The Effect of Smoking on Insulin Resistance and Serum Resistin Levels

Sigaranın İnsülin Rezistansı ve Serum Rezistin Seviyeleri Üzerine Etkisi

Onur EŞBAH, MD,[a]
Gül GÜRSOY, MD,[a]
Nazlı KIRNAP GÜLSOY, MD,[a]
Yaşar ACAR, MD,[a]
Berrin DEMİRBAŞ, MD,[a]
Zuhal KILIÇ, MD,[a]
Aslı GÜNGÖR, MD,[a]
Süleyman ALKAN, MD[a]

[a]Clinic of Internal Medicine,
Ankara Education and Research Hospital,
Ankara

Geliş Tarihi/*Received:* 23.09.2010
Kabul Tarihi/*Accepted:* 27.12.2010

Yazışma Adresi/*Correspondence:*
Gül GÜRSOY, MD
Ankara Education and Research Hospital,
Clinic of Internal Medicine, Ankara,
TÜRKİYE/TURKEY
gulgursoyyener@yahoo.com

ABSTRACT Objective: The relationship between smoking and insulin resistance is controversial. There are conflicing reports as cigarette smoking impairs insulin secretion, augments insulin resistance or has no effect on glucose metabolism. Resistin is an adipokine, demonstrated to induce insulin resistance in vivo or in vitro. In our study, we intended to examine the relationship of smoking with insulin resistance and resistin levels in serum. **Material and Methods:** The study included 52 male smokers and 33 age matched non-smoker male control subjects. As well as making physical and anthropometric examinations, fasting plasma glucose and insulin, post prandial plasma glucose, lipid profile, and resistin levels were measured in all male subjects. We compared all parameters in smoker and non-smoker groups. Then we classified our smoker and non-smoker groups according to their homeostasis model assesment index and compared the parameters again. **Results:** Smoker group had significantly higher plasma resistin and low density lipoprotein cholesterol levels, body mass index, waist circumference and indirect measure of insulin resistance such as homeostasis model assessment, than non- smoker group ($p < 0.05$, $p < 0.01$, $p < 0.05$, $p < 0.02$, $p < 0.01$, respectively) When we grouped smoker and non-smoker groups as homeostasis model assessment ≥ 2.7 and < 2.7 we found that in the smoker group the men with homeostasis model assessment ≥ 2.7 had significantly high resistin levels ($p< 0.05$), but in non- smoker group the subjects with homeostasis model assessment ≥ 2.7 and <2.7 had similar resistin levels. **Conclusion:** In conclusion we may speculate that smoking seems to be related to resistin levels and this relationship may be correlated with insulin resistance.

Key Words: Insulin resistance; resistin; smoking

ÖZET Amaç: İnsülin rezistansı ve sigara arasındaki ilişki çelişkilidir. Sigara içiminin insülin sekresyonunu bozduğu, insülin rezistansını arttırdığı veya glukoz metabolizması üzerine hiçbir etkisi olmadığı şeklinde değişik raporlar mevcuttur. Rezistin in vivo veya in vitro insülin rezistansına neden olduğu gösterilen bir adipokindir. Bu çalışmamızda sigara ile insülin rezistansı ve serum rezistin seviyeleri arasındaki ilişkiyi araştırmayı planladık. **Gereç ve Yöntemler:** Çalışmamız 52 sigara içen erkek ile yaşları uyumlu sigara içmeyen 33 erkek kontrol kişilerden oluştu. Tüm erkeklerde fizik muayene ve antropometrik ölçümlere ek olarak açlık kan şekeri, açlık insülin, tokluk kan şekeri, lipid profili ve rezistin seviyelerine bakıldı. Sigara içen ve içmeyen gruplarda tüm parametrelerin kıyaslamasını yaptık. Sonra, sigara içen ve içmeyen grupları indirekt insülin rezistansı indeksi 'homeostasis model assesment index' lerine göre sınıfladık ve parametrelerin kıyaslanmasını tekrarladık. **Bulgular:** Sigara içen grup, sigara içmeyen gruptan istatistiksel olarak daha yüksek serum rezistin, düşük dansiteli lipoprotein kolesterol seviyeleri, vücut kitle indeksi, bel çevresi ve 'homeostasis model assesment index'ine (sırasıyla $p< 0.05$, $p< 0.01$, $p< 0.05$, $p< 0.02$, $p< 0.01$) sahipti. Sigara içen ve içmeyen grupları'homeostasis model assesment index'si ≥ 2.7 ve < 2.7 olarak sınıflandırdığımızda, sigara içen grupta 'homeostasis model assesment index' ≥ 2.7 olan erkeklerde istatistiksel olarak belirgin yüksek rezistin seviyelerinin olduğunu bulduk ($p< 0.05$), sigara içmeyen grupta 'homeostasis model assesment index' ≥ 2.7 ve < 2.7 olanlar arasında rezistin seviyeleri açısından fark yoktu. **Sonuç:** Sonuç olarak; sigaranın serum rezistin seviyeleri ile ilgisinin olduğunu ve bu ilişkinin insülin rezistansı ile bağlantılı olabileceğini söyleyebiliriz kanısındayım.

Anahtar Kelimeler: İnsülin direnci; rezistin; sigara içme

Turkiye Klinikleri J Endocrin 2011;6(1):23-8

Cigarette smoking is a well known risk factor of coronary heart disease and stroke.[1] Although diabetes and coronary heart disease have many common causal factors, the effect of smoking on the pathogenetic factors for the development of diabetes has been little explored.[2-6]

It was shown that cigarette smoking can impair insulin action both in normal subjects and in patients with type 2 diabetes mellitus (T2DM).[7-10] It was also demonstrated that nondiabetic cigarette smokers are insulin resistant and hyperinsulinemic, when compared with non-smokers.[11]

Cigarette smokers tend to have high triglyceride (TG) and low high density lipoprotein cholesterol (HDL-C) concentrations.[12] It is not clear if the dyslipidemia seen in cigarette smokers is secondary to smoking, or simply to the fact that smokers tend to be insulin resistant. Now data suggest that the dyslipidemia previously attributed to smoking occurs may primarily be seen in those smokers who are also insulin resistant.[8]

Resistin, an adipocyte secreted factor, has been suggested to link obesity with T2DM.[13,14] There are conflicting results about the effects of resistin on insulin resistance and diabetes.[15-20]

Having in mind all these knowledge, we planned to explore the association between smoking and insulin resistance and serum resistin levels in a group of Turkish population.

MATERIAL AND METHODS

MATERIAL

A total of 52 male smokers aged from 25-45 years, were recruited from the outpatient Clinic of Ankara Education and Research Hospital from January 2009 to May 2009. 33 aged matched male subjects formed the control group. Smokers have been smoking at least for 2 years and at least ten cigarettes daily. As resistin serum and mRNA levels were significantly higher in females than males at all ages, in order to obtain an homogenous group we examined only males.[21]

Subjects with female gender, hypertension, diabetes mellitus, glucose intolerance, hyperlipidemia, conditions which may effect metabolic parameters (such as thyroid dysfunctions in history or nowadays), chronic diseases, infection and coronary artery disease were excluded.

After detailed physical examination, in all subjects body weight and height were measured. Waist circumference was measured when fasting, in standing position halfway between costal edge and iliac crest, whereas hip was measured at the greatest circumference around the buttocks, by a non elastic measure. Waist to hip ratio (WHR) was calculated. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. Body fat was estimated by Tanita body composition analyser TBF -300 after the subjects rested 30 minutes.

Blood was withdrawn after 12h of overnight fasting, at 08.30 a.m. for fasting plasma glucose (FPG), fasting plasma insulin (FI), serum total and HDL-C, triglyceride, and resitin levels. Another blood sample was taken for postprandial plasma glucose (PPPG) 2 h after breakfast.

Systolic and diastolic blood pressure (SBP and DBP) were measured after a 5 min rest in the semi-sitting position with a sphygmomanometer. Blood pressure was determined at least three times at the right upper arm, and the mean was used in the analysis. The patients who were taking antihypertensive drugs or patients whose determined mean blood pressure levels ≥140/90 mmHg were diagnosed as hypertensive and excluded.

This sudy was performed according to the Helsinki decleration 2008. The local ethics committee approved this study and all the subjects gave written informed consent.

LABORATORY METHODS

Plasma glucose, total cholesterol, TG and HDL-C concentrations were determined by enzymocalorimetric spectrophotometric method in a Roche/Hitachi molecular PP autoanalyser. LDL-C was calculated by the Friedewald Formula (LDL: Total cholesterol–HDL-TG/5). Insulin was measured by means of DRG Diagnostics (DRG Instruments GmbH, Germany) ELISA kits.

An indirect measure of insulin resistance was calculated from the fasting plasma insulin (μunite

/ ml) x fasting plasma glucose (mmol /l) / 22. 5 formula as homeostasis model assessment (HOMA-IR). As in normal person HOMA-IR level was stated to be < 2.7, it was chosen a cut-point for insulin resistance [22].

For the measurements of resistin, after fasting blood samples were drawn, put into a dry tube and were santrifuged 5000 cycle / min in 10 minutes. Serum was then separated and put into another dry tube before storing at -80˚C. Serum resistin levels were assayed by a commercial resistin ELISA kit.

STATISTICAL ANALYSIS

Calculations were performed using SPSS version 11,5 (Customer ID 30000105 930). Data were presented as mean ± SD. Student t- test was used to compare the groups in a parametric way. A p value of < 0.05 was considered as statistically significant. Pearson correlation coefficient was used for the correlation analysis.

RESULTS

This study was performed with 52 male smoker, and 33 male non-smoker control subjects. All the demographic and laboratory findings of the groups were compared and illustrated in Table 1.

Waist circumference, WHR, LDL-C, HOMA-IR and resistin levels of smoker group were found statistically higher than the non-smoker control group (p< 0.05, p< 0.001, p< 0.05, p< 0.02, p< 0.01 respectively). We could not find any difference between the age, SBP, DBP, BMI, hip circumference, body fat, FPG, PPPG, total cholesterol, HDL-C, body fat, HDL-C, FI levels of the two groups (Table 1).

We then grouped our smokers and non-smokers according to their HOMA-IR levels as HOMA-IR<2.7 and HOMA-IR≥2.7. The data of smoker group with HOMA-IR < 2.7 and ≥2.7 were demonstrated in Table 2.

In the smoker group the males with HOMA-IR ≥ 2.7, had statistically higher WHR and resistin levels than smokers with HOMA-IR <2.7 (p< 0.05 both). Any difference between other parameters was not found (Table 2). The data of non-smoker group with HOMA-IR < 2.7 and ≥ 2.7 were demonstrated in Table 3.

TABLE 1: Characteristics of smoker and non-smoker males.

	Smoker (n= 52)	Non-Smoker (n= 33)	P
Age (yr)	36.8 ± 6.8	36.7 ± 7.1	NS
SBP (mmHg)	115.7 ± 12.1	117.4 ± 12.7	NS
DBP (mmHg)	78.0 ± 7.6	78.3 ± 8.5	NS
BMI (kg/m2)	26.2 ± 2.0	26.7 ± 2.2	NS
Waist Circum. (cm)	93.1 ± 8.5	89.6 ± 6.5	<0.05
Hip Circum. (cm)	104.1 ± 5.9	103.5 ± 5.9	NS
WHR	0.9 ± 0.1	0.8 ± 0.,1	<0.001
Body fat (%)	25.7 ± 6.0	26.7 ± 7.1	NS
FPG (mg/dl)	87.1 ± 9.1	88.7 ± 8.1	NS
PPPG (mg/dl)	96.3 ± 22.7	100.7 ± 22.9	NS
Cholesterol	190.6 ± 46.9	179.7 ± 36.4	NS
TG (mg/dl)	129.8 ± 58.0	124.1 ± 61.3	NS
LDL-C (mg/dl)	127.6 ± 34.7	109.5 ± 34.0	<0.05
HDL-C (mg/dl)	46.3 ± 13.7	45.7 ± 10.9	NS
FI (µu/ml)	12.2 ± 6.6	13.4 ± 4.9	NS
HOMA-IR	3.3 ± 2.0	2.5 ± 0.9	<0.02
Resistin (ng/ml)	5.7 ± 2.5	3.2 ± 1.4	<0.001

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, Waist circum.: Waist Circumference, Hip Circum.: Hip circumference, WHR: Waist- hip ratio, FPG: Fasting blood glucose, PPPG: Post prandial blood glucose, TG: Triglyceride, LDL-C: Low density lipoprotein cholesterol, HDL-C: High density lipoprotein cholesterol, FI: Fasting insulin, HOMA-IR: Homeostasis model assessment insulin resistance index, Data were presented as mean ± SD. NS: nonsignificant.

In the non- smoker group the males with HOMA-IR <2.7 had statistically higher HDL-C levels than smokers with HOMA-IR ≥2.7 (p<0.02). Any difference between other parameters was not found (Table 3).

DISCUSSION

In this study we decided to investigate the effects of smoking on anthropometric – metabolic parameters and resistin. Since the augmented risk for T2DM in cigarette smokers was revealed, there has been an increasing interest in its causes.[2-6] The finding of elevated risk for diabetes in smokers may be paradoxical, as cigarette smoking is inversely associated with BMI.[23,24]

Authors have reported conflicting results about cigarette smoking and insulin resistance.[7,9,11]

TABLE 2: Characteristics of smoker group whose HOMA-IR was < 2.7 and ≥2.7.

	HOMA-IR<2.7 (n:22)	HOMA-IR ≥ 2.7 (n: 30)	P
Age (year)	36.7 ± 5.7	36.8 ± 7.7	NS
SBP (mmHg)	113.6 ± 11.7	117.3 ± 12.2	NS
DBP (mmHg)	77.7 ± 6.1	78.3 ± 8.7	NS
BMI (kg/m2)	26.2 ± 1.8	26.2 ± 2.2	NS
Waist circum. (cm)	9.4 ± 7.2	95.1 ± 8.9	NS
Hip Circum. (cm)	102.5 ± 6.1	105.3 ± 5.5	NS
WHR	0.8 ± 0.5	1.0 ± 0.01	<0.05
Body fat (%)	25.0 ± 5.3	26.2 ± 6.5	NS
FPG (mg/dl)	85.9 ± 8.2	87.9 ± 9.8	NS
PPPG (mg/dl)	96.9 ± 26.7	95.8 ± 19.7	NS
Cholesterol (mg/dl)	175.9 ± 48.0	201.3 ± 43.9	NS
TG (mg/dl)	119.2 ± 53.8	137.6 ± 60.5	NS
LDL (mg/dl)	123.7 ± 31.1	133.0 ± 37.5	NS
HDL-C (mg/dl)	42.8 ± 14.1	48.8 ± 13.1	NS
Resistin (ng/ml)	4.8 ± 2.0	6.4 ± 2.7	<0.05

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, Waist circum.: Waist Circumference, Hip Circum.: Hip circumference, WHR: Waist- hip ratio, FPG: Fasting blood glucose, PPPG: Post prandial blood glucose, TG: Triglyceride, LDL-C: Low density lipoprotein cholesterol, HDL-C: High density lipoprotein cholesterol, HOMA-IR: Homeostasis model assessment insulin resistance index, Data are presented as mean ± SD. NS: nonsignificant.

TABLE 3: Characteristics of non-smoker group whose HOMA-IR was < 2.7 and ≥2.7.

	HOMA-IR<2.7 (n: 19)	HOMA-IR ≥ 2.7 (N:14)	P
Age (year)	37.4 ± 7.0	35.7 ± 7.4	NS
SBP (mmHg)	114.7 ± 14.2	121.0 ± 9.6	NS
DBP (mmHg)	76.3 ± 9.5	81.0 ± 6.2	NS
BMI (kg/m2)	26.2 ± 2.1	27.4 ± 2.2	NS
Waist circum. (cm)	89.0 ± 6.6	90.5 ± 6.4	NS
Hip Circum. (cm)	102.5 ± 6.9	104.7 ± 4.2	NS
WHP	0.8 ± 0.04	0.8 ± 0.07	NS
Body fat (%)	28.0 ± 7.3	29.7 ± 7.0	NS
FPG (mg/dl)	87.0 ± 8.5	91.1 ± 7.0	NS
PPPG (mg/dl)	99.0 ± 12.3	103.1 ± 32.8	NS
Cholesterol (mg/dl)	184.2 ± 37.1	173.6 ± 35.8	NS
TG (mg/dl)	119.7 ± 57.7	130.0 ± 67.7	NS
LDL (mg/dl)	111.2 ± 34.2	107.1 ± 34.8	NS
HDL-C (mg/dl)	49.7 ± 11.4	40.4 ± 7.8	<0.02
Resistin (ng/ml)	3.0 ± 1.4	3.5 ± 1.3	NS

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, Waist circum.: Waist Circumference, Hip Circum. Hip circumference, WHR: Waist- hip ratio, FPG: Fasting blood glucose, PPPG: Post prandial blood glucose, TG: Triglyceride, LDL-C: Low density lipoprotein cholesterol, HDL-C: High density lipoprotein cholesterol, HOMA-IR: Homeostasis model assessment insulin resistance index, Data are presented as mean ± SD. NS: nonsignificant.

Some examiners have suggested that cigarette smoking increases insulin resistance by altering the distribution of body fat or by exerting a direct toxic effect on pancreatic tissue. High incidence of pancreatic carcinomas among smokers may be a support of direct toxic effect of smoking on pancreas.[25] A chemical component of cigarettes may directly effect intracellular glucose transport, or may indirectly alter it through changes in serum chemistry or diminished vascular blood flow.[26] High epinephrine and norepinephrine levels were demonstrated in smokers.[27,28] Catecholamines are antagonistic hormones to insulin, they have long term effects on the synthesis of insulin regulated proteins such as GLUT-4.[29] In concordant with most of the studies in the literature we demonstrated higher HOMA-IR levels in our smokers.

In the present study we did not show any difference of BMI in our smoker and non-smoker males. It was stated that with a normal BMI smokers tend to have a greater risk of abdominal fat accumulation compared with non-smokers.[24,30] The mechanism was not well understood but as smoking had a slight anti-estrogenic effect, it could be related to a hormonal imbalance that could lead to central obesity. Moreover, concordant with the statement that insulin resistance with smoking is related to waist-hip measures not to BMI, we found higher waist circumference and WHR, not BMI in our smoker group than the non-smoker group. In the smoker group the men with HOMA-IR ≥2.7 had higher WHR, as well as resistin, than the men with HOMA-IR<2.7. This result supports the finding of the relation of waist hip measures with resistin and insulin resistance in smokers.

Resistin is an adipokine involved in glucose homeostasis, lipid metabolism and insulin action in mice. Some papers reported that in humans plasma resistin levels correlate with obesity, insulin resistance and Type 2 DM, while others failed to observe any correlation of plasma resistin levels with either metabolic or lipid parameters and no significant difference was observed in plasma resistin levels in subjects with the metabolic syndrome compared to controls.[18,19,31,32]

In our study resistin levels were statistically higher in our smoker males than non- smoker ones. In our smoker group the males who were insulin resistant (Having HOMA-IR ≥2.7) had higher resistin levels than non-insulin resistant males. But we could not show this difference in non-smokers. In non-smokers resistin levels did not change as insulin resistance were absent or present. This results made us think that resistin levels are related to insulin resistance.

There were reports suggesting a decrease in fasting insulin level in smokers,[33] while other reports showed an unimpaired or somewhat overstimulated insulin secretion in smokers.[34] It was also stated that former smoking was associated with low beta cell function, and current smoking with high beta cell function, independent of diabetes, suggesting that smoking might have acute and post cessation effects on beta cells.[27] In our study fasting insulin levels were similar between smokers and non-smokers. This result does not suggest a significant advers effect of smoking on pancreatic insulin secretion.

A number of authors examined the relationship of parameters of metabolic syndrome with smoking. Several studies have shown that smokers tend to have high TG, total cholesterol, LDL-C and low HDL-C concentrations.[8,9,35] An indirect effect of smoking on insulin action such as elevated levels of free fatty acids was stated.[36] Studies examining the effect of resistin on basal and catecholamine stimulated lipolysis in adipocytes may define the contribution of resistin to incresed free fatty acids.[37] Plasma resistin levels were reported to be correlated with HDL- C and TG especially in females.[31] In ours study we only found high LDL-C levels in smokers, total and HDL-C and TG levels were not different in spite of high resistin levels in the smoker group. In the smoker group the subjects with HOMA-IR <2.7 had lower resistin levels than subjects with HOMA-IR ≥2.7, but did not have different lipid levels. In the non-smoker group as HOMA-IR was concerned, resistin levels did not change as well as total and LDL- C, TG but only HDL-C levels were higher in HOMA-IR <2.7 subjects. We may say that in our smoker population lipid parameters were not effected by resistin levels. The difference of our results and the ones in the literature may be explained by different assay methods, difference of gender, concomittant disorders or low number of patients enrolled in our study. It must also be remembered that we have included only non-diabetic, non-hypertensive healthy males in our study.

Positive correlation between resistin and blood pressure values especially systolic blood pressure was demonstrated.[31,38,39] We did not find any difference in blood pressure levels in our smoker and non-smoker groups, in spite of higher resistin levels in smokers. In smoker and non-smoker groups blood pressures did not differ as HOMA-IR was concerned, whereas in HOMA-IR high smoker group, resistin level was high. A different role of resistin according to gender was observed by authors, and it was speculated that associations between plasma resistin levels with metabolic and anthropometric parameters were different in men compared with women.[18,31] We think that the gender specific effect of resistin could depend on different adipose tissue depots that are responsible for its production in females and males.

In conclusion we speculate that smoking effects insulin resistance and resistin levels and resistin may be involved in glucose homeostasis, and insulin action. Confirmation of this observation is needed through additional research. But it is certain that smokers must be councelled that discontinuation of smoking would be useful and could bring substantial reversal of the damage caused.

REFERENCES

1. Jarrett RJ, Shipley MJ. Type 2 (non-insulin-dependent) diabetes mellitus and cardiovascular disease--putative association via common antecedents; further evidence from the Whitehall Study. Diabetologia 1988;31(10):737-40.
2. Perry IJ, Wannamethee SG, Walker MK, Thomson AG, Whincup PH, Shaper AG. Prospective study of risk factors for development of non-insulin dependent diabetes in middle aged British men. BMJ 1995;310(6979):560-4.
3. Haire-Joshu D, Glasgow RE, Tibbs TL. Smoking and diabetes. Diabetes Care 1999;22(11):1887-98.
4. Wannamethee SG, Shaper AG, Perry IJ; British Regional Heart Study. Smoking as a modifiable risk factor for type 2 diabetes in middle-aged men. Diabetes Care 2001;24(9):1590-5.
5. Targher G, Alberiche M, Zenere MB, Bonadonna RC, Muggeo M, Bonora E. Cigarette smoking and insulin resistance in patients with noninsulin-dependent diabetes mellitus. J Clin Endocrinol Metab 1997;82(11):3619-24.
6. Wakabayashi I. Associations between alcohol drinking and multiple risk factors for atherosclerosis in smokers and nonsmokers. Angiology 2010;61(5):495-503.
7. Attvall S, Fowelin J, Lager I, Von Schenck H, Smith U. Smoking induces insulin resistance--a potential link with the insulin resistance syndrome. J Intern Med 1993;233(4):327-32.
8. Masulli M, Riccardi G, Galasso R, Vaccaro O. Relationship between smoking habits and the features of the metabolic syndrome in a non-diabetic population. Nutr Metab Cardiovasc Dis 2006;16(5):364-70.
9. Farin HM, Abbasi F, Kim SH, Lamendola C, McLaughlin T, Reaven GM. The relationship between insulin resistance and dyslipidaemia in cigarette smokers. Diabetes Obes Metab 2007;9(1):65-9.
10. Kowall B, Rathmann W, Strassburger K, Heier M, Holle R, Thorand B, et al. Association of passive and active smoking with incident type 2 diabetes mellitus in the elderly population: the KORA S4/F4 cohort study. Eur J Epidemiol 2010;25(6):393-402.
11. Eliasson B, Attvall S, Taskinen MR, Smith U. The insulin resistance syndrome in smokers is related to smoking habits. Arterioscler Thromb 1994;14(12):1946-50.
12. Facchini FS, Hollenbeck CB, Jeppesen J, Chen YD, Reaven GM. Insulin resistance and cigarette smoking. Lancet 1992;339(8802):1128-30.
13. Steppan CM, Bailey ST, Bhat S, Brown EJ, Banerjee RR, Wright CM, et al. The hormone resistin links obesity to diabetes. Nature 2001;409(6818):307-12.
14. Menzaghi C, Trischitta V. Genetics of serum resistin: a paradigm of population-specific regulation? Diabetologia 2010;53(2):226-8.
15. Al-Daghri NM, Al-Attas OS, Hussain T, Sabico S, Bamakhramah A. Altered levels of adipocytokines in type 2 diabetic cigarette smokers. Diabetes Res Clin Pract 2009;83(2):e37-9.
16. Nogueiras R, Novelle MG, Vazquez MJ, Lopez M, Dieguez C. Resistin: regulation of food intake, glucose homeostasis and lipid metabolism. Endocr Dev 2010;17:175-84.
17. Banerjee RR, Rangwala SM, Shapiro JS, Rich AS, Rhoades B, Qi Y, et al. Regulation of fasted blood glucose by resistin. Science 2004;303(5661):1195-8.
18. Chen BH, Song Y, Ding EL, Roberts CK, Manson JE, Rifai N, et al. Circulating levels of resistin and risk of type 2 diabetes in men and women: results from two prospective cohorts. Diabetes Care 2009;32(2):329-34.
19. de Luis DA, Sagrado MG, Conde R, Aller R, Izaola O, de la Fuente B, et al. Relation of resistin levels with cardiovascular risk factors, insulin resistance and inflammation in naïve diabetes obese patients. Diabetes Res Clin Pract 2010;89(2):110-4.
20. Stofkova A. Resistin and visfatin: regulators of insulin sensitivity, inflammation and immunity. Endocr Regul 2010;44(1):25-36.
21. Gui Y, Silha JV, Murphy LJ. Sexual dimorphism and regulation of resistin, adiponectin, and leptin expression in the mouse. Obes Res 2004;12(9):1481-91.
22. Wallace JM, Levy JC, Matthews DR. Use and abuse of HOMA modelling. Diabetes Care 2007;27(2):1487-95.
23. Ostgren CJ, Lindblad U, Ranstam J, Melander A, Råstam L; Skaraborg Hypertension and Diabetes Project. Associations between smoking and beta-cell function in a non-hypertensive and non-diabetic population. Skaraborg Hypertension and Diabetes Project. Diabet Med 2000;17(6):445-50.
24. Shimokata H, Muller DC, Andres R. Studies in the distribution of body fat. III. Effects of cigarette smoking. JAMA 1989;261(8):1169-73.
25. Will JC, Galuska DA, Ford ES, Mokdad A, Calle EE. Cigarette smoking and diabetes mellitus: evidence of a positive association from a large prospective cohort study. Int J Epidemiol 2001;30(3):540-6.
26. Rimm EB, Chan J, Stampfer MJ, Colditz GA, Willett WC. Prospective study of cigarette smoking, alcohol use, and the risk of diabetes in men. BMJ 1995;310(6979):555-9.
27. Daniel M, Cargo MD. Association between smoking, insulin resistance and beta-cell function in a North-western First Nation. Diabet Med 2004;21(2):188-93.
28. Eliasson B, Mero N, Taskinen MR, Smith U. The insulin resistance syndrome and postprandial lipid intolerance in smokers. Atherosclerosis 1997;129(1):79-88.
29. Benwitz NL. Pharmacological aspects of cigarette smoking and nicotine action. F Eng J Med 1988;319(1):1318-30.
30. Willi C, Bodenmann P, Ghali WA, Faris PD, Cornuz J. Active smoking and the risk of Type 2 diabetes. JAMA 2007;298(22):2654-64.
31. Norata GD, Ongari M, Garlaschelli K, Raselli S, Grigore L, Catapano AL. Plasma resistin levels correlate with determinants of metabolic syndrome. Eur J Endocrinol 2007; 156(2):279-84.
32. Kim SK, Choe JY, Park SH, Lee SW, Lee GH, Chung WT. Increased insulin resistance and serum resistin in Korean patients with Behçet's diesease. Arch Med Res 2010; 41(4):269-74.
33. Grunberg NE, Popp KA, Bowen DJ, Nespor SM, Winders SE, Eury SE. Effects of chronic nicotine administration on insulin, glucose, epinephrine and norepinephrine. Life Sci 1988;42(12):161-70.
34. Ko GT, Tong PC, SO W, Cockram CS, Chan JC. Association between smoking, pancretic insulin secretion and insulinresistance in Chinese subjects with or without glucose intolerance. Chinese Med J 2007;120(24):2233-7.
35. Gupta V, Tiwari S, Agarwal CG, Shukla P, Chandra H, Sharma P. "Effect of short-term cigarette smoking on insulin resistance and lipid profile in asymptomatic adults". Indian J Physiol Pharmacol 2006;50(3):285-90.
36. Boden G, Chen X, Ruiz J, White JV, Rosetti L. Mechanism of fatty acid induced inhibition of glucose uptake. J Clin Invest 1994;93(6):2438-46.
37. McTernan PG, Fisher FM, Valsamakis G, Chetty R, Harte A, McTernan CL, et al. Resistin and type 2 diabetes: regulation of resistin expression by insulin and rosiglitazone and the effects of recombinant resistin on lipid and glucose metabolism in human differentiated adipocytes. J Clin Endocrinol Metab 2003;88(12):6098-106.
38. Li M, Fisette A, Zhao XY, Deng JY, Mi J, Cianflone K. Serum resistin correlates with central obesity but weakly with insulin resistance in Chinese children and adolescents. Int J Obes (Lond) 2009;33(4):424-39.
39. Papadopoulos DP, Perrea D, Thomopoulos C, Sanidas E, Daskalaki M, Papazachou U, et al. Masked hypertension and atherogenesis: the impact on adiponectin and resistin plasma levels. J Clin Hypertens (Greenwich) 2009;11(2):61-5.