www.endocrinologia.org.mx

PERMANYER

Check for updates

REVISTA MEXICANA DE ENDOCRINOLOGÍA, METABOLISMO & NUTRICIÓN

ORIGINAL ARTICLE

Effect of the rs9939609-*FTO* marker in Mexican adults under nutritional intervention

Efecto del marcador rs9939609-FTO en adultos mexicanos bajo intervención nutricional

Diana A. Vela-Vásquez[1], *Ivan Delgado-Enciso*[2], *Gilberto Ruiz-de-la-Cruz*[1], *Pascuala Ambriz-Morales*[1], *and Ana Ma. Sifuentes-Rincón*[1]*

[1]Laboratorio de Biotecnología Animal, Centro de Biotecnología Genómica, Instituto Politécnico Nacional (IPN), Reynosa, Tamps; [2]Facultad de Medicina, Universidad de Colima, Col. Mexico

ABSTRACT

Background: Obesity is a disease importantly influenced by genetic factors. The rs9939609 variant of the gene associated with fat mass and obesity (*FTO*) has been associated with weight gain, body mass index (BMI), and influence on the individual response to macronutrient intake. **Objectives:** To evaluate the effect of the rs9939609-*FTO* (A>T) marker on the response of volunteers under a dietary intervention that included beef with different compositions: high in saturated fatty acids and high in monounsaturated fatty acids (MUFA). **Methods:** The rs9939609-*FTO* marker genotype was obtained from 49 volunteers under a dietary intervention, and parametric tests were performed to determine its influence on anthropometric measurements between genotypes. **Results:** Both groups showed reductions in post-intervention measurements. The rs9939609-*FTO* polymorphism had no significant impact on weight loss, except at the hip measurement, where the A allele carriers (TA/AA) those that consumed more MUFA showed significantly smaller reductions between genotypes. **Conclusion:** This study provides insights from a Mexican population about the influence of *FTO* genotypes and diet composition on weight loss.

Keywords: Saturated fatty acids. Monounsaturated fatty acids. Weight loss. Body mass index. Single-nucleotide polymorphism.

RESUMEN

Antecedentes: La obesidad es una enfermedad en la que los factores genéticos desempeñan un papel importante. La variante rs9939609 del gen asociado a la masa grasa y la obesidad (*FTO*) se ha relacionado con aumento de peso y el índice de masa corporal, y tiene influencia en la respuesta individual a la ingesta de macronutrientes. **Objetivo:** Evaluar el efecto del marcador rs9939609-*FTO* (A>T) en la respuesta de voluntarios bajo una intervención dietética que incluyó carne de res con diferente composición: alta en ácidos grasos saturados (AGS) y alta en ácidos grasos monoinsaturados (AGM). **Método:** Se obtuvo el genotipo del marcador rs9939609-*FTO* de 49 voluntarios sometidos a intervención alimentaria y se realizaron pruebas paramétricas para determinar su influencia en las medidas antropométricas entre genotipos. **Resultados:** Ambos grupos mostraron reducciones en las mediciones tras la intervención, el polimorfismo rs9939609-*FTO* no tuvo un impacto significativo en la pérdida de peso, excepto en la cadera, donde los portadores del alelo A (TA/AA) que consumieron más AGM mostraron reducciones significativamente menores entre genotipos. **Conclusión:** Este estudio aporta información en una población mexicana sobre la influencia de los genotipos *FTO* y la composición de la dieta en la pérdida de peso.

Palabras clave: Ácidos grasos saturados. Ácidos grasos monoinsaturados. Pérdida de peso. Índice de masa corporal. Polimorfismo de un solo nucleótido.

*Correspondence:
Ana Ma. Sifuentes-Rincón
E-mail: asifuentes@ipn.mx

Date of reception: 01-04-2025
Date of acceptance: 03-07-2025
DOI: 10.24875/RME.25000019

Available online: 27-03-2026
Rev Mex Endocrinol Metab Nutr. 2026;13:1-6

INTRODUCTION

Obesity is the result of a chronic imbalance between energy expenditure and energy intake and is considered a multifactorial disease in which dietary and non-dietary factors are involved[1]. It has been described that between 40 and 70% of the variation in body mass index (BMI) in a population can be explained by genetic factors[2].

The fat mass and obesity-associated (*FTO*) gene is so far considered an important candidate gene for obesity. *FTO* gene polymorphisms may influence the growth, proliferation, and function of cells, as well as weight, BMI, and related traits[3,4]. The rs9939609-*FTO* single-nucleotide polymorphism (SNP) is an A/T transversion located in the first intron of *FTO* gene[4], and this polymorphism has been worldwide associated with obesity and related traits such as increased food intake, reduced hunger, and satiety responses[5].

The A allele (also referred to as obesity-predisposing allele), carriers have been reported to exhibit hyperphagia and an altered preference for macronutrients, including a higher intake of sugar and saturated fats than homozygous TT carriers[6]. In the Mexican population, the allele frequencies of rs9939609-*FTO* have been reported between 0.74 for the T allele and 0.26 for the A allele, these frequencies are close to those observed in the American population (T: 0.68, A: 0.32), but lower than the observed frequencies in African and European populations, where the A allele frequencies are 0.48 and 0.41, respectively[7].

Gene-diet interactions have been observed. De Luis et al.[8] reported a significant difference between individuals with the TT and TA/AA genotypes of the rs9939609-*FTO* polymorphism after 3 months of intervention. Carriers of the TA/AA genotype showed a greater reduction in weight, BMI, and fat mass levels compared to those with the TT genotype after following a hypocaloric high in polyunsaturated fatty acids (FA) diet. In addition, different studies have shown that the type of diet and genotype have been found to influence the outcomes[9-11]. Vela-Vásquez et al.[12,13] reported two clinical trials evaluating the effect of beef fatty acid composition including weight loss. Two types of beef were evaluated: high-monounsaturated FA (MUFA) beef containing 42.9% saturated FA (SFA), and 51.4% MUFA and the high-SFA beef contained significantly 2.27% more SFA and 1.81% less MUFA compared to high-MUFA beef. It was found that volunteers who consumed a high-MUFA beef experienced a higher reduction in body measurements and related indices than the consumption of high-SFA beef. Here we study a subsample from these two trials to evaluate the impact of rs9939609-*FTO* marker on the response of volunteers under a dietary intervention that included beef with varying content and composition of FA.

MATERIALS AND METHODS

Study design and subjects

This study was conceived as an exploratory clinical trial to evaluate the effect of a genotype-based nutritional intervention. *A priori* sample size estimation was conducted based on the maximum weighted mean difference in body weight reduction observed in a previous dietary intervention study comparing individuals with AA versus TT genotypes (−0.72 kg; PMID: 26888713). Using this effect size, a total of 30 participants per group (TT vs. TA/AA) would be required to achieve 80% statistical power with a two-sided α of 0.05, as calculated using the ClinCalc sample size calculator (http://clincalc.com/stats/samplesize.aspx; accessed 1 November 2024). Due to technical constraints – specifically, the genomic deoxyribonucleic acid (DNA) sample availability – the number of participants enrolled was lower than anticipated (21 and 28 volunteers from each group were included).

The clinical trials were randomized, controlled, double-blinded, and were carried out according to the Consolidated Standards of Reporting Trials guidelines. The inclusion and exclusion criteria, beef processing, dietary plan features, and dietary restrictions are detailed elsewhere[12,13]. Briefly, volunteers were randomly assigned to a study group "A" (control) for food intervention with high-SFA beef or group "B" for high-MUFA beef. NUTRIRES trial[12] had 2-week duration and NUTRIRES2[13] 4 weeks; in this last one,

the data at 2 weeks were analyzed to adjust the duration period with NUTRIRES trial. Volunteers followed a calorie-restricted menu and consumed 120 g of beef 3 times over a 2-week period. To avoid generating an additional caloric expenditure, moderate or intense physical activities and exercise were restricted. All volunteers gave written informed consent, approved by the Bioethics Committee of the Escuela Nacional de Medicina y Homeopatía (CBE/013/2019 and CBE/007/2021). The clinical trials were registered in the Cuban Public Registry of Clinical Trials (RPCEC) under the identifiers NUTRIRES: RPCEC00000302 and NUTRIRES2: RPCEC00000403.

ANTHROPOMETRIC MEASUREMENTS

Body weight, waist, and hip circumferences (cm) were measured according to standard procedures using a digital scale (OMRON, HBF-514C-LA) and an anthropometric tape (Lufkin W606PM). All measurements were assessed by the same individual to reduce variation[14]; using these data, BMI (kg/m^2) and waist–hip ratio (WHR) (waist circumference/hip circumference given in cm) were calculated.

GENOTYPING

Venous blood samples were obtained before the food intervention for the DNA extraction. DNA extraction was performed using GenElute™ Mammalian Genomic DNA Miniprep Kits. The sequences of the selected primers were based on the reported sequence (GenBank number 79068): forward 5'-GTATCTTTTGGCAGATCAGAAC-3'; and reverse, 5´-CAAGGATGTGTTTCTAAGGA-3´, which amplified a 416 bp product. For allelic discrimination of the SNP rs9939609-*FTO* in each sample analyzed, automated sequencing was performed in Operon Eurofins (Lincoln, U.S.A.). The alleles and genotype data of the population were generated using the Excel tool in the Microsoft Office package. The software Cervus 3.0.7 was used for computed frequencies and Hardy–Weinberg equilibrium[15].

STATISTICAL ANALYSIS

Due to the normal distribution of the data, verified by the Shapiro-Wilk test, statistical analyses were performed using parametric tests (t-test for independent samples and paired t-test for dependent samples). The anthropometric measures from each volunteer were analyzed at baseline and at the end of the dietary intervention, as well as the change between the two periods (final value minus basal value). The statistical analysis was performed using the DATAtab: Online Statistics Calculator, grouping the genotypes with the risk allele, i.e., TA + AA (TA/AA), and wild-type TT as the second group. A $p < 0.05$ was considered statistically significant.

RESULTS

Forty-nine volunteers were analyzed in this study, all of whom completed the 2-week follow-up period without any dropouts in either group. The mean age was 33.08 ± 8.18 years and the mean BMI was 27.95 ± 5.05, with 23 males (46.94%) and 26 females (53.06%) ($p = 0.877$). Seventeen were classified with obesity (at different levels, six men and eleven women), 17 with overweight (eleven men and six women), and normal weight (six men and nine women). Overweight was more frequent in men, whereas obesity was more frequent in women.

The rs9939609-*FTO* marker allele frequencies were 0.4 and 0.6 for A and T alleles, respectively. No deviation from Hardy–Weinberg equilibrium was observed. The genotype distribution was TT (42.85%), TA (34.69%), and AA (22.44%). The genotype frequency of the homozygous AA risk allele was higher in the group with high-SFA diet, while the number of heterozygous carriers was higher in the volunteers with high-MUFA diet.

Anthropometric parameters of volunteers at baseline and after 2 weeks of intervention are shown in table 1.

After the intervention, all volunteers showed a reduction in anthropometric measurements. Although there were no significant differences between groups, significant intragroup differences were observed in most measurements for both genotypes (Table 1). The TT volunteers in the high-MUFA beef group exhibited the greatest reductions

Table 1. Anthropometric measurements before and after intervention

Time	High-SFA beef		p^	High-MUFA beef		p^
	TT (n = 11)	TA or AA (n = 14)		TT (n = 10)	TA or AA (n = 14)	
Weight (kg)						
Basal	82.10 ± 17.23	80.58 ± 16.51	0.824	80.81 ± 12.39	71.16 ± 15.89	0.124
Final	81.22 ± 17.39	79.56 ± 16.31	0.808	79.45 ± 12.18	70.45 ± 15.31	0.138
p†	0.003	0.003		< 0.001	0.062	
Change	−0.88 ± 0.75	−1.02 ± 1.03	0.708	−1.36 ± 0.69	−0.71 ± 1.3	0.163
BMI						
Basal	28.52 ± 4.65	28.88 ± 5.13	0.858	29.19 ± 4.74	25.7 ± 5.3	0.112
Final	28.2 ± 4.69	28.51 ± 5.02	0.878	28.71 ± 4.74	25.46 ± 5.18	0.132
p†	0.005	0.002		< 0.001	0.061	
Change	−0.32 ± 0.29	−0.37 ± 0.37	0.696	−0.48 ± 0.22	−0.24 ± 0.43	0.120
Waist (cm)						
Basal	90.9 ± 11.41	94.61 ± 11.35	0.427	93.35 ± 10.84	85.66 ± 9.72	0.082
Final	88.9 ± 11.25	93.00 ± 10.55	0.359	91.77 ± 10.56	83.49 ± 10.18	0.066
p†	0.002	0.025		0.038	0.007	
Change	−2.00 ± 1.54	−1.61± 2.37	0.639	−1.58 ± 2.05	−2.17 ± 2.5	0.547
Hip (cm)						
Basal	108.69 ± 12.55	108.64 ± 9.53	0.991	107.87 ± 6.41	100.32 ± 7.09	0.014
Final	107.45 ± 12.84	106.61 ± 8.67	0.846	105.82 ± 6.56	100.23 ± 6.71	0.055
p†	0.041	0.068		0.010	0.838	
Change	−1.24 ± 1.75	−2.04 ± 3.83	0.529	−2.05 ± 1.98	−0.09 ± 1.66	0.016
WHR						
Basal	0.84 ± 0.07	0.87 ± 0.07	0.283	0.86 ± 0.08	0.85 ± 0.05	0.662
Final	0.83 ± 0.08	0.87 ± 0.05	0.130	0.87 ± 0.08	0.83 ± 0.06	0.227
p†	0.195	0.836		0.656	0.029	
Change	−0.01 ± 0.02	0.00 ± 0.04	0.473	0.00 ± 0.02	−0.02 ± 0.04	0.073

No statistical differences between genotypes in different diet groups ($p < 0.05$). Values are means and S.D.
†p: baseline versus final, t-test (two related samples).
^p: TT versus TA/AA of the same diet group, t-test (independent samples).
BMI: body mass index; MUFA: monounsaturated fatty acids; SFA: saturated fatty acids.

in weight, BMI, and hip circumference, while the TA/AA volunteers of the same group showed the smallest decreases in these measurements. Only the WHR showed a significant difference after the consumption of the high-MUFA beef in TA/AA volunteers' group. These intragroup differences were not observed after the consumption of the high-SFA beef. Interestingly, when comparing changes according to genotype within each beef group, only the hip measurement showed a significant difference in the high-MUFA group. In this group, the TA/AA volunteers presented 1.96 cm more in hip circumference (Table 1) compared to the TT volunteers of the same group.

DISCUSSION

Men in our study population had a higher prevalence of overweight, while women had a higher prevalence of obesity. This tendency has been described by Barquera et al.[16] in a Mexican population where overweight is more predominant in men (42.5%) and obesity in women (40.2%). The allelic frequencies of the rs9939609-*FTO* in this study were 0.4 for the A allele and 0.6 for the T allele. These results are close to previously reported frequencies in southeastern Mexico[7].

Here, we found that no matter their FA composition, beef consumption did not affect the weight loss; however, it had an important impact on the anthropometric measurements regardless of the rs9939609-*FTO* genotype. At the intragroup level, the TA/AA genotype carriers of the high-MUFA group showed significantly lower reductions in hip circumference. These results were not observed in the TA/AA volunteers of the high-SFA-beef diet group.

Different studies have reported a greater weight loss response in A-allele carriers following Mediterranean-style, high-protein, or low-fat diets; this response was not observed in our study, as A-allele carriers showed the smallest reductions when following a high-MUFA beef diet. As it was previously described, the sample size studied was lower than the expected; consequently, the present analysis should be considered a hypothesis-generating exploratory trial. Despite the reduced sample size, the observed results and trends provide preliminary evidence of an interaction between genetic background and dietary response, warranting confirmation in adequately powered future studies. It is also applicable for other variables such as the intervention extension, since previous studies have typically ranged from 3 months to 3 years[9-11].

MUFA consumption could influence body fat redistribution, as TA/AA volunteers showed a significant reduction in WHR due to decreased waist circumference; however, this group showed less reduction in the hip, which could reflect a specific resistance of this genotype to changes in this measure. In terms of body composition, Di Renzo et al.[17] observed a gene-diet interaction, where A carriers in the control group experienced an increase in total body fat (+ 6.11 kg), while A carriers on the Mediterranean diet reduced total body fat (−3.97 kg) following a 4-week intervention. Although this difference was not statistically significant and cannot be treated as if it was a dual-energy X-ray absorptiometry results, these findings emphasize the potential role of diet in influencing fat distribution and highlight the need for further research on gene-diet interactions and their effects on body fat redistribution using appropriate assessment tools. Carriers of the AA genotype has been found to have larger waist sizes, although this trend has not been observed in all populations[18,19]. In our study, both genotypes exhibited high values in the waist measurements (> 80 cm). Interestingly, A allele carriers showed a greater reduction in waist circumference after MUFA consumption compared to T homozygotes in both groups, although not significant. This is noteworthy, as waist circumference is a key indicator of central adiposity[20].

On the other hand, it has been reported that SFA consumption has a greater impact on the BMI of *FTO* A allele carriers compared to other macronutrients[3,21]. However, in our study, SFA consumption did not increase weight, BMI, or any anthropometric measurements. In our population, carriers of the rs9939609-*FTO* risk allele showed contrasting results. First, we observed that a tendency toward smaller decreases in various anthropometric measurements when a more favorable FA profile was consumed. Second, greater reductions were seen with the high-SFA diet, although these differences were not statistically significant. Finally, the possible influence of MUFA consumption on body fat composition in the A-allele carriers is an interesting point to explore as a strategy to reduce cardiovascular risk.

CONCLUSION

In this study, the rs9939609-*FTO* polymorphism did not have a major impact on weight reduction or anthropometric measurements during the short-term consumption of either a high-MUFA or high-SFA diet, except for hip circumference, where A allele carriers (TA/AA) on the MUFA-rich diet showed significantly smaller reductions. Further long-term studies are

needed to expand knowledge about specific nutrition components and its interaction with consumer-genetic background.

ACKNOWLEDGMENTS

The authors want to thank SECIHTI for support through the P.A.M. and D.A.V.V. scholarships and Ing. Paola Mares and the staff of Agroindustrias Cohuayana for beef collection and donation.

FUNDING

This research was funded by Instituto Politécnico Nacional through SIP project 20241271.

CONFLICTS OF INTEREST

The authors report that there are no conflicts of interest.

ETHICAL CONSIDERATIONS

Protection of humans and animals. The authors declare to have followed the ethical standards of the relevant experimentation committee, according to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from all patients, and secured approval from the Ethics Committee. SAGER guidelines have been followed as applicable to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

REFERENCES

1. Stroebe W. Is the energy balance explanation of the obesity epidemic wrong? Appetite. 2023;188:106614.
2. Attaoua R, El Mkadem SA, Lautier C, Kaouache S, Renard E, Brun JF, et al. Association of the FTO gene with obesity and the metabolic syndrome is independent of the IRS-2 gene in the female population of Southern France. Diabetes Metab. 2009;35:476-83.
3. Abdollahi S, Ardekanizadeh NH, Poorhosseini SM, Gholamalizadeh M, Roumi Z, Goodarzi MO, et al. Unraveling the complex interactions between the fat mass and obesity-associated (FTO) gene, lifestyle, and cancer. Adv Nutr. 2022;13:2406-19.
4. Baručija-Özçoban I, Ašić A, Bešić L, Halilović S, Marjanović D, Dogan S. A decade of the common FTO Rs9939609 polymorphism: a systematic review. Coll Antropol. 2018;42:147-58.
5. Qi Q, Kilpeläinen TO, Downer MK, Tanaka T, Smith CE, Sluijs I, et al. FTO genetic variants, dietary intake and body mass index: insights from 177,330 individuals. Hum Mol Genet. 2014;23:6961-72.
6. Poosri S, Boonyuen U, Chupeerach C, Soonthornworasiri N, Kwanbunjan K, Prangthip P. Association of FTO variants rs9939609 and rs1421085 with elevated sugar and fat consumption in adult obesity. Sci Rep. 2024;14:25618.
7. Ortega PE, Meneses ME, Delgado-Enciso I, Irecta-Nájera CA, Castro-Quezada I, Solís-Hernández R, et al. Association of rs9939609-FTO with metabolic syndrome components among women from Mayan communities of Chiapas, Mexico. J Physiol Anthropol. 2021;40:11.
8. De Luis DA, Aller R, Izaola O, Pacheco D. Role of rs9939609 *FTO* gene variant in weight loss, insulin resistance and metabolic parameters after a high monounsaturated vs a high polyunsaturated fat hypocaloric diets. Nutr Hosp 2015;32:175-81.
9. Razquin C, Martinez JA, Martinez-Gonzalez MA, Bes-Rastrollo M, Fernandez-Crehuet J, Marti A. A 3-year intervention with a mediterranean diet modified the association between the rs9939609 gene variant in FTO and body weight changes. Int J Obes (Lond). 2010;34:266-72.
10. Zhang X, Qi Q, Zhang C, Smith SR, Hu FB, Sacks FM, et al. FTO genotype and 2-year change in body composition and fat distribution in response to weight-loss diets: the POUNDS LOST Trial. Diabetes. 2012;61:3005-11.
11. De Luis DA, Aller R, Izaola O, De la Fuente B, Conde R, Sagrado MG, et al. Evaluation of weight loss and adipocytokines levels after two hypocaloric diets with different macronutrient distribution in obese subjects with rs9939609 gene variant. Diabetes Metab Res Rev. 2012;28:663-8.
12. Vela-Vásquez DA, Sifuentes-Rincón AM, Delgado-Enciso I, Delgado-Enciso OG, Ordaz-Pichardo C, Arellano-Vera W, et al. Improvement of serum lipid parameters in consumers of Mexican Wagyu-Cross beef: a randomized controlled trial. J Food Sci. 2021;86:2713-26.
13. Vela-Vasquez DA, Sifuentes-Rincón AM, Delgado-Enciso I, Ordaz-Pichardo C, Arellano-Vera W, Treviño-Alvarado V, et al. Effect of consuming beef with varying fatty acid compositions as a major source of protein in volunteers under a personalized nutritional program. Nutrients. 2022;14:3711.
14. Marfell-Jones F, Vaquero-Cristóbal R. Protocolo Internacional para la Valoración Antropométrica. Murcia, Spain: Perfil Restrito, Universidad Católica de Murcia; 2019.
15. Kalinowski ST, Taper ML, Marshall TC. Revising how the computer program CERVUS accommodates genotyping error increases success in paternity assignment. Mol Ecol. 2007;16:1099-106.
16. Barquera S, Hernández-Barrera L, Trejo-Valdivia B, Shamah T, Campos-Nonato I, Rivera-Dommarco J. Obesity in Mexico, prevalence andtrends in adults. Ensanut 2018-19. Salud Pública Méx. 2020;62:682-92.
17. Di Renzo L, Cioccoloni G, Falco S, Abenavoli L, Moia A, Sinibaldi SP, et al. Influence of FTO rs9939609 and mediterranean diet on body composition and weight loss: a randomized clinical trial. J Transl Med. 2018;16:308.
18. Mehrdad M, Fardaei M, Fararouei M, Eftekhari MH. The association between FTO rs9939609 gene polymorphism and anthropometric indices in adults. J Physiol Anthropol 2020;39:14.
19. Ağagündüz D, Gezmen-Karadağ M. Association of FTO common variant (rs9939609) with body fat in Turkish individuals. Lipids Health Dis. 2019;18:212.
20. Xi B, Zong XN, Kelishadi R, Litwin M, Hong YM, Poh BK, et al. International waist circumference percentile cutoffs for central obesity in children and adolescents aged 6 to 18 years. J Clin Endocrinol Metab. 2020;105: e1569-83.
21. Corella D, Arnett DK, Tucker KL, Kabagambe EK, Tsai M, Parnell LD, et al. A high intake of saturated fatty acids strengthens the association between the fat mass and obesity-associated gene and BMI. J Nutr. 2011;141:2219-25.