Dyslipidemia

Subjects: Cardiac & Cardiovascular Systems | Medicine, General & Internal | Nutrition & Dietetics

Contributor: Mihnea-Alexandru Gaman

Dyslipidemia is a significant threat to public health worldwide and the identification of its pathogenic mechanisms, as well as novel lipid-lowering agents, are warranted. Magnesium (Mg) is a key element to human health and its deficiency has been linked to the development of lipid abnormalities and related disorders, such as the metabolic syndrome, type 2 diabetes mellitus, or cardiovascular disease.

magnesium | magnesemia | hypomagnesemia | lipids | cholesterol | triglycerides | dyslipidemia | hyperlipidemia | diabetes | metabolic syndrome

1. Introduction

Dyslipidemia has emerged as a significant threat to public health worldwide, with recent statistics revealing that its prevalence reaches 42.7% in China and 56.8% in the United States of America (USA). In addition, Lu et al. (2018) have pointed out that an alarming rate of the population suffering from this disorder is not aware of its lipid profile (26.7% in the USA versus 80.4% in China), leading to poor treatment and control rates of lipid abnormalities (13.2% and 4.6% in China versus 54.1 and 35.7% in the USA) [1]. Thus, identifying novel strategies to combat dyslipidemia are warranted, particularly due to its involvement in the development of and crosstalk with metabolic syndrome (MetS), type 2 diabetes mellitus (T2DM), cardiovascular disease, obesity, hypertension, chronic kidney disease (CKD), and others [1][2][3].

Magnesium (Mg) seems to play a key role in a myriad of disorders, e.g., MetS, T2DM, obesity, hypertension, and its deficiency has been regarded as highly prevalent, with Piuri et al. (2021) ranking it as the most common electrolyte imbalance in high-income countries [4][5][6]. Taking this information into consideration, we may hypothesize that there is a crosstalk between Mg and serum lipids which may impact on the pathogenesis of dyslipidemia and its associated comorbidities, as well as that Mg supplementation might provide health benefits in patients suffering from cardiometabolic disorders.

2. Crosstalk of Magnesium and Serum Lipids in Dyslipidemia and Associated Disorders

Mg deficits may arise both from primary (insufficient intake, decreased absorption or elevated excretion) and secondary causes, e.g., disorders that accompany the advancement in age, several comorbidities (T2DM, MetS) or it can occur due to the use of certain medications such as loop diuretics [7]. In addition, particular attention should be given to the methods employed in the measurement of Mg concentrations. Barbagallo et al. (2014) demonstrated that, in elderly patients diagnosed with T2DM, serum ionized rather than total serum Mg may emerge as a superior predictor of the subclinical deficit of this micronutrient. In addition, they also detected that TG may be a confounding factor in the crosstalk between Mg levels and markers of glucose metabolism. For example, after multiple adjustments for TG, BMI, and glomerular filtration rate, the associations of serum total Mg with FPG and HbA1c, respectively, failed to reach statistical significance. However, serum-ionized Mg remained associated with these variables despite multiple adjustments [8]. Moreover, in their recent umbrella review of systematic reviews and meta-analyses of observational and intervention studies focused on the crosstalk between Mg concentrations and health outcomes, Veronese et al. (2019) evidenced that an elevated intake of this micronutrient can result in a reduction of the risk of both stroke and T2DM. However, Mg intake was not linked to any other cardiovascular endpoints based on their results [9].

The potential lipid-lowering effects of Mg warrant further investigation, with a myriad of studies linking the serum concentrations of this micronutrient to cardiometabolic disorders, e.g., obesity, T2DM, MetS, cardiovascular disorders, neurological ailments, and even cancer, all of which are worldwide public health threats [5][10][11]. Mg supplements stand out as one of the most popular supplements in Europe and the United States [12]. In particular, Mg orotate supplementation, due to the Mg-fixing capacity of this salt, has exerted health benefits [12][13]. For example, in an RCT, patients with heart failure who were prescribed Mg orotate had better 1-year survival versus subjects receiving placebo [13]. Similarly, patients diagnosed with concomitant heart failure and hypertension who were administered Mg orotate registered a decrease in both blood pressure and N-terminal (NT)-pro hormone BNP (NT-proBNP) [14].

In terms of Mg supplementation, the most reliable data included in our paper were obtained from 29 RCTs with a total number of 1724 subjects who received different forms of Mg supplementation for a period of time ranging from 4 to 24 weeks [15][16][17][18][19][20][21][22][23][24][25][26][27][28][29][30][31][32][33][34][35][36][37][38][39][40][41][42][43]. Overall, the vast majority of the analyzed RCTs reported no variations in HDL-C (n = 19), LDL-C (n = 16), TG (n = 17), TC (n = 14), TC/HDL-C (n = 4), VLDL (n = 2), or LDL-C/HDL-C (n = 1). However, some RCTs reported elevations of the HDL-C (n = 8), apoA1 (n = 1), or HDL-C/TG (n = 1), as well as reductions in LDL-C (n = 7), TC (n = 4), TG (n = 7), TC/HDL-C (n = 2), or VLDL (n = 3) in the participants exposed to the Mg intervention [15][16][17][18][19][20][21][22][23][24][25][26][27][28][29][30][31][32][33][34][35][36][37][38][39][40][41][42][43].

References

1. Lu, Y.; Wang, P.; Zhou, T.; Lu, J.; Spatz, E.S.; Nasir, K.; Jiang, L.; Krumholz, H.M. Comparison of Prevalence, Awareness, Treatment, and Control of Cardiovascular Risk Factors in China and the United States. J. Am. Heart Assoc. 2018, 7, e007462.
2. Epingeac, M.E.; Gaman, M.A.; Diaconu, C.C.; Gaman, A.M. Crosstalk between Oxidative Stress and Inflammation in Obesity. Rev. Chim. 2020, 71, 228–232.

3. Munteanu, M.A.; Gheorghe, G.; Stanescu, A.M.A.; Bratu, O.G.; Diaconu, C.C. What Is New Regarding the Treatment of Dyslipidemia in the 2019 European Society of Cardiology Guidelines? Arch. Balk. Med. Union 2019, 54, 749–752.
4. Orlova, S.; Dikke, G.; Pickering, G.; Konchits, S.; Starostin, K.; Bevz, A. Magnesium Deficiency Questionnaire: A New Non-Invasive Magnesium Deficiency Screening Tool Developed Using Real-World Data from Four Observational Studies. Nutrients 2020, 12, 2062.
5. Piuri, G.; Zocchi, M.; Della Porta, M.; Ficara, V.; Manoni, M.; Zuccotti, G.V.; Pinotti, L.; Maier, J.A.; Cazzola, R. Magnesium in Obesity, Metabolic Syndrome, and Type 2 Diabetes. Nutrients 2021, 13, 320.
6. Rosanoff, A.; Costello, R.B.; Johnson, G.H. Effectively Prescribing Oral Magnesium Therapy for Hypertension: A Categorized Systematic Review of 49 Clinical Trials. Nutrients 2021, 13, 195.
7. Barbagallo, M.; Veronese, N.; Dominguez, L.J. Magnesium in Aging, Health and Diseases. Nutrients 2021, 13, 463.
8. Barbagallo, M.; Di Bella, G.; Brucato, V.; D’Angelo, D.; Damiani, P.; Monteverde, A.; Belvedere, M.; Dominguez, L.J. Serum Ionized Magnesium in Diabetic Older Persons. Metabolism 2014, 63, 502–509.
9. Veronese, N.; Demurtas, J.; Pesolillo, G.; Celotto, S.; Barnini, T.; Calusi, G.; Caruso, M.G.; Notarnicola, M.; Reddavide, R.; Stubbs, B.; et al. Magnesium and Health Outcomes: An Umbrella Review of Systematic Reviews and Meta-Analyses of Observational and Intervention Studies. Eur. J. Nutr. 2020, 59, 263–272.
10. Fiorentini, D.; Cappadone, C.; Farruggia, G.; Prata, C. Magnesium: Biochemistry, Nutrition, Detection, and Social Impact of Diseases Linked to Its Deficiency. Nutrients 2021, 13, 1136.
11. Găman, M.-A.; Cozma, M.-A.; Dobrică, E.-C.; Bacalbașa, N.; Bratu, O.G.; Diaconu, C.C. Dyslipidemia: A Trigger for Coronary Heart Disease in Romanian Patients with Diabetes. Metabolites 2020, 10, 195.
12. Frank, J.; Kisters, K.; Stirban, O.A.; Obeid, R.; Lorkowski, S.; Wallert, M.; Egert, S.; Podszun, M.C.; Eckert, G.P.; Pettersen, J.A.; et al. The Role of Biofactors in the Prevention and Treatment of Age-Related Diseases. Biofactors 2021.
13. Stepura, O.B.; Martynow, A.I. Magnesium Orotate in Severe Congestive Heart Failure (MACH). Int. J. Cardiol. 2009, 131, 293–295.
14. Kisters, K.; Gremmler, B.; Gröber, U. Magnesium deficiency in hypertensive heart disease. J. Hypertens. 2015, 33, e273.
15. Itoh, K.; Kawasaka, T.; Nakamura, M. The Effects of High Oral Magnesium Supplementation on Blood Pressure, Serum Lipids and Related Variables in Apparently Healthy Japanese Subjects.

Br. J. Nutr. 1997, 78, 737–750.

16. Marken, P.A.; Weart, C.W.; Carson, D.S.; Gums, J.G.; Lopes-Virella, M.F. Effects of Magnesium Oxide on the Lipid Profile of Healthy Volunteers. Atherosclerosis 1989, 77, 37–42.
17. Aslanabadi, N.; Habibi Asl, B.; Bakhshalizadeh, B.; Ghaderi, F.; Nemati, M. Hypolipidemic Activity of a Natural Mineral Water Rich in Calcium, Magnesium, and Bicarbonate in Hyperlipidemic Adults. Adv. Pharm. Bull. 2014, 4, 303–307.
18. Rodríguez-Moran, M.; Guerrero-Romero, F. Oral Magnesium Supplementation Improves the Metabolic Profile of Metabolically Obese, Normal-Weight Individuals: A Randomized Double-Blind Placebo-Controlled Trial. Arch. Med. Res. 2014, 45, 388–393.
19. Joris, P.J.; Plat, J.; Bakker, S.J.L.; Mensink, R.P. Effects of Long-Term Magnesium Supplementation on Endothelial Function and Cardiometabolic Risk Markers: A Randomized Controlled Trial in Overweight/Obese Adults. Sci. Rep. 2017, 7, 106.
20. Solati, M.; Kazemi, L.; Shahabi Majd, N.; Keshavarz, M.; Pouladian, N.; Soltani, N. Oral Herbal Supplement Containing Magnesium Sulfate Improve Metabolic Control and Insulin Resistance in Non-Diabetic Overweight Patients: A Randomized Double Blind Clinical Trial. Med. J. Islam. Repub. Iran 2019, 33, 2.
21. Jamilian, M.; Sabzevar, N.K.; Asemi, Z. The Effect of Magnesium and Vitamin E Co-Supplementation on Glycemic Control and Markers of Cardio-Metabolic Risk in Women with Polycystic Ovary Syndrome: A Randomized, Double-Blind, Placebo-Controlled Trial. Horm. Metab. Res. 2019, 51, 100–105.
22. Jamilian, M.; Maktabi, M.; Asemi, Z. A Trial on the Effects of Magnesium-Zinc-Calcium-Vitamin D Co-Supplementation on Glycemic Control and Markers of Cardio-Metabolic Risk in Women with Polycystic Ovary Syndrome. Arch. Iran. Med. 2017, 20, 640–645.
23. Karandish, M.; Tamimi, M.; Shayesteh, A.A.; Haghighizadeh, M.H.; Jalali, M.T. The Effect of Magnesium Supplementation and Weight Loss on Liver Enzymes in Patients with Nonalcoholic Fatty Liver Disease. J. Res. Med. Sci. 2013, 18, 573–579.
24. Lima de Souza, E.; Silva, M.d.L.; Cruz, T.; Rodrigues, L.E.; Ladeia, A.M.; Bomfim, O.; Olivieri, L.; Melo, J.; Correia, R.; Porto, M.; et al. Magnesium Replacement Does Not Improve Insulin Resistance in Patients with Metabolic Syndrome: A 12-Week Randomized Double-Blind Study. J. Clin. Med. Res. 2014, 6, 456–462.
25. Hamedifard, Z.; Farrokhian, A.; Reiner, Ž.; Bahmani, F.; Asemi, Z.; Ghotbi, M.; Taghizadeh, M. The Effects of Combined Magnesium and Zinc Supplementation on Metabolic Status in Patients with Type 2 Diabetes Mellitus and Coronary Heart Disease. Lipids Health Dis. 2020, 19, 112.
26. Rashvand, S.; Mobasseri, M.; Tarighat-Esfanjani, A. Effects of Choline and Magnesium Concurrent Supplementation on Coagulation and Lipid Profile in Patients with Type 2 Diabetes

Mellitus: A Pilot Clinical Trial. Biol. Trace Elem. Res. 2020, 194, 328–335.

27. Whitfield, P.; Parry-Strong, A.; Walsh, E.; Weatherall, M.; Krebs, J.D. The Effect of a Cinnamon-, Chromium- and Magnesium-Formulated Honey on Glycaemic Control, Weight Loss and Lipid Parameters in Type 2 Diabetes: An Open-Label Cross-over Randomised Controlled Trial. Eur. J. Nutr. 2016, 55, 1123–1131.
28. Ham, J.Y.; Shon, Y.H. Natural Magnesium-Enriched Deep-Sea Water Improves Insulin Resistance and the Lipid Profile of Prediabetic Adults: A Randomized, Double-Blinded Crossover Trial. Nutrients 2020, 12, 515.
29. Cosaro, E.; Bonafini, S.; Montagnana, M.; Danese, E.; Trettene, M.S.; Minuz, P.; Delva, P.; Fava, C. Effects of Magnesium Supplements on Blood Pressure, Endothelial Function and Metabolic Parameters in Healthy Young Men with a Family History of Metabolic Syndrome. Nutr. Metab. Cardiovasc. Dis. 2014, 24, 1213–1220.
30. Asemi, Z.; Karamali, M.; Jamilian, M.; Foroozanfard, F.; Bahmani, F.; Heidarzadeh, Z.; Benisi-Kohansal, S.; Surkan, P.J.; Esmaillzadeh, A. Magnesium Supplementation Affects Metabolic Status and Pregnancy Outcomes in Gestational Diabetes: A Randomized, Double-Blind, Placebo-Controlled Trial. Am. J. Clin. Nutr. 2015, 102, 222–229.
31. Navarrete-Cortes, A.; Ble-Castillo, J.L.; Guerrero-Romero, F.; Cordova-Uscanga, R.; Juárez-Rojop, I.E.; Aguilar-Mariscal, H.; Tovilla-Zarate, C.A.; Lopez-Guevara, M.D.R. No Effect of Magnesium Supplementation on Metabolic Control and Insulin Sensitivity in Type 2 Diabetic Patients with Normomagnesemia. Magnes. Res. 2014, 27, 48–56.
32. Guerrero-Romero, F.; Simental-Mendía, L.E.; Hernández-Ronquillo, G.; Rodriguez-Morán, M. Oral Magnesium Supplementation Improves Glycaemic Status in Subjects with Prediabetes and Hypomagnesaemia: A Double-Blind Placebo-Controlled Randomized Trial. Diabetes Metab. 2015, 41, 202–207.
33. Solati, M.; Ouspid, E.; Hosseini, S.; Soltani, N.; Keshavarz, M.; Dehghani, M. Oral Magnesium Supplementation in Type II Diabetic Patients. Med. J. Islam. Repub. Iran 2014, 28, 67.
34. de Valk, H.W.; Verkaaik, R.; van Rijn, H.J.; Geerdink, R.A.; Struyvenberg, A. Oral Magnesium Supplementation in Insulin-Requiring Type 2 Diabetic Patients. Diabet. Med. 1998, 15, 503–507.
35. Talari, H.R.; Zakizade, M.; Soleimani, A.; Bahmani, F.; Ghaderi, A.; Mirhosseini, N.; Eslahi, M.; Babadi, M.; Mansournia, M.A.; Asemi, Z. Effects of Magnesium Supplementation on Carotid Intima-Media Thickness and Metabolic Profiles in Diabetic Haemodialysis Patients: A Randomised, Double-Blind, Placebo-Controlled Trial. Br. J. Nutr. 2019, 121, 809–817.
36. Afzali, H.; Jafari Kashi, A.H.; Momen-Heravi, M.; Razzaghi, R.; Amirani, E.; Bahmani, F.; Gilasi, H.R.; Asemi, Z. The Effects of Magnesium and Vitamin E Co-Supplementation on Wound Healing

and Metabolic Status in Patients with Diabetic Foot Ulcer: A Randomized, Double-Blind, Placebo-Controlled Trial: Supplementation and Diabetic Foot. Wound Repair Regen. 2019, 27, 277–284.

37. Karamali, M.; Bahramimoghadam, S.; Sharifzadeh, F.; Asemi, Z. Magnesium–Zinc–Calcium–Vitamin D Co-Supplementation Improves Glycemic Control and Markers of Cardiometabolic Risk in Gestational Diabetes: A Randomized, Double-Blind, Placebo-Controlled Trial. Appl. Physiol. Nutr. Metab. 2018, 43, 565–570.
38. Sadeghian, M.; Azadbakht, L.; Khalili, N.; Mortazavi, M.; Esmaillzadeh, A. Oral Magnesium Supplementation Improved Lipid Profile but Increased Insulin Resistance in Patients with Diabetic Nephropathy: A Double-Blind Randomized Controlled Clinical Trial. Biol. Trace Elem. Res. 2020, 193, 23–35.
39. Farshidi, H.; Sobhani, A.R.; Eslami, M.; Azarkish, F.; Eftekhar, E.; Keshavarz, M.; Soltani, N. Magnesium Sulfate Administration in Moderate Coronary Artery Disease Patients Improves Atherosclerotic Risk Factors: A Double-Blind Clinical Trial Study. J. Cardiovasc. Pharmacol. 2020, 76, 321–328.
40. Zemel, P.C.; Zemel, M.B.; Urberg, M.; Douglas, F.L.; Geiser, R.; Sowers, J.R. Metabolic and Hemodynamic Effects of Magnesium Supplementation in Patients with Essential Hypertension. Am. J. Clin. Nutr. 1990, 51, 665–669.
41. Guerrero-Romero, F.; Rodríguez-Morán, M. The Effect of Lowering Blood Pressure by Magnesium Supplementation in Diabetic Hypertensive Adults with Low Serum Magnesium Levels: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial. J. Hum. Hypertens. 2009, 23, 245–251.
42. Cunha, A.R.; D’El-Rei, J.; Medeiros, F.; Umbelino, B.; Oigman, W.; Touyz, R.M.; Neves, M.F. Oral Magnesium Supplementation Improves Endothelial Function and Attenuates Subclinical Atherosclerosis in Thiazide-Treated Hypertensive Women. J. Hypertens. 2017, 35, 89–97.
43. Mortazavi, M.; Moeinzadeh, F.; Saadatnia, M.; Shahidi, S.; McGee, J.C.; Minagar, A. Effect of Magnesium Supplementation on Carotid Intima-Media Thickness and Flow-Mediated Dilatation among Hemodialysis Patients: A Double-Blind, Randomized, Placebo-Controlled Trial. Eur. Neurol. 2013, 69, 309–316.