version of MMSE was validated and found to be suitable for usage among the local elderly population (Zarina et al. 2007). Respondents were categorised as normal in the cognitive assessment if their MMSE scores were 24 or above, while those obtaining a score of 21 to 23 are categorized as having MCI. The Clock Drawing Test according to the method introduced by Sunderland et al. (1989) was used in this study, and the maximum score is ten. A score of six and above is categorized as normal in cognitive function.

The DRS is a useful tool to screen for cognitive impairment and dementia (Mattis 1976; Mattis 1988). It consists of 36 tasks, divided into five subscales, which were Attention (8 items), Initation and Perseveration (11 items), Construction (6 items), Conceptualization (6 items) and lastly, Memory (5 items). The cut-off score for dementia is 122 and below. Respondents are categorized as normal if they had scores of 123 and above. The short Geriatric Depression Scale (GDS) form (Sheikh & Yesavage 1986) modified from the original GDS was used in this study to measure depression level. It consisted of 15 questions and was more suitable to be used among the elderly who generally had low attention-span. Scores of zero to four indicated negative for depression symptoms, five to nine indicated mild depression, while 10 and above indicated severe depression (Sheikh & Yesavage 1986). Part C consisted of dietary intake, where food intake was assessed using the Diet History Questionnaire (DHQ) (Suzana et al. 2000), while antioxidants supplement was assessed using the Food Frequency Questionnaire (FFQ). However, the FFQ only focused on the types and form of supplement taken, but not the dosage.

Antioxidant and carotenoids intake was determined using the Malaysian Food Composition Table (Tee et al. 1997) and USDA Nutrient Data Laboratory obtained from Nutritionist Pro version 3.00. All data were analysed using SPSS 16.0. Descriptive statistics were used to analyse socio-demography, antioxidant intake levels and test scores. All data were checked for normality before analysis. Multiple linear regression was used to test for the association between antioxidants and cognitive impairment, after adjusting according to each model.

RESULTS

A total of 84 elderly were interviewed and 70 of them with mean age 67.1 ± 4.0 years for men and 65.7 ± 4.3 years for women completed the assessment (Table 1). Majority of the subjects were Malay (54.3% men and 51.4% women), followed by 37.1% Chinese and 10.0% Indian. Most of the subjects were married (68.6%), and there is a significant difference ($p<0.05$) in marital status between gender where more (40%) women were reported to be widowed (none were divorced) as compared to 14.3% men. This could be due to the shorter life span of men compared to women, with a mean difference of 4.2 years worldwide (Lunenfeld 2002). Besides, there was also a significant difference ($p<0.01$) in total years of education between gender. Mean years of education received was higher for men (7.6 ± 3.8) and the education level for men was generally higher than women. On the other hand, mean BMI for both genders were similar, which are 25.7 ± 4.1 kg/m^2 for men and 25.8 ± 3.8 kg/m^2 for women, indicating that most subjects were overweight (WHO Expert Consultation 2004).

As for dietary intake, it was found that mean energy intake for both men and women were below Recommended Nutrient Intake for Malaysia (NCCFN 2005), with men achieving 72.4% of RNI and women 73.2% (Table 2). Mean intake for vitamin C was satisfactory, a total of 117.9 ± 99.2 mg and 87.7 ± 82.7 mg were recorded for men and women, respectively. However, this is not the case for mean vitamin E intake, where 82.9% of men and women did not meet the RNI (Figure 1). Intake levels for four carotenoids were measured and it was found that intakes of beta-carotene

TABLE 1. Socio-demographic characteristics, BMI and IADL score according to Gender (presented as mean ± SD or number (%) and p)

Charateristics	Men (n=35) mean ± SD	Women (n=35) mean ± SD
Age (years)	67.1 ± 4.0	65.7 ± 4.3
Ethnicity	n (%)	n (%)
Malay	19 (54.3)	18 (51.4)
Chinese	13 (37.1)	13 (37.1)
Indian	3 (8.6)	4 (11.4)
Marital Status	n (%)	n (%)
Single	1 (2.9)	0 (0)
Married	27 (77.1)	21 (60)
Divorced/Widowed*	7 (20.0)	14 (40)
Education (years)*	7.6 ± 3.8	5.2 ± 3.3
BMI (kg/m^2)	25.7 ± 4.1	25.8 ± 3.8
IADL	13.6 ± 0.7	13.2 ± 1.6

*p<0.05, independent t-test

TABLE 2. Intake of energy, antioxidants, and cognitive test scores according to gender (presented as mean ± SD or number (%) and p)

Parameters	Men (n=35) mean ± SD	Women (n=35) mean ± SD	p
Energy intake (kcal)	1455 ± 400.9	1303 ± 350.3	0.096
Vitamin C (mg)	117.9 ± 99.2	87.7 ± 82.7	0.17
Vitamin E (mg)	5.0 ± 4.3	4.3 ± 3.0	0.444
Beta-carotene (µg)	3894 ± 3544	2781 ± 2742	0.146
Alpha-carotene (µg)	3 ± 9	8 ± 37	0.957
Lutein/ Zeaxanthin (µg)	36 ± 69	109 ± 471	0.371
Lycopene (µg)	65 ± 383	0	0.317
Antioxidant supplement use	n (%)	n (%)	
Yes	12 (34.3)	3 (8.6)	0.009[a]
No	23 (65.7)	32 (91.4)	0.016[b]
MMSE	23.0 ± 3.0	20.7 ± 4.5	0.029[b]
CDT	6.0 ± 2.0	4.6 ± 3.1	0.060
DRS	125.1 ± 16.9	115.2 ± 25.6	0.417
GDS	3.5 ± 2.4	4.0 ± 2.8	

[a]p<0.01, chi-square test, [b]p<0.05, independent t-test
MMSE = Mini-mental State Examination
CDT = Clock Drawing Test
DRS = Dementia Rating Scale
GDS = Geriatric Depression Scale

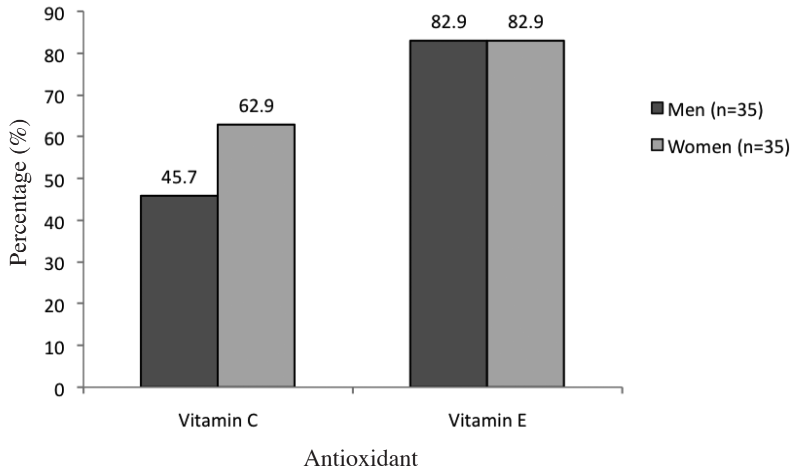

FIGURE 1. Percentage of subjects who do not meet RNI Malaysia for vitamin C and vitamin E intake according to gender

were the highest (3894 ± 3544 µg for men and 2781 ± 2742 µg for women) among the four. Mean intake of alpha-carotene, lutein (zeaxanthin) and lycopene were low, where the highest value achieved was 109 ± 471 µg for lutein intake among women, but none of them were reported taking foods containing lycopene. There was no significant difference in antioxidant intake from food between gender. Nevertheless, a significant difference ($p<0.01$) was found between gender in antioxidant supplement use. More men (34.3%) compared to women (8.6%) were reported to be taking antioxidant supplements at time of the study, with 25.7% of men were taking vitamin C supplement regularly (Figure 2). Interestingly, other than antioxidant supplements, 22.9% of men and women were using B complex supplements. The reason for such consumption is explained by the fact that it was either prescribed by a medical doctor or encouraged by their family members.

As shown in Table 2, a significant ($p<0.05$) difference was found between gender in the mean score for two cognitive tests, namely MMSE and CDT. Men scored higher in both tests, achieving a mean score of 23.0 ± 3.0 for MMSE and 6.0 ± 2.0 for CDT, while women obtained 20.7 ± 4.5 and 4.6 ± 3.1 for MMSE and CDT respectively. By taking into account all the criteria, it was found that 15.7% (10.0% men and 5.7% women) were having a-MCI, while 34.3% were demented and 32.9% were depressed (Figure 3). Using multiple regression analysis and after adjusting for education, a weak but significant association was found between beta-carotene intake and cognitive performance in CDT ($\beta = 0.325$, $p<0.05$) (Table 3).

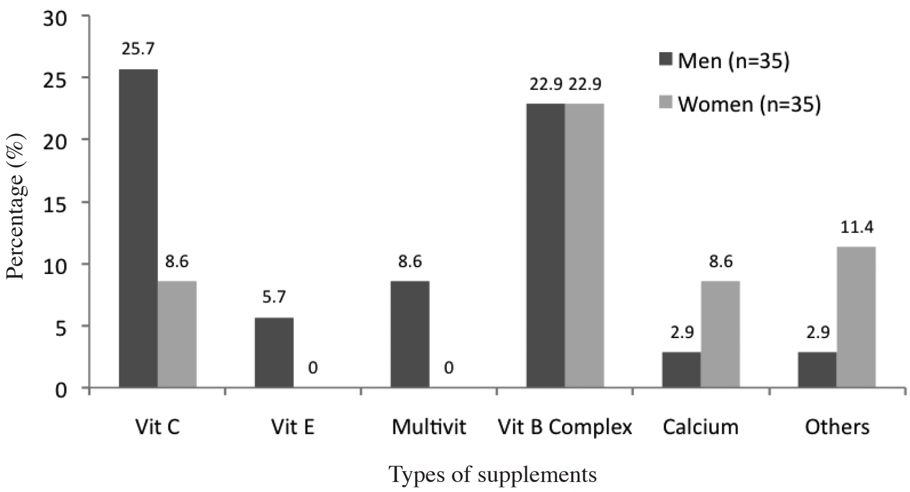

FIGURE 2. Types of supplements taken according to gender (presented as percentage)

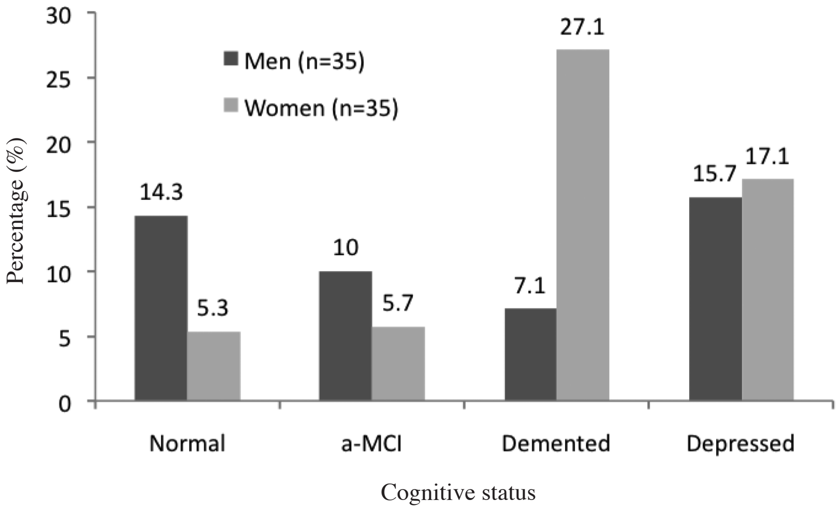

FIGURE 3. Cognitive status of subjects according to gender (presented as percentage)

TABLE 3. Correlation of antioxidants and cognitive test scores (presented as β and p)

	MMSE		CDT		DRS	
	β	p	β	p	β	p
Vitamin C						
Model 1	0.034	0.826	0.001	0.994	0.013	0.932
Model 2	-0.039	0.983	-0.095	0.520	0.004	0.979
Model 3	0.022	0.876	-0.046	0.754	0.027	0.845
Vitamin E						
Model 1	-0.128	0.466	0.254	0.139	-0.099	0.574
Model 2	0.039	0.808	0.225	0.123	0.087	0.601
Model 3	0.042	0.766	0.216	0.147	0.124	0.363
Beta-carotene						
Model 1	0.02	0.906	0.287	0.076	0.195	0.24
Model 2	-0.154	0.392	0.233	0.148	0.108	0.555
Model 3	-0.02	0.893	0.325	0.045*	0.098	0.503
Alpha-carotene						
Model 1	-0.05	0.654	0.116	0.304	-0.043	0.172
Model 2	0.005	0.969	0.100	0.363	0.034	0.788
Model 3	-0.049	0.644	0.094	0.401	-0.034	0.738
Lutein/Zeaxanthin						
Model 1	-0.061	0.597	0.185	0.101	0.109	0.345
Model 2	-0.067	0.609	0.197	0.092	0.085	0.515
Model 3	-0.106	0.316	0.145	0.196	0.109	0.293
Lycopene						
Model 1	0.034	0.776	-0.031	0.788	0.012	0.917
Model 2	0.02	0.874	-0.042	0.712	0.028	0.833
Model 3	-0.017	0.881	-0.042	0.72	-0.029	0.786

*p<0.05, multiple linear regression
MMSE = Mini-mental State Examination
CDT = Clock Drawing Test
DRS = Dementia Rating Scale
Model 1 = Adjusted for age, sex, ethnicity and energy intake (kcal)
Model 2 = Adjusted for marital status, BMI (kg/m^2) and antioxidant supplement use
Model 3 = Adjusted for education (years)

DISCUSSION

The incidence of MCI among the general population is between 2 to 30%, while it is more common in the clinical setting, ranging between 6 to 85% (Visser 2000). As for this study which was performed in the community setting, the incidence of MCI was 15.7%. This is similar to the results of a recent study involving 1969 elderly aged 70 to 89 years from Olmsted County, Minnesota, where 16.5% of the participants were reported to have MCI, and men were 1.67 times more likely than women to develop MCI (Roberts et al. 2008). In the present study, it was found that men were 1.8 times more likely to develop MCI compared to women. This could be attributed to a higher number (27.1%) of the female subjects who were identified as demented when assessed with DRS. The women (17.1%) were also found to be more depressed as compared to men (15.7%).

The average vitamin E intake among subjects did not meet the RNI (NCCFN 2005). This may be due to the low intake of vitamin E-rich foods such as whole grains, egg yolk, nuts and seeds, as well as the general low intake of energy. However, underreporting may be the cause of low mean energy intake, despite a high mean BMI among both men and women. The average intake of vitamin C and beta-carotene were satisfactory. The main sources of these antioxidants among the subjects were green leafy vegetables such as kale, Chinese mustard leaves, sweet potato shoots, as well as papaya.

Although studies have shown that oxidative stress is the main pathogenic mechanism for various neurodegenerative diseases including Alzheimer's disease (AD) and MCI (Delanty & Ditchter 2000; Emerit et al. 2004; Perry et al. 1998), but this study did not show any significant association between intakes of antioxidant vitamins and MCI in all 3 models. The finding of this study is similar to two large randomized, double blind, placebo-controlled trial of vitamin E supplementation (Kang et al. 2006; Petersen et al. 2005). After 3 years and 10 years of treatment, respectively, it was found that long-term use of vitamin E supplements did not provide cognitive benefits among the general healthy older subjects. Nevertheless, the results are controversial as previous studies indicated a low serum concentration of vitamin E is associated with declined memory performance (Perkins et al. 1999).

After adjusting for education (years), there was significant positive ($\beta = 0.325$, $p<0.05$) association between beta-carotene intake and CDT score. Education was shown to be positively associated with cognitive performance (Crum et al. 1993; Monsch et al. 1995). Subjects who received higher education obtain more knowledge and social exposure, thus might have helped in problem solving tasks. The result obtained was consistent with a recent study where long-term beta-carotene supplementation was shown to improve performance in verbal memory test (Grodstein et al. 2007). This was supported by two biological data, where retinoic acid was found to be able to normalise beta-amyloid protein processing *in-vitro* (König et al. 1990), and beta-amyloid accumulation in the brain was associated with AD pathogenesis (Hardy & Selkoe 2002). Moreover, carotenoids being fat-soluble antioxidants may help in protecting poly-unsaturated fatty acids in the brain from lipid peroxidation.

CONCLUSION

The intake levels of antioxidants are generally low among the elderly subjects and there is a weak but significant positive ($\beta = 0.325$, $p<0.05$) association between beta-carotene intake and cognitive performance, even after adjusting for education. Further studies are needed to confirm the association and also to look into the types of food that may confer protection in delaying the onset of MCI and progression to AD. There is an urgent need for early identification of those at risk of developing malnutrition as well as cognitive decline in order to prevent further health complications. Health education and intervention programmes can be specifically developed to increase awareness on the importance of diet in preventing cognitive impairment.

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