

**EFFECTO EN EL MANEJO DE LOS NIVELES DE
HEMOGLOBINA GLICOSILADA DE LA METFORMINA VS
LIRAGLUTIDA INYECTABLE VS SEMAGLUTIDA
INYECTABLE EN PACIENTES OBESOS ($IMC \geq 30$) DE UN
PROGRAMA DE MANEJO DE SÍNDROME METABÓLICO
EN UNA CLÍNICA DE MAICAO (LA GUAJIRA, CO)
DURANTE LOS AÑOS 2022 A 2023**

LUIS CARLOS HERRERA DÍAZ

Código estudiantil: 2022114038103

JAIRO JOSÉ QUIROZ BARRAZA

Código estudiantil: 2022114038120

Trabajo de Investigación presentado como requisito para optar el título de:

ESPECIALISTA EN MEDICINA INTERNA

Tutor Disciplinar:

ALBERTO ENRIQUE POLO BARRANCO

MD | SPC MEDICINA INTERNA

Tutor Metodológico:

HENRY JOSETH GONZÁLEZ TORRES

BIO | Spc App Stat | MSc Bio (GenPop) | DrSc (C) BioMed

RESUMEN

La obesidad es un factor de riesgo crítico para enfermedades metabólicas y cardiovasculares, exacerbando el síndrome metabólico en poblaciones vulnerables. En respuesta a esta problemática, los agonistas GLP-1 (liraglutida y semaglutida) y la metformina han sido estudiados ampliamente por su potencial para mejorar los niveles de hemoglobina glicosilada (HbA1c), peso, presión arterial y perfil lipídico en pacientes obesos.

Objetivo: Comparar del efecto Metformina vs Liraglutida Inyectable vs Semaglutida Inyectable en pacientes Obesos ($IMC \geq 30$) de un Programa de Manejo de Síndrome Metabólico en una Clínica de Maicao (La Guajira, CO) durante los años 2022 a 2023.

Metodología: Se realizó un estudio observacional, analítico y de cohorte longitudinal con 45 pacientes obesos ($IMC \geq 30$) tratados con liraglutida, semaglutida o metformina durante el período de 2022-2023. Se analizaron datos de HbA1c, IMC, presión arterial (PAS y PAD) y perfil lipídico (colesterol total, HDL-C y LDL-C) mediante análisis de varianza (ANOVA) para muestras pareadas e independientes.

Resultados: En este estudio con 45 pacientes obesos (60% mujeres, edad promedio 53.1 años), no hubo diferencias significativas entre sexos en PAS, PAD, IMC, ni HbA1C. Los hombres presentaron mayor hipertensión (72%) y uso de liraglutida ($p=0.04$). Entre los tratamientos (liraglutida, metformina y semaglutida), no se hallaron diferencias significativas en parámetros basales. La PAS disminuyó en todos los grupos, siendo mayor en liraglutida y semaglutida; sin embargo, la PAD solo mejoró significativamente con metformina. El grupo de semaglutida mostró la mayor reducción en IMC ($p<0.001$) y HbA1C (-1.0%), además de una mejora significativa en HDL-C y reducción en colesterol total.

Conclusión: Los agonistas GLP-1, especialmente la semaglutida, demostraron mayor efectividad en el control de HbA1c y en la reducción de IMC en pacientes obesos, además de ofrecer beneficios adicionales en el perfil lipídico. Estos hallazgos respaldan el uso de semaglutida y liraglutida como opciones prometedoras en el manejo integral del síndrome metabólico en pacientes con obesidad.

Palabras clave: Obesidad; Síndrome Metabólico; Hemoglobina Glicosilada (HbA1c); Liraglutida; Semaglutida; Metformina; Índice de Masa Corporal (IMC); Perfil Lipídico; Presión Arterial.

ABSTRACT

Obesity is a critical risk factor for metabolic and cardiovascular diseases, exacerbating metabolic syndrome in vulnerable populations. In response to this issue, GLP-1 agonists (liraglutide and semaglutide) and metformin have been widely studied for their potential to improve hemoglobin A1c (HbA1c) levels, weight, blood pressure, and lipid profile in obese patients.

Objective: To compare the effect of Metformin vs. Injectable Liraglutide vs. Injectable Semaglutide in obese patients (BMI \geq 30) enrolled in a Metabolic Syndrome Management Program at a clinic in Maicao (La Guajira, CO) from 2022 to 2023.

Methodology: An observational, analytical, and longitudinal cohort study was conducted with 45 obese patients (BMI \geq 30) treated with liraglutide, semaglutide, or metformin during the 2022-2023 period. Data on HbA1c, BMI, blood pressure (SBP and DBP), and lipid profile (total cholesterol, HDL-C, and LDL-C) were analyzed using analysis of variance (ANOVA) for paired and independent samples.

Results: In this study with 45 obese patients (60% women, mean age 53.1 years), there were no significant differences between sexes in SBP, DBP, BMI, or HbA1c. Men presented with higher rates of hypertension (72%) and liraglutide use ($p=0.04$). Among treatments (liraglutide, metformin, and semaglutide), no significant differences were found in baseline parameters. SBP decreased in all groups, with a greater reduction in liraglutide and semaglutide; however, DBP only significantly improved with metformin. The semaglutide group showed the largest reduction in BMI ($p<0.001$) and HbA1c (-1.0%), as well as a significant increase in HDL-C and reduction in total cholesterol.

Conclusion: GLP-1 agonists, especially semaglutide, demonstrated greater effectiveness in controlling HbA1c and reducing BMI in obese patients, in addition to providing additional benefits in lipid profile. These findings support the use of semaglutide and liraglutide as promising options for comprehensive management of metabolic syndrome in obese patients.

Keywords: Obesity; Metabolic Syndrome; Glycated Hemoglobin (HbA1c); Liraglutide; Semaglutide; Metformin; Body Mass Index (BMI); Lipid Profile; Blood Pressure

REFERENCIAS BIBLIOGRÁFICAS

1. Ndumele CE, Neeland IJ, Tuttle KR, Chow SL, Mathew RO, Khan SS, et al. A Synopsis of the Evidence for the Science and Clinical Management of Cardiovascular-Kidney-Metabolic (CKM) Syndrome: A Scientific Statement From the American Heart Association. *Circulation*. 2023 Nov;148(20):1636–64.
2. Koenen M, Hill MA, Cohen P, Sowers JR. Obesity, Adipose Tissue and Vascular Dysfunction. *Circ Res*. 2021 Apr;128(7):951–68.
3. Yaribeygi H, Maleki M, Nasimi F, Jamialahmadi T, Stanford FC, Sahebkar A. Benefits of GLP-1 Mimetics on Epicardial Adiposity. *Curr Med Chem*. 2023 Nov;30(37):4256–65.
4. Elmaleh-Sachs A, Schwartz JL, Bramante CT, Nicklas JM, Gudzone KA, Jay M. Obesity Management in Adults. *JAMA*. 2023 Nov;330(20):2000.
5. Rubino DM, Greenway FL, Khalid U, O'Neil PM, Rosenstock J, Sørrig R, et al. Effect of Weekly Subcutaneous Semaglutide vs Daily Liraglutide on Body Weight in Adults With Overweight or Obesity Without Diabetes: The STEP 8 Randomized Clinical Trial. *JAMA*. 2022 Jan;327(2):138–50.
6. Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: Understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. *Comput Biol Med*. 2021 Sep;136:104754.
7. Mitchell NS, Catenacci VA, Wyatt HR, Hill JO. Obesity: Overview of an Epidemic. *Psychiatr Clin North Am*. 2011 Dec;34(4):717–32.
8. Azhar S. Peroxisome proliferator-activated receptors, Metabolic Syndrome and Cardiovascular Disease. *Future Cardiol*. 2010 Sep;6(5):657–91.
9. Engin A. The Definition and Prevalence of Obesity and Metabolic Syndrome. In 2017. p. 1–17.
10. Tune JD, Goodwill AG, Sassoon DJ, Mather KJ. Cardiovascular consequences of metabolic syndrome. *Transl Res*. 2017 May;183:57–70.
11. Wu H, Ballantyne CM. Metabolic Inflammation and Insulin Resistance in Obesity. *Circ Res*. 2020 May;126(11):1549–64.
12. Ferrante SC, Nadler EP, Pillai DK, Hubal MJ, Wang Z, Wang JM, et al. Adipocyte-derived exosomal miRNAs: a novel mechanism for obesity-related disease. *Pediatr Res*. 2015 Mar;77(3):447–54.
13. Anderson MR, Shashaty MGS. Impact of Obesity in Critical Illness. *Chest*. 2021 Dec;160(6):2135–45.
14. Seidell JC, Halberstadt J. The Global Burden of Obesity and the Challenges of Prevention. *Ann Nutr Metab*. 2015;66(Suppl. 2):7–12.
15. Hoffman DJ, Powell TL, Barrett ES, Hardy DB. Developmental origins of metabolic diseases. *Physiol Rev*. 2021 Jul;101(3):739–95.
16. Anekwe CV, Jarrell AR, Townsend MJ, Gaudier GI, Hiserodt JM, Stanford FC. Socioeconomics of Obesity. *Curr Obes Rep*. 2020 Sep;9(3):272–9.
17. Riaz H, Khan MS, Siddiqi TJ, Usman MS, Shah N, Goyal A, et al. Association Between Obesity and Cardiovascular Outcomes. *JAMA Netw Open*. 2018 Nov;1(7):e183788.

18. Kushner RF, Calanna S, Davies M, Dicker D, Garvey WT, Goldman B, et al. Semaglutide 2.4 mg for the Treatment of Obesity: Key Elements of the STEP Trials 1 to 5. *Obesity*. 2020 Jun;28(6):1050–61.
19. Yerevanian A, Soukas AA. Metformin: Mechanisms in Human Obesity and Weight Loss. *Curr Obes Rep*. 2019 Jun;8(2):156–64.
20. Khera R, Murad MH, Chandar AK, Dulai PS, Wang Z, Prokop LJ, et al. Association of Pharmacological Treatments for Obesity With Weight Loss and Adverse Events. *JAMA*. 2016 Jun;315(22):2424.
21. Kahleova H, Lloren JI, Mashchak A, Hill M, Fraser GE. Meal Frequency and Timing Are Associated with Changes in Body Mass Index in Adventist Health Study 2. *J Nutr*. 2017 Sep;147(9):1722–8.
22. Samuels JM, Niswender KD, Roumie CL, Spann MD, Flynn CR, Ye F, et al. Adverse event comparison between glucagon-like peptide-1 receptor agonists and other antiobesity medications following bariatric surgery. *Diabetes, Obes Metab*. 2024 Sep;26(9):3906–13.
23. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet*. 2014 Aug;384(9945):766–81.
24. Huang PL. A comprehensive definition for metabolic syndrome. *Dis Model Mech*. 2009 Apr;2(5–6):231–7.
25. Jastreboff AM, Kushner RF. New Frontiers in Obesity Treatment: GLP-1 and Nascent Nutrient-Stimulated Hormone-Based Therapeutics. *Annu Rev Med*. 2023 Jan;74(1):125–39.
26. Xie Z, Yang S, Deng W, Li J, Chen J. Efficacy and Safety of Liraglutide and Semaglutide on Weight Loss in People with Obesity or Overweight: A Systematic Review. *Clin Epidemiol*. 2022 Dec;Volume 14:1463–76.
27. Deng Y, Park A, Zhu L, Xie W, Pan CQ. Effect of semaglutide and liraglutide in individuals with obesity or overweight without diabetes: a systematic review. *Ther Adv Chronic Dis*. 2022 Jan;13.
28. Rentzeperi E, Pegiou S, Koufakis T. Sex Differences in Response to Treatment with Glucagon-like Peptide 1 Receptor Agonists : Opportunities for a Tailored Approach to Diabetes and Obesity Care. 2022;
29. Nowrouzi-Sohrabi P, Soroush N, Tabrizi R, Shabani-Borujeni M, Rezaei S, Jafari F, et al. Effect of Liraglutide on Cardiometabolic Risk Profile in People with Coronary Artery Disease with or without Type 2 Diabetes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Front Pharmacol*. 2021 Mar;12.
30. Verma S, Poulter NR, Bhatt DL, Bain SC, Buse JB, Leiter LA, et al. Effects of Liraglutide on Cardiovascular Outcomes in Patients With Type 2 Diabetes Mellitus With or Without History of Myocardial Infarction or Stroke. *Circulation*. 2018 Dec;138(25):2884–94.
31. Wong HJ, Toh KZX, Teo YH, Teo YN, Chan MY, Yeo LLL, et al. Effects of glucagon-like peptide-1 receptor agonists on blood pressure in overweight or obese patients: a meta-analysis of randomized controlled trials. *J Hypertens*. 2024 Oct;

32. Michos ED, Lopez-Jimenez F, Gulati M. Role of Glucagon-Like Peptide-1 Receptor Agonists in Achieving Weight Loss and Improving Cardiovascular Outcomes in People With Overweight and Obesity. *J Am Heart Assoc.* 2023 Jun;12(11).
33. Zhao D, Liu H, Dong P. Liraglutide reduces systolic blood pressure in patients with type 2 diabetes mellitus: A meta-analysis of randomized trials. *Clin Exp Hypertens.* 2020 Jul;42(5):393–400.
34. Muzurović E, Mikhailidis DP. Impact of glucagon-like peptide 1 receptor agonists and sodium-glucose transport protein 2 inhibitors on blood pressure and lipid profile. *Expert Opin Pharmacother.* 2020 Nov;21(17):2125–35.
35. Alhindi Y, Avery A. The efficacy and safety of oral semaglutide for glycaemic management in adults with type 2 diabetes compared to subcutaneous semaglutide, placebo, and other GLP-1 RA comparators: A systematic review and network meta-analysis. *Contemp Clin Trials Commun.* 2022 Aug;28:100944.
36. Wang S, Wang S, Wang Y, Luan J. Glycemic Control, Weight Management, Cardiovascular Safety, and Cost-Effectiveness of Semaglutide for Patients with Type 2 Diabetes Mellitus: A Rapid Review and Meta-analysis of Real-World Studies. *Diabetes Ther.* 2024 Feb;15(2):497–519.
37. Rizzo M, Nikolic D, Patti AM, Mannina C, Montalto G, McAdams BS, et al. GLP-1 receptor agonists and reduction of cardiometabolic risk: Potential underlying mechanisms. *Biochim Biophys Acta - Mol Basis Dis.* 2018 Sep;1864(9):2814–21.
38. Kim HJ, Park SO, Ko SH, Rhee SY, Hur KY, Kim NH, et al. Glucagon-Like Peptide-1 Receptor Agonists for the Treatment of Type 2 Diabetes Mellitus: A Position Statement of the Korean Diabetes Association. *Diabetes Metab J.* 2017;41(6):423.
39. Hu EH, Tsai ML, Lin Y, Chou TS, Chen TH. A Review and Meta-Analysis of the Safety and Efficacy of Using Glucagon-like Peptide-1 Receptor Agonists. *Medicina (B Aires).* 2024 Feb;60(3):357.
40. Cornell S. A review of GLP-1 receptor agonists in type 2 diabetes: A focus on the mechanism of action of once-weekly agents. *J Clin Pharm Ther* [Internet]. 2020 Sep 10;45(S1):17–27. Available from: <https://onlinelibrary.wiley.com/doi/10.1111/jcpt.13230>
41. Szekeres Z, Nagy A, Jahner K, Szabados E. Impact of Selected Glucagon-like Peptide-1 Receptor Agonists on Serum Lipids, Adipose Tissue, and Muscle Metabolism—A Narrative Review. *Int J Mol Sci* [Internet]. 2024 Jul 27;25(15):8214. Available from: <https://www.mdpi.com/1422-0067/25/15/8214>
42. Nikolic D, Giglio RV, Rizvi AA, Patti AM, Montalto G, Maranta F, et al. Liraglutide Reduces Carotid Intima-Media Thickness by Reducing Small Dense Low-Density Lipoproteins in a Real-World Setting of Patients with Type 2 Diabetes: A Novel Anti-Atherogenic Effect. *Diabetes Ther* [Internet]. 2021 Jan 18;12(1):261–74. Available from: <https://link.springer.com/10.1007/s13300-020-00962-3>
43. Ajabnoor GMA, Hashim KT, Alzahrani MM, Alsuheili AZ, Alharbi AF, Alhozali AM, et al. The Possible Effect of the Long-Term Use of Glucagon-like Peptide-

- 1 Receptor Agonists (GLP-1RA) on Hba1c and Lipid Profile in Type 2 Diabetes Mellitus: A Retrospective Study in KAUH, Jeddah, Saudi Arabia. *Diseases* [Internet]. 2023 Mar 14;11(1):50. Available from: <https://www.mdpi.com/2079-9721/11/1/50>
44. Verrijken A, Francque S, Van Gaal L. The metabolic syndrome and the liver. *Acta Gastroenterol Belg* [Internet]. 2008;71(1):48–59. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/18396752>
45. Vargas M, Cardoso Toniasso S de C, Riedel PG, Baldin CP, dos Reis FL, Pereira RM, et al. Metabolic disease and the liver: A review. *World J Hepatol* [Internet]. 2024 Jan 27;16(1):33–40. Available from: <https://www.wjgnet.com/1948-5182/full/v16/i1/33.htm>
46. Patel V, Joharapurkar A, Shah G, Jain M. Effect of GLP-1 Based Therapies on Diabetic Dyslipidemia. *Curr Diabetes Rev* [Internet]. 2014 Jul 6;10(4):238–50. Available from: <http://www.eurekaselect.com/openurl/content.php?genre=article&issn=1573-3998&volume=10&issue=4&spage=238>
47. Bu T, Sun Z, Pan Y, Deng X, Yuan G. Glucagon-Like Peptide-1: New Regulator in Lipid Metabolism. *Diabetes Metab J* [Internet]. 2024 May;48(3):354–72. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/38650100>
48. Yabut JM, Drucker DJ. Glucagon-like Peptide-1 Receptor-based Therapeutics for Metabolic Liver Disease. *Endocr Rev* [Internet]. 2023 Jan 12;44(1):14–32. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/35907261>
49. Le R, Nguyen MT, Allahwala MA, Psaltis JP, Marathe CS, Marathe JA, et al. Cardiovascular Protective Properties of GLP-1 Receptor Agonists: More than Just Diabetic and Weight Loss Drugs. *J Clin Med* [Internet]. 2024 Aug 9;13(16):4674. Available from: <https://www.mdpi.com/2077-0383/13/16/4674>
50. Yang JL, Chen WY, Chen SD. The Emerging Role of GLP-1 Receptors in DNA Repair: Implications in Neurological Disorders. *Int J Mol Sci* [Internet]. 2017 Aug 26;18(9). Available from: <http://www.ncbi.nlm.nih.gov/pubmed/28846606>
51. Albahli OM, Ali S, Alblaihi F, Aljaman AA. The Effect of Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists on the Lipid Profile of Diabetic Patients Using Statins: A Retrospective Cohort Study in the Diabetic Center of King Salman Bin Abdulaziz Hospital, Saudi Arabia. *Cureus* [Internet]. 2024 Jul 27; Available from: <https://www.cureus.com/articles/279066-the-effect-of-glucagon-like-peptide-1-glp-1-receptor-agonists-on-the-lipid-profile-of-diabetic-patients-using-statins-a-retrospective-cohort-study-in-the-diabetic-center-of-king-salman-bin-abdulaziz-hospital-saudi-arabia>
52. Patti AM, Rizvi AA, Giglio RV, Stoian AP, Ligi D, Mannello F. Impact of Glucose-Lowering Medications on Cardiovascular and Metabolic Risk in Type 2 Diabetes. *J Clin Med* [Internet]. 2020 Mar 26;9(4):912. Available from: <https://www.mdpi.com/2077-0383/9/4/912>