

STRATEGY FOR WEIGHT LOSS IN OVERWEIGHT PEOPLE

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INTRODUCTION

Until the 1960s, undernutrition and starvation were major causes of disease and mortality in Korea. Diseases resulting from undernutrition, such as tuberculosis, were severe problems until the 1970s. But now, we are facing an opposite problem, that of energy surplus. Over the past decade, Korean adults have increased the percent of fat in their diets from about 14% in 1990 (1) to 18% in 1998 (2). For adults aged 20-49 yr, daily fat intake increased from about 35g in 1990, to 45g in 1998. Average calorie intake of adults was slightly below 2,000 kcal in 1998, close to the recommended 2,000 kcal per day for women and below the recommended 2,500 kcal per day for men.

The prevalence of obesity continues to increase. In 1995, nearly 20% of Korean males were overweight, meaning that they had a body mass index (BMI) of 25kg/m^2 and above (2). Being overweight leads to major health hazards and it is associated to most of the chronic diseases that affect industrialized populations, such as type II diabetes and cardiovascular disease (CVD), including hypertension, stroke, and coronary artery disease (CAD) (3). However, a high waist/hip circumference ratio (WHR), an approximation of centrally distributed adipose tissue, has been suggested to be a strong risk factor for CVD, independent of BMI (4,5). Thus, greater interest has recently been focused on patterns of body fat distribution rather than amounts of fat per se as the real risk factor for CVD. Stronger relationship between CVD and WHR has been demonstrated repeatedly by visceral fat mass, determined by computerized tomography (CT) scans (4).

Regional body fat distribution may result from interactions between different factors controlling the environment and polymorphisms in several genes acting synergistically to dispose for obesity. In overweight people with abdominal fat accumulation, weight losses of 5% of initial body weight improve metabolic risk factors (6,7). However, the response to a weight reduction intervention is not homogeneous and some people improve body fat distribution and metabolic syndrome more easily than others. Genetic factors could be associated with a resistance in these improvements in response to weight loss (8).

This paper focuses on recent data of Koreans: 1) age-related changes in fat deposition, 2) influence of lifestyle factors on body fat distribution and cardiovascular risk factors, 3) central body fat and cardiovascular risk factors clustering in CAD patients, 4) beneficial effects of weight loss in overweight subjects, and 5) effects of the mutations in the β_3 -adrenergic receptor (β_3 AR) and uncoupling protein-3 (UCP3) genes on body fat and cardiovascular risk factors in response to weight loss.

Age-related changes in fat deposition in Korean men: relationships with cardiovascular disease risk factors

Aging is associated to an increase in obesity and central body fat (9). Being overweight and increased waist circumference are linked to cardiovascular risk factors common in old age, including elevated blood pressure, lipid abnormalities, and glucose intolerance. Understanding the correlations of CVD risks to being overweight and accumulation of abdominal fat in old age is important because the proportion of overweight and central obese persons in Korean old population has recently increased.

According to cross-sectional age relations of blood pressure, anthropometric indexes and serum lipids in 240 Korean males aged 30-69 years, regional body fat distribution of older men was different from that of younger men (6). Older men had higher WHR and larger amounts of visceral fat at L1 and L4 levels. The greater amount of visceral fat observed in older subjects was independent of differences in body weight because there was no significant difference in BMI across the age groups. Although diastolic blood pressure increased with age only in normal weight males, systolic blood pressure was higher in older men than in younger men of both weight groups. Serum total cholesterol concentration increased with age in normal weight males. The age-associated increase in visceral adiposity might contribute to the increase in blood pressure and total cholesterol with age in Korean men.

Aging and visceral fat accumulation may predispose individuals to CVD and dyslipidemia (9). Several possible factors may explain central fat accumulation and metabolic aberrations in older men but the mechanism is not yet understood. A decrease in serum testosterone concentrations observed in older men may be associated to both redistribution of body fat and metabolic abnormalities; further studies are necessary to evaluate the relative contribution of this factor and other endocrine function in Korean males.

Influence of lifestyle factors on body fat distribution and cardiovascular risk factors

Lifestyle factors play an important role in determining regional pattern for body fat distribution. Korean men have poor lifestyle habits including low physical activity levels, excessive calorie intake *due to frequent dinner parties, high alcohol consumption, and frequent cigarette smoking*. These patterns contribute to upper-body fat deposition, impaired antioxidant defense system and increased incidence of CAD.

One hundred sixty six Korean men aged 30-69 yrs participated in the study of influence of lifestyle factors on body fat distribution and cardiovascular risk factors (10). Smokers were categorized as nonsmoker, as moderate smokers when they smoked <15 cigarettes/d or as heavy smokers when they smoked >15 cigarettes/d. Drinkers were subdivided into non, moderate (10-25g alcohol/d) and heavy (>25g alcohol/d). Despite their similar body mass index, heavy drinkers showed the higher mean value of WHR and subcutaneous fat area at L1 and L4 than nondrinkers. Serum triglyceride levels and plasma homocysteine concentrations were higher in heavy-drinker and heavy-smoker than in nondrinker-nonsmoker. Compared to nondrinker-nonsmoker, serum concentrations of β -carotene, cryptoxanthin and lycopene were 30-40% lower in heavy smoker or heavy drinker, and 50-70% lower in heavy drinker-heavy smoker(10).

The poor lifestyle pattern including simultaneous abuses of excessive alcohol and cigarette consumption in Korean men relate with central body fat deposition, abnormal serum lipid profiles and low antioxidant levels. Data for Korean men are consistent with other reported world health literature.

Central body fat and cardiovascular risk factors clustering in patients with coronary artery disease

In addition to the traditional cardiovascular risk factors (hypertension, diabetes, smoking and hypercholesterolemia), abdominal obesity, impaired antioxidant status, and hyperinsulinemia have been reported to be effective markers of CAD risk. The differences in body fat distribution and antioxidant status were determined in 64 healthy Korean men, and in 56 men with CAD with or without diabetes (11). Despite their similar age and body mass index, CAD patients with diabetes showed higher mean value of WHR than control subjects. The visceral fat area at the L1 vertebra was higher in CAD patients than the control and those at the L4 vertebra was the highest in CAD patients with diabetes. Both groups of CAD patients had lower serum levels of HDL-cholesterol, testosterone,

and IGF-1 and superoxide dismutase activity and higher plasma homocysteine levels than did control subjects. Serum β -carotene, cryptoxanthin and lycopene concentrations were lowest in the CAD patients with diabetes.

Excessive visceral fat accumulation in CAD patients may accelerate the progression of type 2 diabetes. Increased visceral fat accumulation in CAD patients with diabetes can show a further decrease in serum levels of HDL-cholesterol, testosterone and carotenoids (10). The concurrent presence of CAD and diabetes is associated with a greater negative effect on the risk factors typically associated with significant declines in health status.

Beneficial effects of weight reduction in overweight individuals

With abdominal obesity being recognized as an important risk factor of metabolic disease and atherosclerosis, the diets or functional materials for decreasing body weight and CVD risk in Korean adults have been actively studied (12,13). Healthy overweight men aged 40-49 yrs participated in a 3-month weight-management program with low-calorie diet and exercise (13). The diet and exercise program reduced daily energy intake by 300-400 kcal from daily energy need and expended about 100 kcal in walking and other light exercise. After 3 months of diet and exercise, body weight fell an average of 4.9kg (6.3%) and waist circumference reduced an average of 5cm. Visceral and subcutaneous fat areas at L1 and L4 levels showed about 20% reduction after weight loss. Mean values of serum total cholesterol, even though within normal range before weight loss, decreased significantly after weight loss. Serum triglyceride concentration fell from 192 to 143mg/dl in association the weight reduction. Modest weight loss showed a 30% decrease in fasting insulin and response areas of insulin during oral glucose tolerance test (OGTT).

Healthy overweight young women (20-39 yrs) consumed 120ml functional beverage or placebo beverage in 8 weeks with usual food intake and physical activity. Functional beverage (Cheiljedang Corporation) was composed of 2000mg soy peptide, 20mg L-carnitine, 300mg garcinia (40% HCA). All subjects did not have any weight loss/gain over the previous 12 months. This study was carried out by randomized trial, consisting of two phases; a 2-week washout phase and an 8-week intervention phase of placebo or functional beverage. During the 2-week washout period, all participants were advised to continue their usual diet and exercise and baseline measurements were performed. After the washout period, thirty-six women were randomly subdivided into 2 groups and assigned to consume either placebo beverage or the functional beverage during 8-week intervention

without any change in diet and physical activity. To check participants' compliance during the study period, the dietitian checked by personal interviews on weekly visit-basis, whether they were following the program well. Taste and preference for functional beverage were checked together with energy intake and expenditure and weight changes.

After 8-week consumption of functional beverage with usual diet and exercise, body weight fell an average of 1.4kg (2.1%)(Fig.1). Visceral fat area reduced an average of 7.8% at L1 (69.6 ± 8.7 vs 64.2 ± 7.5 cm², NS) and 5.1% (60.7 ± 4.9 vs 57.6 ± 4.8 cm², $P<0.05$) at L4 level after weight loss in test group (Fig.2). Calf fat area in test group showed about 10% reduction (31.0 ± 2.7 vs 27.7 ± 1.7 cm², $P<0.05$) after weight loss(Fig. 2). These reductions in fat areas were not shown in placebo group. There were tendencies of increase in serum levels of β -hydroxybutyrate (26.8 ± 5.3 vs 41.0 ± 17.5 $\mu\text{mol/L}$), acetoacetate (1.64 ± 0.2 vs 1.83 ± 0.3 $\mu\text{mol/L}$), and total ketone (28.5 ± 5.5 vs 42.8 ± 17.9 $\mu\text{mol/L}$) in test group (Fig.3). There was 7% and 17% insignificant increase in fasting free fatty acid (517 ± 57 vs 558 ± 82 $\mu\text{U/ml}$) and response area of free fatty acid during OGTT (493 ± 61 vs 554 ± 84 $\mu\text{U/mlxhr}$), respectively, in test group (Fig.4). In addition, little weight loss in test group showed 8% but not significant reduction in insulin response area during OGTT (96 ± 10 vs 88 ± 8 $\mu\text{U/mlxhr}$) (Fig.4).

Modest weight loss (6% of initial body weight) with low-calorie diet and exercise can show a rapid decrease in abdominal fat and be a viable approach to help decrease serum lipids and hyperinsulinemia and improve insulin responsiveness to glucose challenge. Daily functional beverage consumption can cause an average of 1.4kg reduction after 8-week in overweight young women without any change in usual diet and physical activity. Functional materials for weight loss may contribute to increase fat oxidation. Although weight reduction with functional food is negligible, the simultaneous use of functional beverage and low-calorie diet may help obese people to lose weight more easily and rapidly than in the use of low-calorie diet alone.

Effects of the mutations in the β_3 -AR and UCP-3 genes on body fat and glycemic control in response to mild weight loss

Mutation of certain genes have been studied in relation to weight changes. One of such variant the trp64arg mutation in β_3 -adrenergic receptor (β_3 AR) gene in white adipose tissue. As does β_3 AR variant, a variant (-55C→T) in the putative promoter region of uncoupling protein-3 (UCP3) has been also associated with body weight and fat metabolism.

The recent study for Korean overweight individuals determined whether the trp64arg mutation in

β_3 AR gene and -55C→T mutation in the promoter region of UCP3 have association with abdominal fat loss and insulin-resistant glucose metabolism in response to mild weight loss (14). One hundred forty five overweight ($BMI \geq 25 \text{ kg/m}^2$) subjects with CAD or metabolic syndrome (abdominal obesity, dyslipidemia or high blood pressure) completed the 12 weeks weight loss program by low calorie diet (-300kcal/d). The subjects were divided into 4 groups according to their β_3 AR and UCP3 promoter genotype: no mutation (control; n=48), only C→T mutation in the UCP3 promoter (n=57), only trp64arg in the β_3 AR (n=16), and both mutations (n=24). Despite similar 5% loss of initial body weight in 4 groups, the control showed reductions in visceral (7%, $P < 0.01$) and subcutaneous (7%, $P < 0.05$) fat areas at the levels of L1 and L4, and subjects with only UCP3 variant showed a decrease in those areas (4%, $P < 0.05$) at L1 level. However, subjects with both mutation showed 7% reduction in mid-thigh muscle without any reduction in fat area. In response to weight loss, the fasting insulin levels decreased to the same extent across the four groups but only control subjects showed a decrease in insulin response area during OGTT. Fasting glucose levels and glucose response area during OGTT improved to the similar extent except subjects with mutation in both genes. The results suggest that a combination of the trp64arg mutation in the β_3 AR and -55C→T mutation in the UCP3 promoter may be associated with difficulties in losing fat and improving glucose control in response to mild weight loss.

CONCLUSION

With increasing affluence, foods have become more various and abundant in Korea. Koreans have relatively shorter stature than Western people and require less energy, so they may have an increased risk of obesity. Lifestyle factors such as excessive calorie intake, lack of exercise, stress, alcohol intake and cigarette smoking can contribute to the increased risk of abdominal obesity. Because intra-abdominal fats are mobilized readily, energy restriction and increased physical activity are associated to reductions in central fat mass and may ameliorate the metabolic consequences associated to visceral obesity. For the purpose of health promotion to prevent CVD associated to being overweight and visceral fat accumulation, the general public should be advised to be aware of the risk associated to large waist circumference as well as the importance of reducing visceral fat through weight loss in abdominal obese people.

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