Role of retinol intake in nutritional status and metabolic syndrome in the Korean Genomic Rural Cohort

Song Yi Kim

The Graduate School

Yonsei University

Department of Meicine

Feb, 2010

Role of retinol intake in nutritional status and metabolic syndrome in the Korean Genomic Rural Cohort

A Master thesis

submitted to the Department of Medicine

and the Graduate School of Yonsei University

in partial fulfillment of the

requirements for the degree of

Master of Medical Science

Song Yi Kim

Feb, 2010

This certifies that the dissertation of Song Yi Kim is approved

[signature]_____

Thesis Supervisor: Choon Hee Chung

[signature]_____

Thesis Committee Member: Sang Baek Koh

[signature]_____

Thesis Committee Member: Young Goo Shin

The Graduate School

Yonsei University

Feb, 2010

Acknowledgement

어느덧 짧지 않은 대학원 생활을 마무리하며 지난 시간들을 돌이켜보니 많은 아쉬움과 후회가 남습니다. 학업적 성취에 있어서의 아쉬움만이 아닌, 고마운 많은 분들께 감사의 마음을 제대로 전하지 못했기에 더욱 그러한 것 같습니다. 논문이 완성되기까지 오랜 시간이 걸렸지만 그 동안 힘이 되고 방향을 잡아주셨던 많은 분들께 감사의 말씀을 전하고자 합니다.

먼저 본 논문이 완성되기까지 세심한 지도와 많은 격려로 이끌어 주신 정춘희 교수님께 진심으로 감사드립니다. 또한 논문 심사 과정에서 아낌없는 지도로 많은 가르침을 주신 신영구 교수님, 고상백 교수님께도 감사드리며 논문 작성에 대한 조언과 논문을 다듬어 주신 이미영 선생님께도 감사드립니다. 그리고 논문에 사용된 통계해석을 마치 자신의 일처럼 도와준 김민영 선생님께도 감사드립니다.

시험준비와 논문준비를 병행하는 며느리 때문에 육아를 전담하고 계신 시부모님, 전공의 때부터 항상 옆에서 지지해주는 사랑하는 남편 노진규 선생님, 그리고 사랑하는 딸 도연이에게 감사의 마음을 전합니다. 마지막으로 언제나 제 편이 되어 힘을 주시고 바르게 생각하고 행동할 수 있도록 가르쳐주신 부모님께 감사드리며 앞으로 맡은 분야에서 더욱 성장하도록 노력하겠습니다.

2009 년 12 월

김 송 이

Table of Contents

List of Table

List of Figure

Abstract

Background: Numerous dietary factors are related to the development of metabolic syndrome(MS). Several studies suggest that antioxidant nutrients may play a protective role in this complex disorder. The goal of the present study was to characterize the relationship between retinol intake and the prevalence of metabolic syndrome in a defined population sample.

Methods: This cross-sectional study was conducted in a sample of 2983 men drawn from the Korean Genomic Rural Cohort Study. Dietary intake, including retinol intake, was assessed using a semiquantitative food frequency questionnaire. We evaluated the prevalence and odds ratios of metabolic syndrome by quartile of retinol intake.

Results: Participants with metabolic syndrome reported significantly lower retinol intake than normal subjects. The prevalence of metabolic syndrome and the adjusted odds ratio were both decreased in the highest quartile of retinol intake [OR: 0.64 (95% CI, 0.483-0.847)] compared with the lowest quartile. Participants in the highest quartile also had higher body mass indexes (BMI), and waist and hip circumferences, but lower systolic blood pressures and serum triglyceride levels than those in

the lowest quartile. Retinol intake showed significant negative correlations with each metabolic component except HDL cholesterol.

Conclusion: Our analysis revealed an inverse association between retinol consumption and the prevalence of metabolic syndrome in a large sample of Korean men. In this study, systolic blood pressure and serum triglycerides were the main risk factors associated with retinol intake.

Key Wards: Retinol, Metabolic syndrome, Korean Genomic Rural Cohort

Introduction

Metabolic syndrome(MS) is influenced by a cluster of risk factors that are associated to type 2 diabetes mellitus and cardiovascular disease, all of which may lead to mortality (1-4). Diabetes and cardiovascular disease are showed features of oxidative stress, and some studies suggests that antioxidant nutrients, which suppress oxidative injury by inactivating free radicals, may offer protection from these conditions (5).

Reports documented that various dietary factors are related not only to individual components of metabolic syndrome but also to the prevalence of metabolic syndrome. For example, higher intakes of fruits and vegetables are associated with lower prevalence of metabolic syndrome (6-8). But few studies have investigated the relationships between individual antioxidant nutrients and metabolic syndrome. In data from the Third National Health and Nutrition Examination Survey (NHANES), subjects with metabolic syndrome showed suboptimal concentrations of antioxidants such as vitamin A, C, E, carotenoids, and selenium (9). Another study reported an inverse correlation between metabolic syndrome and concentrations of dietary vitamin A and E (10). However, data regarding the relationship between dietary retinol intake and the prevalence of metabolic syndrome are lacking.

In this study, we investigated the relationship between dietary retinol intake and the prevalence of metabolic syndrome in a large sample of Korean men drawn from the Korean Genomic Rural Cohort (KGRC). In addition, we

evaluated the relationship between retinol intake and metabolic syndrome components.

Subjects and methods

1. Study sample

For this cross-sectional study, we enrolled subjects from the Korean Rural Genomic Cohort (KGRC) of 2006. The 4089 male KGRC participants, ranging in age from 40 to 70 years, came from the five communities of Wonju, Pyeongchang, Naju, Keumsan, Kangreung in South Korea. We excluded participants who were taking medications for hypertension, hyperlipidemia, and diabetes mellitus, and subjects with missing data (n=1106). In total, we included 2983 participants in the present study.

2. Data collection

After obtaining written informed consent from participants, we conducted interviews and anthropometric examinations. Trained interviewers obtained basic demographic data, medical histories, and information about personal habits, including diet, smoking, alcohol intake, physical activity, family history and medication use. After eight hours of fasting, blood samples were collected for analysis of biochemical markers. Insulin resistance was calculated using the homeostasis model assessment (HOMA-IR) (11), using the following formula: fasting insulin (μU/mL) x fasting plasma glucose (mg/dL) /22.5. The usual dietary intakes were assessed by a 103-item interviewer-administered semiquantitative food

frequency questionnaire (FFQ) (12). The dietary record was analyzed using the DS 24 (Human Nutrition Lab, Seoul National University and AI/DB Lab., Sookmyung Women's University) with values drawn from the Food Composition Table of Korea, Seventh Edition (13).

3. Metabolic syndrome

Metabolic syndrome was defined according to modified NCEP-ATP III guidelines, applying the Asia-Pacific waist circumference values (14,15). A diagnosis of metabolic syndrome was made if a subject showed three or more of the following abnormalities: waist circumference ≥90 cm in men or ≥80 cm in women, serum triglycerides ≥ 150 mg/dL, HDL cholesterol <40 mg/dL in men or <50 mg/dL in women, blood pressure ≥ 130/85 mm Hg, and fasting blood glucose ≥ 100 mg/dL.

4. Statistical analysis

Statistical calculations were performed using SPSS for Windows (v.11). We used Student's t-test to compare the dietary, anthropometric, and biochemical characteristics of subjects with and without metabolic syndrome. Multivariate stepwise logistic regression analyses were performed to estimate odds ratios and 95% confidence intervals for the prevalence of metabolic syndrome by quartile of retinol intake. We performed ANOVA to evaluate anthropometric and biochemical

characteristics by quartile of retinol intake. *P*-values less than 0.05 were considered statistically significant.

Results

1. Anthropometric and biochemical characteristics of subjects

Subjects with metabolic syndrome had significantly higher BMIs, waist circumferences, hip circumferences, and waist-to-hip ratios (WHR) than normal subjects. Total cholesterol, triglyceride, LDL cholesterol, AST, ALT, GGT, HOMA-IR, fasting and postprandial glucose and insulin levels were significantly higher in subjects with metabolic syndrome, while HDL cholesterol and adiponectin levels were significantly lower than in normal subjects (Table 1).

Table 1. Characteristics of subjects with and without metabolic syndrome

	Non-MS (n=2178)	MS (n=805)
Age	56.76±8.16	55.57±8.02
Height (cm)	165.73±5.64	166.94±5.58
Weight (kg)	63.56±8.48	72.09±9.45
BMI (kg/m^2)	23.25±2.61	25.92±3.05*
Waist circumference (cm)	83.06±7.12	90.68±7.08*
Hip circumference (cm)	93.45±5.80	97.96±6.58*
WHR	0.88±0.06	0.92±0.06*
SBP (mmHg)	128.24±16.38	139.28±16.31
DBP (mmHg)	82.01±10.74	88.53±10.93
FPG (mg/dL)	93.27±13.85	105.21±29.36*
PPG (mg/dL)	105.42±60.24	122.37±87.31*
Fasting insulin (mIU/L)	6.94±3.54	9.97±6.19*

Table 1. Characteristics of subjects with and without metabolic syndrome (continued)

	Non-MS (n=2178)	MS (n=805)
Postprandial insulin (mIU/L)	20.06±19.89	28.61±28.34*
HOMA-IR	29.23±18.49	47.82±42.71*
HbA1C (%)	5.53±0.69	5.81±0.88
Adiponectin (μg/dL)	8.93±4.46	6.60±3.65*
AST (IU/L)	31.55±18.75	34.48±23.25*
ALT (IU/L)	27.82±17.77	35.69±22.38*
GGT (IU/L)	53.47±97.03	87.03±171.92*
Total cholesterol (mg/dL)	196.25±36.16	204.26±41.82*
Triglyceride (mg/dL)	135.99±86.88	251.90±178.56*
HDL-cholesterol (mg/dL)	47.92±11.73	38.15±8.47*
LDL-cholesterol (mg/dL)	112.89±31.34	114.56±33.36*
WBC(10^9/L)	7.29±2.02	7.66±2.00
CRP(mg/dL)	2.07±5.43	2.55±7.16
Alcohol(g/day)	31.32±113.70	45.46±213.89
Smoking(pack years)	19.99±19.63	21.55±21.45
Exercise(%)	22.6	26.0

Data are represented by mean ± SD. MS, metabolic syndrome; BMI, body mass index; WHR, waist-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; PPG, postprandial glucose; HOMA-IR, homeostasis assessment model for insulin resistance; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, γ-glutamyltransferase; HDL, high density lipoprotein; LDL, low density lipoprotein; WBC, white blood cells; CRP, C-reactive protein. *: $p<0.05$ compared with non-MS group.

2. Comparison of dietary factors between subjects with and without metabolic syndrome

Of all dietary factors analyzed, only retinol intake was significantly lower in subjects with metabolic syndrome than in those without metabolic syndrome (Table 2).

Table 2. Dietary factors in subjects with and without metabolic syndrome

	Non-MS (n=2178)	MS (n=805)
Total Energy (kcal/d)	1849.83±528.95	1889.04±552.85
Protein (g/d)	59.81±25.13	61.79±26.78
Fat (g/d)	27.48±25.79	27.55±21.56
Carbohydrates (g/d)	332.73±85.52	339.16±86.88
Calcium (mg/d)	418.65±260.46	419.54±264.39
Phosphorus (mg/d)	910.88±347.17	929.47±335.63
Iron (mg/d)	9.98±6.39	10.13±5.49
Sodium (g/d)	3137.22±1960.63	3157.66±1936.17
Potassium (g/d)	2200.27±1247.04	2235.22±1133.64
Fiber (g/d)	5.97±3.38	6.07±3.21
Vit A (mg/d)	500.87±477.73	503.66±410.94
Vit B1 (mg/d)	1.07±0.69	1.08±0.53
Vit B2 (mg/d)	0.88±0.57	0.89±0.48
Vit B12 (μg /d)	14.09±8.52	14.43±6.69
Vit C (mg/d)	99.86±75.54	102.43±6.69
Zinc (mg/d)	7.64±4.89	7.93±4.15
Folate (μg /d)	211.73±145.74	216.87±135.72
Retinol (μg /d)	52.24±53.80	51.18±58.14*
Carotene (mg/d)	2602.89±2529.11	2624.55±2258.14

Data are represented by mean ± SD. MS, metabolic syndrome; vit, vitamin.

*: $p<0.05$ compared with non-MS group.

3. Prevalence of metabolic syndrome by the quartile of various dietary factors

The prevalence of metabolic syndrome decreased significantly with increasing quartile of retinol intake (Table 3). The distribution of retinol intake by quartile was less than 15.7 μg in the lowest quartile; 15.7 to 35.05 μg in the second quartile; 35.06 to 68.55 μg in the third quartile; and more than 68.55 μg in the highest quartile. Compared to the lowest quartile of retinol intake, multivariate-adjusted odds ratios for metabolic syndrome in the higher quartiles were as follows: 0.85 (95% CI, 0.67-1.08), 0.85 (95% CI, 0.66-1.09) and 0.64 (95% CI, 0.48-0.84), respectively.

Table 3. Prevalences and odds ratios of metabolic syndrome by the quartile of retinol intake

	Quartile of retinol intake				
	1Q	2Q	3Q	4Q	*P* for trend
Prevalence of MS (%)	192/674 (28.5%)	216/801 (27.0%)	212/752 (28.2%)	185/756 (24.5%)	0.290
Odds ratio (95% CI)					
Model 1	1	0.91 (0.72-1.15)	0.95 (0.75-1.20)	0.78 (0.61-0.99)	0.154
Model 2	1	0.85 (0.67-1.08)	0.85 (0.66-1.09)	0.64 (0.48-0.84)	0.068

C.I., confidence interval; Q, quartile. Model 1 was adjusted for age. Model 2 was adjusted for Model 1 plus total energy, smoking, alcohol, and exercise.

4. Metabolic risk factors in male participants by the quartile of retinol intake.

Compared with participants in the lowest quartile, those in the highest quartile of retinol intake were younger and had higher body mass indexes (BMI), and waist and hip circumferences, but lower systolic blood pressures and serum triglyceride levels. Diastolic blood pressure, HDL cholesterol and fasting plasma glucose did not differ significantly by quartile. Interestingly, mean adiponectin concentrations decreased significantly with increasing quartile retinol intake but HOMA-IR did not change. Also, the prevalence of subjects who exercised increased significantly with quartile of retinol intake (Table 4).

Retinol intake was lower in participants with each components of metabolic syndrome as defined by the modified NCEP-ATP III guidelines except for waist circumference than in normal participants (Figure 1A), and proportionately lower in participants as the number of metabolic syndrome components increased (Figure 1B).

Table 4. Metabolic risk factors in male participants by the quartile of retinol intake

Characteristics	Quartile of retinol intake				*P value*
	1Q (n=674)	2Q (n=801)	3Q (n=752)	4Q (n=756)	
Total energy intake (kcal/d)	1522.49±318.08	1723.94±368.81	1918.46±456.84	2248.25±644.87	<0.001
Age (year)	58.36±7.74	56.31±7.93	55.88±8.19	55.42±8.38	<0.001
Height(cm)	165.27±5.69	166.12±5.30	166.19±5.87	166.56±5.66	<0.001
Weight (Kg)	64.63±7.95	66.13±8.91	65.74±9.79	66.88±9.99	<0.001
BMI (kg/m^2)	23.62±2.89	23.94±2.84	23.76±3.04	24.06±3.01	0.030
Waist (cm)	84.59±7.96	85.27±7.57	84.83±7.90	85.78±8.06	0.025
Hip (cm)	94.13±6.22	94.68±5.75	94.51±6.49	95.34±6.89	0.004
WHR	0.89±0.05	0.90±0.05	0.89±0.05	0.90±0.05	0.749
HOMA-IR	34.26±33.86	34.69±25.69	33.34±23.23	34.68±30.66	0.769
HbA1C(%)	5.62±0.72	5.62±0.81	5.59±0.74	5.57±0.71	0.482
SBP (mmHg)	132.53±17.77	131.13±16.80	132.05±19.65	129.87±16.44	0.030
DBP (mmHg)	84.37±11.52	83.43±10.73	83.47±11.25	83.72±11.25	0.434
FPG (mg/dL)	96.25±22.69	97.25±18.09	96.20±18.89	96.20±20.53	0.670
PPG (mg/dL)	113.59±66.18	112.78±69.65	105.17±70.35	108.63±69.17	0.069

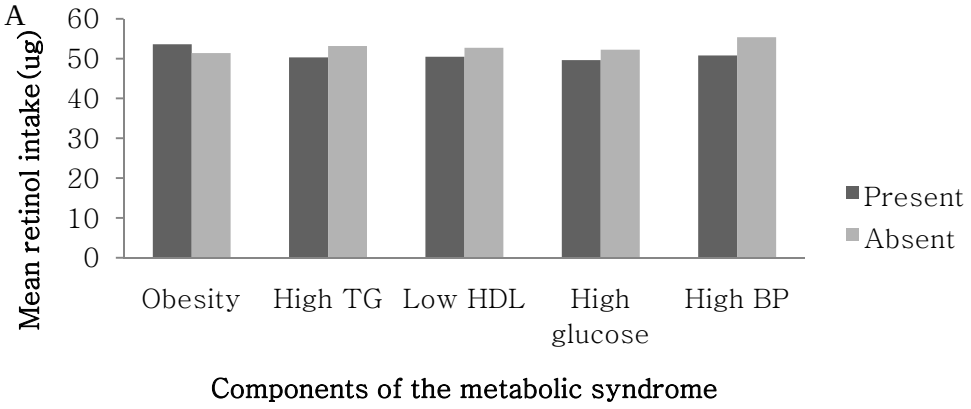
Table 4. Metabolic risk factors in male participants by the quartile of retinol intake (continued)

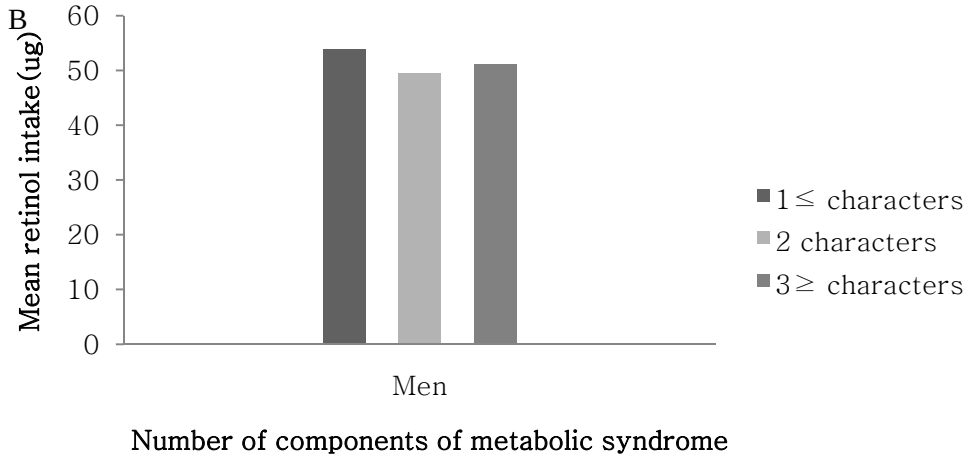
Characteristics	Quartile of retinol intake				*P value*
	1Q (n=674)	2Q (n=801)	3Q (n=752)	4Q (n=756)	
Fasting insulin(mIU/L)	7.69±4.28	7.83±4.53	7.64±4.29	7.87±5.27	0.731
Postprandial insulin	23.84±26.74	22.55±21.89	20.52±18.75	22.35±23.12	0.067
Adiponectin(μg/dL)	8.81±4.65	8.19±4.11	8.26±4.49	8.13±4.28	0.025
T. Cholesterol(mg/dL)	197.21±36.70	201.46±41.62	196.64±36.91	198.03±35.73	0.056
HDL-C (mg/dL)	45.23±12.15	45.34±12.29	44.90±11.13	45.66±11.52	0.654
LDL-C (mg/dL)	112.96±31.22	114.39±33.41	111.58±31.44	114.32±31.32	0.266
TG (mg/dL)	165.56±107.85	177.25±160.43	168.98±128.98	156.54±108.49	0.017
AST(IU/L)	32.83±20.95	32.06±17.10	32.23±21.23	32.33±21.13	0.902
ALT(IU/L)	29.88±20.33	29.96±18.84	29.85±18.80	30.07±19.92	0.996
GGT(IU/L)	68.19±176.58	59.27±92.98	65.04±127.77	58.45±79.09	0.370
WBC(10^9/L)	7.45±2.11	7.40±2.02	7.32±1.93	7.39±2.03	0.710
CRP(mg/dL)	2.04±4.64	2.28±7.20	2.50±6.73	1.97±4.51	0.306
Smoking (pack years)	21.32±20.47	20.74±19.73	19.92±19.81	19.44±20.59	0.310
Alcohol (g/day)	23.85±117.71	39.76±208.69	33.98±104.65	40.79±112.39	0.366
Exercise (%)†	15.8	21.9	23.8	31.7	<0.001

Data are represented by the mean ± SD. BMI, body mass index; HOMA-IR, homeostasis assessment model for insulin resistance; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; TG, triglyceride; FPG, fasting plasma glucose; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, γ-glutamyltransferase; WBC, white blood cells; CRP, C-reactive protein; Q, quartile.

†Percentage of the study participants who consistently exercised enough to perspire.

Figure 1. Mean retinol intake according to the presence or absence of multiple components of metabolic syndrome. (A) Mean retinol intake was lower in subjects who had components of metabolic syndrome than in normal subjects. (B) Increase in number of metabolic syndrome components corresponds to decreased mean retinol intake





5. Relationships between retinol intake and components of metabolic syndrome

Retinol intake showed inverse correlations with waist-hip ratio, HbA1c, LDL cholesterol, postprandial insulin, postprandial glucose and systolic blood pressure. The correlation with HDL cholesterol, however, was positive (Table 5).

Table 5. Correlations between retinol intake and components of metabolic syndrome

	r	*P value*
Waist-hip ratio	−0.071	<0.007
HbA1C	−0.045	0.009
LDL	−0.031	0.047
TG	−0.090	<0.001
HDL	0.068	<0.001
Postprandial insulin	−0.054	<0.001
Postprandial glucose	−0.075	<0.001
SBP	−0.039	0.014

r; coefficient of pearsons' correlation

Discussion

In this study, we determined the prevalence of metabolic syndrome in a Korean male population with respect to intakes of various dietary factors, and detected a negative correlation between MS and retinol intake only.

Retinol, one of the most usable forms of vitamin A, is a fat-soluble vitamin that functions in vision and bone growth (16). Animal sources such as liver and eggs contain the retinyl ester precursor forms, which are converted to retinol in the small intestine (17). The pro-vitamin A carotenoids from darkly colored fruits and vegetables also serve as dietary retinol precursors.

Previous study supports an association between metabolic syndrome with increased oxidative stress (18), which is implicated in diabetes mellitus, obesity, and coronary vascular disease, and may also be involved in insulin resistance (19, 20). Oxidative stress may contribute to diabetes mellitus through impairment of insulin signaling or dysfunction in pancreatic β-cells, which contain only low concentrations of radical scavengers (21-24). Recent data show that specific nutrients or representative food groups can reduce the risk of oxidative stress-related chronic disease (25). Aantioxidant components of these foods, including β-carotene, vitamin C, and vitamin E, can directly suppress oxidative stress by inactivating free radicals. From this, we hypothesized that retinol, as an antioxidant, may reduce the risk for metabolic syndrome. This is consistent with results of

prospective studies, which showed a lower prevalence of metabolic syndrome at higher carotenoid intake (26), and an association of metabolic syndrome or type 2 diabetes mellitus with lower concentrations of serum carotenoids (27,28).

The results of our study revealed a relationship between higher retinol consumption and decreased prevalence of metabolic syndrome. Subjects in the highest quartile of retinol intake showed a prevalence of metabolic syndrome 36% lower than in the lowest quartile. This inverse relationship extended to each component of the metabolic syndrome, including serum triglyceride concentration and systolic blood pressure. However, we also found that subjects in the highest retinol intake group had higher weight, body mass index (BMI), and waist and hip circumference compared with those who had lowest retinol intake. This discrepancy may reflect an increased intake of other nutrients in the highest quartile of retinol intake. Retinol intake was lower in subjects with each component of metabolic syndrome except for waist circumference than in normal subjects. Furthermore, retinol consumption in subjects with multiple components of metabolic syndrome was proportionately lower than in subjects with fewer components. From these findings, we surmised that retinol may have a protective effect in the development of metabolic syndrome.

Adiponectin is a novel adipose tissue-specific polypeptide that may counteract atherosclerosis and insulin resistance (29). Studies show lower adiponectin levels in type 2 diabetes mellitus, obesity and insulin resistance

(30). In this study, we found significantly lower mean adiponectin levels as retinol intake increased. HOMA-IR and CRP , which are predictive factors for diabetes mellitus and metabolic syndrome, also were not correlated with retinol intake. We suggest that the lower adiponectin level in subjects with the highest retinol intake is related to the proportionately higher waist circumference and BMI in this group, independent of metabolic syndrome status.

Although our findings support a protective role for retinol in metabolic syndrome, we did not measure oxidative stress markers, and thus could not test the relationship between oxidative stress and retinol intake. Studies show, however, that vitamin A supplementation may reduce hypertension by enhancing synthesis of prostaglandin E_1 and platelet aggregation inhibitors, and may also influence lipid metabolism (31). Barber *et al.* found significant changes in mitochondrial membrane lipid composition and function, and suggested that chronic vitamin A deficiency may decrease membrane lipid turnover (32). Based on measurements of lipid peroxidation in the mitochondria, they emphasized the antioxidant role of vitamin A in the maintenance of lipid composition (32).

In conclusion, of the nutritional factors we tested, only retinol intake showed a significant negative correlation with the prevalence of metabolic syndrome. Our findings suggest that higher retinol intake may reduce the risk for metabolic syndrome, and also for components of metabolic syndrome. We identified systolic blood pressure and serum triglyceride level as the

main risk factors associated with retinol intake in this study. However, to determine whether the antioxidant properties of retinol offer protection from metabolic abnormalities will require further cohort or intervention studies.

References

1. Resnick HE, Jones K, Ruotolo G, Jain AK, Henderson J, Lu W, Howard BV. Insulin resistance, the metabolic syndrome, and risk of incident cardiovascular disease in nondiabetic American Indians: the Strong Heart Study. Diabetes Care 26:861-867, 2003
2. Sattar N, Gaw A, Scherbakova O, Ford I, O' 'Reilly DSJ, Haffner SM, Isles C, Macfarlane PW, Packard CJ, Cobbe SM, Shepherd J. Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. Circulation 108:414-419, 2003
3. McNeill AM, Rosamond WD, Girman CJ, Golden SH, Schmidt MI, East HE, Ballantyne CM, Heiss G. The metabolic syndrome and 11-year risk of incident cardiovascular disease in the Atherosclerosis Risk in Communities Study. Diabetes Care 28:385-390, 2005
4. Lakka H-M, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, Salonen JT. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. JAMA 288: 2709-2716, 2002
5. Ruhe RC, McDonald RB. Use of antioxidant nutrients in the prevention and treatment of type 2 diabetes. J Am Coll Nutr 20:363S-369S, 2001
6. Yoo S, Nicklas T, Baranowski T, Zakeri IF, Yang SJ, Srinivasan SR, et al. Comparision of diatary intakes associated with metabolic syndrome risk

factors in young adults: he Bogalusa Heart Study. Am J Clin Nutr 80:841-848, 2004

7. Esmaillzadeh A, Kimiagar M, Mehrabi Y, Azadbakht L, Hu FB, Willett WC. Fruit and vegetable intakes, C-reactive protein, and the metabolic syndrome. Am J Clin Nutr 84:1489-1497, 2006

8. Esmaillzadeh A, Kimiagar M, Mehrabi Y, Azadbakht L, Hu FB, Willett WC. Dietary patterns, insulin resistance, and prevalence of the metabolic syndrome in women. Am J Clin Nutr 85:910-918, 2007

9. Ford ES, Mokdad AH, Giles WH, Brown DW. The Metabolic Syndrome and Antioxidant Concentration: findings from the Third National Health and Nutritional Examination Survey. Diabetes 52:2346-2352, 2003

10. Kim MH, Lee HS, Park HJ, Kim WY. Risk factors associated metabolic syndrome in Korean elderly. Ann Nutr Metab 6:533-540, 2007

11. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and b cell fuction from fasting plasma glucose and insulin concentrations in man. Diabetologia 28:412-419, 1985

12. Sudha V, Radhika G, Sathya RM, Ganesan A, Mohan V. Reproducibility and validity of an interviewer administered semi-quantitative food frequency questionnaire to assess dietary intake of urban adults in Southern India. Int J Food Sci Nutr 57:481-493, 2006

13. Kim CI, Lee HS, Kim BH, Jang YA, Suh HJ. Change in nutritional status of the elderly population in Korea. J Food composition and Analysis 17:449-457, 2004

14. Executive summary of the third report of the National Cholesterol Education Program (NECP) Expert Panel on Detection, Evaluation and Treatment of High Blood Chlesterol in Adult (Adult Treatment Panel III). JAMA 285:2486-2497, 2001

15. World Health Organization, International Association for the Study of Obesity and International Obesity Task Force. The Asia Pacific perspective: redefining obesity and its treatment. Sydney: Health Communications Australia Pty Limited. 17-21, 2001

16. Bonet ML, Ribot J, Felipe F, Palou A. Vitamin A and the regulation of fat reserves. Cell Mol Life Sci 60: 1311-1321, 2003

17. de Pee S, Bloem MW. The bioavailability of (pro) vitamin A carotenoids and maximizing of contribution of homestead food production to combating vitamin A deficiency. Int J Vitam Nutr Res 77:182-192, 2007

18. Hansel B, Giral P, Nobecourt E, et al. Metabolic syndrome is associated with elevated oxidative stress and dysfunctional dense high-density lipoprotein particles displaying impaired antioxidative activity. J Clin Endocrinol Metab 89:4963-4971, 2004

19. Bhatt DL. Anti-inflammatory agents and antioxidants as a possible "tird reat wave" in cardiovascular secondary prevention. Am J Cardiol 101:4D-13D, 2008

20. Willcox , Curb JD, Rodriguez BL. Antioxidants in cardiovascular health and disease: key lessons from epidemiologic studies. Am J Cardiol 101:75D-86D, 2008

21. Oberly LW: Free radicals and disbetes. Free Radic Biol Med 5:113-124, 1988

22. Rosen P, Nawroth PP, King G, Moller W, Tritschler HJ, Packer L: The role of oxidative stress in the onset and progression of diabetes and its complications: a summary of a Congress Series sponsored by UNESCOMCBN, the American Diabetes Association and the German Diabetes Society. Diabetes Metab Res Rev 17:189-212, 2001

23. Jain SK, Palmer M: The effect of oxygen radicals metabolites and vitamin E on glycosylation of proteins. Free Radic Biol Med 22:593-596, 1997

24. Beales PE, Williams AJ, Albertini MC, Pozzilli P: Vitamin E delays diabetes onset in the non-obese diabetic mouse. Horm Metab Res 26:450-452, 1994

25. Schulze MB, Hoffmann K, Manson JE, Willett WC, Meigs JB, Weikert C, Heidemann C, Colditz GA, Hu FB. Dietary pattern, inflammation, and incidence of type 2 diabetes in women. Am J Clin Nutr 82:675-684, 2005

26. Sluijs I, Beulens JWJ, Grobbee DE, van der Schouw YT. Dietary Carotenoid intake Is Associated with Lower prevalence of metabolic syndrome in middle-aged and elderly men. J Nutr 139:987-992, 2009

27. Coyne T, Ibiebele T, Baade PD, McClintock CS, Shaw JE. Metabolic syndrome and serum carotenoids: finding of a cross-sectional stud in

Queensland, Australia. Br J Nutr 27:1-10, 2009

28. Coyne T, Ibiebele T, Baade PD, Dobson A, McClintock CS, Dunn S, Leonard D, Shaw JE. Diabetes mellitus and serum carotenoids: findings of a population-based study in Queensland, Australia. Am J Clin Nutr 82:685-693, 2005

29. Díez JJ, Iglesias P. The role of the novel adipocyte-derived hormone adiponectin in human disease. Eur J Endocrinol. 148:293-300, 2003

30. Ukkola O, Santaniemi M. Adiponectin: a link between excess adiposity and associated comorbidities? J. Mol. Med. 80:696-702, 2002

31. Das UN. Nutritional factors in the pathobiology of human essential hypertension. Nutrition 17:337-346, 2001

32. Barber T, Borrás E, Torres L, García C, Cabezuelo F, Lloret A, Pallardó FV, Viña JR. Vitamin A deficiency causes oxidative damage to liver mitochondria in rats. Free Radic Biol Med. 29:1-7, 2000

국 문 요 약

연구배경: 대사증후군은 제 2 형 당뇨병 및 심혈관 질환과 연관되어 있고 세계적으로 그 유병률이 증가 추세에 있으나 대사증후군에서 영양 및 식사의 역할은 아직 논란이 많다. 저자들은 한국 지역사회 유전체 코호트에 참여한 남성을 대상으로 영양 및 식사패턴과 대사증후군과의 연관성을 규명하고자 하였다.

방법: 2006 년 한국 지역사회 유전체 코호트 중 원주, 평창, 강릉, 나주, 금산에 거주하는 40 세 이상 70 세 이하의 남자 4089 명을 대상으로 하였다. 이 중 식사패턴에 영향을 줄 수 있는 항고혈압약제, 혈당강하제, 고지혈증약제 처방을 받고 있는 환자를 제외한 총 2983 명이 참여하였다. 이들은 식품섭취빈도조사지를 비롯한 설문을 통하여 생활습관, 의학적 기왕력 및 식사력을 제공하였으며 신장, 체중, 혈압 및 허리-엉덩이 둘레의 비 등의 신체계측과 공복 및 식후 정맥채혈을 시행하였다. 대사증후군의 진단기준으로는 NCEP-ATP III 의 기준을 보완하여 이용하였다.

결과: 대사증후군이 있는 군에서 레티놀의 섭취량이 낮았다. 또한 각 영양소를 4 분위수로 나눈 후 레티놀의 섭취가 증가할수록 대사증후군의 비교위험률은 감소하였다[2nd quartile OR:0.85(95% CI: 0.67-1.08), 3rd quartile OR: 0.85(95% CI: 0.66-1.09), 4th quartile OR: 0.64 (95% CI: 0.48-0.84)]. 레티놀의 섭취가 많은 군에서 대사증후군의 구성요소 중 수축기 혈압과 혈중 중성지방의 수치가 의미있게 감소하였다. 또한 레티놀의 섭취량은 비만도와 당화혈색소, LDL 콜레스테롤, 식후혈당, 식후인슐린 및 수축기혈압과 음의 상관관계를 나타내었고 HDL 콜레스테롤과는 양의 상관관계를 보였다.

결론: 한국인 남성에서 레티놀 섭취는 대사증후군의 각 요소들과 상관관계를 보이고 특히 레티놀의 섭취가 많은 그룹에서 수축기혈압과 중성지방이 의미있게 감소함을 알 수 있었다. 이는 충분한 레티놀의 섭취는 대사증후군의 유병률을 감소시킬 수 있음을 시사한다. 따라서 이에 대한 대규모 임상 연구가 필요할 것으로 생각된다.

중심단어: 레티놀, 대사증후군, 지역사회 코호트