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# **Increase In Levels Of Cholesterol Joined To Low Density Lipoproteins Due To The Consumption Of Ketogenic Diets**

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#### Abstract:

Ketogenic diets are characterized by high fat intake and drastic carbohydrate restriction, in recent years they have become one of the most popular weight loss diets worldwide, and are also used for the treatment of multiple chronic diseases. Despite its beneficial effects, approximately 10% of patients present some type of adverse effect, among which the alteration in lipid metabolism stands out, being evidenced in several studies that show that the implementation of this type of diets it may at some point raise total serum cholesterol and low-density lipoprotein (LDL) cholesterol, a factor associated with an increased risk of stroke.

#### Keywords: Ketogenic, diet, lipoproteins

### Introduction:

The ketogenic diet (DC) or also called Keto diet, has been used as a therapeutic measure since the beginning of the 20th century, this being a special and strict eating plan characterized by a very low-carbohydrate and high-fat diet (LCHF), whose objective is to generate a state of ketosis similar to fasting, due to this it is very effective as anticonvulsant therapy in patients with epilepsy, and also in the treatment of diseases such as Parkinson's, Alzheimer's, traumatic brain injury and amyotrophic lateral sclerosis. [1, 2]

It is important to note that there are four types of DC, and the proportions of the nutrients vary between them, the classic, the medium chain triglycerides, the modified Atkins and the low glycemic index. On the one hand, the classic or traditional ketogenic diet is not a balanced diet, it contains a fixed ratio between grams of fat (it will always be higher), grams of carbohydrates

and proteins; the most used ratios are 4: 1 and 3: 1, the first one indicates that for a total of 5 grams, 4 are fat and the remaining gram can be protein or carbohydrate or a combination of both, that is, 90% of the calories come from fat; and when the ratio is 3: 1, the caloric intake of fat is 87% and the remaining 13% corresponds to proteins and carbohydrates. The DC of medium chain triglycerides, medium chain triglyceride oil is used to provide around half of the caloric intake, which is why a lower amount of fat is required in the diet, which allows a greater intake of protein and carbohydrates and, therefore, a greater variety of foods. On the other hand, the Atkins ketogenic diet was modified, it allows to administer between 10 and 20 grams of carbohydrates daily, the consumption of fat is stimulated. It is easier to use, since it does not require weighing all the foods to be consumed and provides greater amounts of protein, it is not balanced and therefore it is important to supplement with vitamin supplements. Finally, low-glycemic DC, which is low in carbohydrates, restricting its intake to 40 to 60 grams per day, and includes foods with a glycemic index less than 50, is easy to implement and does not require ongoing nutritional monitoring. [3,4]

The LCHF diet establishes a state of glucose deficiency, this being the main energy source, having little availability of this, the body is forced to create another source of energy, this from a process called gluconeogenesis that is nothing more than the synthesis of glucose from precursors that are not carbohydrates, in this case the gluconeogenic precursor of attention is fatty acids (FA). [5,6] In the liver, fat is transformed into fatty acids, so that later ketone bodies are formed from it, thus replacing glucose as the main source of energy. [7,8]

#### Physiology

Usually energy is obtained from glucose through glycolysis, producing acetyl coenzyme A (CoA), which I know condenses with oxaloacetate in the Krebs

cycle, resulting in electrons that will later be used in the electron transport chain to produce adenosine triphosphates (ATP). On the other hand we have the case of DC where the main molecule is the fatty acids which are metabolized through lipolysis, thanks to the beta-oxidation given in the liver the FAs are transformed into ketone bodies (CC), said metabolites later they are used as energy precursors to produce ATP. [9,10] The LCHF regimen recreates the metabolic conditions that occur during fasting, forcing the body to metabolize AG as an energy source (Figure 1).



Figure 1. Diagram of carbohydrate metabolism compared to fatty acid metabolism. In both metabolic pathways ATP is produced.

Keto flu symptoms
Drowsiness
Fatigue
Dizziness
Nausea and vomiting
Hypoglycemia
Abdominal pain
Dyspnoea

The body normally reaches the condition of ketosis within 4 to 5 days after starting the diet. [11,12] This dietary transition is usually followed by include drowsiness, fatigue, concentration problems, nausea, abdominal pain, and a few others; The effects of the keto flu usually subside during the first few weeks, and this is when the body begins to lose faquickly. [13,14]

#### Table 1. Most common symptoms of "keto flu"

Nowadays DC has gained a lot of popularity in patients with obesity, diabetes and also in the healthy young community; Despite its beneficial effects, studies determine that the frequent and high intake of saturated fatty acids and the low consumption of dietary fiber characteristic of this diet favor the increase in lowdensity lipoprotein (LDL) cholesterol, a factor of risk of coronary heart disease. [15,16]

CD is a safe and reliable treatment, but approximately 10% of patients who use it have some type of adverse effect, either short-term (Table 1) or long-term (Table 2). [17,18] Hypercholesterolemia occurs in more than 50% of the people who use DC, this can manifest itself at some point in said diet, this is because ketogenic diets are rich in fat, it is important to rigorously follow the serum lipids of the patients who consume them, since an elevation in fasting values of serum cholesterol, triglycerides and low-density lipoproteins (LDL), and a decrease in high-density lipoproteins (HDL) are commonly seen during the first year of implementation of the diet, but they tend to normalize after this time. [19,20]

Long-term adverse effects
Abnormalities in lipid metabolism
Mineral deficiencies
Cardiomyopathies
Hypoproteinemia
Severe hepatic steatosis
Nephrolithiasis

# Table 2. Most common long-term adverse effects ofthe ketogenic diet

However, there are cases where there may be a previous dyslipidaemia, severe deficiency or that does not present a positive evolution, genetic factors, nutrient deficiency, associated medication or other treatments, which may influence the ketogenic process of the diet. [21,22] there have been studies that have yielded contradictory results related to the probable vascular damage from the LCHF regimen, in patients who participated in the treatment with DC, an increase in the stiffness in the wall of the arteries was evidenced, participating as a an early marker in the detection of damage to the vasculature, in addition to the early appearance of the disturbance of arterial compliance, which can be reversed and is not very relevant after 24 months of treatment with DC. [23,24]

#### Discussion

The purpose of this review is to correlate an increase in low-density lipoprotein cholesterol levels due to the consumption of ketogenic diets.In the reviewed literature, several studies were found that establish such a relationship; moreover, there was a particular study by Jonas Burén et al., entitled "A Ketogenic Low-Carbohydrate High-Fat Diet Increases LDL Cholesterol in Healthy, Young, Normal-Weight Women: A Randomized Controlled Feeding Trial", where a sample of 24 female people was taken and assigned a DC for 4 weeks (this regimen consisted of 4% carbohydrates; 77% fat; 19% protein), then continued with a control diet proposed by the National Food Agency which also lasted 4 weeks (this is based on an intake of 44% carbohydrates; 33% fat; 19% protein), or the reverse sequence thanks to the crossover design it has. Between the treatment phases, a 15-week washing season was incorporated. Of the 24 women who started the study, only 17 finished it, the variables were studied using mixed models. The results concluded that the ingestion of LCHF stimulated the

increase of cholesterol bound to low-density lipoproteins.

Additionally, there is a case report by Nicholas Norwitz and Vyvyane Loh entitled "A Standard Lipid Panel Is Insufficient for the Care of a Patient on a High-Fat, Low-Carbohydrate Ketogenic Diet", which explains about a A male patient who received the ketogenic diet therapeutically to manage ulcerative colitis, he achieved a cure, but also had alterations in his serum lipid profile (increased LDL) associated with CD.

On the other hand, articles were also reviewed in which no relationship with the increase in the levels of cholesterol linked to low-density lipoproteins due to the consumption of ketogenic diets was highlighted, on the contrary, they suggest that DC generates a modification of serum lipid parameters but in a positive way, considered a cardioprotective. Likewise, other studies determine that in the first months of LCHF intake, an increase in LDL cholesterol is evidenced, but this normalizes after a few months.

## Conclusion

The ketogenic diet is effective for weight loss and for therapeutic uses in various pathologies, but there are studies that establish that it carries with it worrisome metabolic alterations, such as an increase in LDL cholesterol, which is associated with a high risk of stroke , but many literatures describe the opposite. Following the above, it is prudent to say that there is controversy in the scientific community because a convincing conclusion regarding the safety, tolerance and long-term effects of such a regimen has not yet been reached.

# References

 Dashti, H. M., Al-Zaid, N. S., Mathew, T. C., Al-Mousawi, M., Talib, H., Asfar, S. K., & Behbahani, A. I. (2006). Long Term Effects of Ketogenic Diet in Obese Subjects with High Cholesterol Level. *Molecular and Cellular Biochemistry*, 286(1–2), 1–9. https://doi.org/10.1007/s11010-005-9001-x

- Pedrón, C. (2021). Manual para la práctica de la dieta cetogénica. 2a edición / SEGHNP: Sociedad Española de Gastroenterología, Hepatología y Nutrición Pediátrica. seghnp. https://www.seghnp.org/documentos/manualpara-practica-de-dieta-cetogenica-2a-edicion
- Alharbi, A., & Al-Sowayan, N. S. (2020). The Effect of Ketogenic-Diet on Health. Food and Nutrition Sciences, 11(04), 301–313. https://doi.org/10.4236/fns.2020.114022
- Lloreda, P. S. (2021). Dietas cetogénicas y su papel en la nutrición clínica / Medicina. Revista Medicina. Vol 43 Núm 2. https://revistamedicina.net/ojsanm/index.php/Med icina/article/view/1607
- Gutiérrez, C. P. (2013). Dietas cetogénicas en el tratamiento del sobrepeso y la obesidad. Dialnet. https://dialnet.unirioja.es/servlet/articulo?codigo= 4399952
- Prabhakar, A., Quach, A., Zhang, H., Terrera, M., Jackemeyer, D., Xian, X., Tsow, F., Tao, N., & Forzani, E. S. (2015). Acetone as biomarker for ketosis buildup capability - a study in healthy individuals under combined high fat and starvation diets. *Nutrition Journal*, 14(1). https://doi.org/10.1186/s12937-015-0028-x
- Li, H., Ouyang, M., Zhang, P., Fei, L., & Hu, X. (2020). The efficacy and safety of a ketogenic diet for children with refractory epilepsy in China: a retrospective single-center cohort study. *Translational Pediatrics*, 9(4), 561–566. https://doi.org/10.21037/tp-20-219
- Feinman, R. D., Pogozelski, W. K., Astrup, A., Bernstein, R. K., Fine, E. J., Westman, E. C., Accurso, A., Frassetto, L., Gower, B. A.,

McFarlane, S. I., Nielsen, J. V., Krarup, T., Saslow, L., Roth, K. S., Vernon, M. C., Volek, J. S., Wilshire, G. B., Dahlqvist, A., Sundberg, R., . . . Worm, N. (2015). Dietary carbohydrate restriction as the first approach in diabetes management: Critical review and evidence base. *Nutrition*, *31*(1), 1–13. https://doi.org/10.1016/j.nut.2014.06.011

- Moreno-Sepúlveda, J., & Capponi, M. (2020). Dieta baja en carbohidratos y dieta cetogénica: impacto en enfermedades metabólicas y reproductivas. *Revista médica de Chile*, 148(11), 1630–1639. https://doi.org/10.4067/s0034-98872020001101630
- Vidali, S., Aminzadeh, S., Lambert, B., Rutherford, T., Sperl, W., Kofler, B., & Feichtinger, R. G. (2015). Mitochondria: The ketogenic diet—A metabolism-based therapy. *The International Journal of Biochemistry & Cell Biology*, 63, 55–59. https://doi.org/10.1016/j.biocel.2015.01.022
- 11. Dąbek, A., Wojtala, M., Pirola, L., & Balcerczyk, A. (2020). Modulation of Cellular Biochemistry, Epigenetics and Metabolomics by Ketone Bodies. Implications of the Ketogenic Diet in the Physiology of the Organism and Pathological States. *Nutrients*, *12*(3), 788. https://doi.org/10.3390/nu12030788
- Dupuis, N., Curatolo, N., Benoist, J. F., & Auvin, S. (2015). Ketogenic diet exhibits antiinflammatory properties. *Epilepsia*, 56(7), e95e98. https://doi.org/10.1111/epi.13038
- 13. Barona, J., & Fernandez, M. L. (2012). Dietary Cholesterol Affects Plasma Lipid Levels, the Intravascular Processing of Lipoproteins and Reverse Cholesterol Transport without Increasing the Risk for Heart Disease. *Nutrients*, 4(8), 1015– 1025. https://doi.org/10.3390/nu4081015
- 14. Pondel, N., Liśkiewicz, D., & Liśkiewicz, A. (2020). Dieta ketogeniczna mechanizm działania

i perspektywy zastosowania w terapii: dane z badań klinicznych. *Postępy Biochemii*. Published. https://doi.org/10.18388/pb.2020\_342

- Lüscher, T. F. (2020). 'The lower the better' revisited: the new lipid targets in high risk patients. *European Heart Journal*, 41(1), 1–3. https://doi.org/10.1093/eurheartj/ehz960
- 16. Laufs, U., Parhofer, K. G., Ginsberg, H. N., & Hegele, R. A. (2019). Clinical review on triglycerides. *European Heart Journal*, 41(1), 99– 109c. https://doi.org/10.1093/eurheartj/ehz785
- 17. Athinarayanan, S. J., Adams, R. N., Hallberg, S. J., McKenzie, A. L., Bhanpuri, N. H., Campbell, W. W., Volek, J. S., Phinney, S. D., & McCarter, J. P. (2019). Long-Term Effects of a Novel Continuous Remote Care Intervention Including Nutritional Ketosis for the Management of Type 2 Diabetes: A 2-Year Non-randomized Clinical Trial. *Frontiers in Endocrinology*, *10*. https://doi.org/10.3389/fendo.2019.00348
- Burén, J., Ericsson, M., Damasceno, N. R. T., & Sjödin, A. (2021). A Ketogenic Low-Carbohydrate High-Fat Diet Increases LDL Cholesterol in Healthy, Young, Normal-Weight Women: A Randomized Controlled Feeding Trial. *Nutrients*, *13*(3), 814. https://doi.org/10.3390/nu13030814.
- 19. Kapourchali, F. R., Surendiran, G., Goulet, A., & Moghadasian, M. H. (2015). The Role of Dietary Cholesterol in Lipoprotein Metabolism and Related Metabolic Abnormalities: A Mini-review. *Critical Reviews in Food Science and Nutrition*, 56(14), 2408–2415. https://doi.org/10.1080/10408398.2013.842887
- 20. Papotti, B., Escolà-Gil, J. C., Julve, J., Potì, F., & Zanotti, I. (2021). Impact of Dietary Lipids on the Reverse Cholesterol Transport: What We Learned from Animal Studies. *Nutrients*, *13*(8), 2643. https://doi.org/10.3390/nu13082643

- Armeno, M., Araujo, C., Sotomontesano, B., Caraballo. R. H. (2018). Actualización sobre los efectos adversos durante la terapia con dieta cetogénica en la epilepsia refractaria pediátrica. Rev Neurol; 66: 193-200
- Burkitt, M. J. (2020). An overlooked danger of ketogenic diets: Making the case that ketone bodies induce vascular damage by the same mechanisms as glucose. *Nutrition*, 75-76, 110763. https://doi.org/10.1016/j.nut.2020.110763
- 23. Norwitz, N. G., & Loh, V. (2020). A Standard Lipid Panel Is Insufficient for the Care of a Patient on a High-Fat, Low-Carbohydrate Ketogenic Diet. *Frontiers in Medicine*, 7. https://doi.org/10.3389/fmed.2020.00097
- 24. Kuchkuntla, A. R., Shah, M., Velapati, S., Gershuni, V. M., Rajjo, T., Nanda, S., Hurt, R. T., & Mundi, M. S. (2019). Ketogenic Diet: An Endocrinologist Perspective. *Current Nutrition Reports*, 8(4), 402–410. https://doi.org/10.1007/s13668-019-00297-x
- 25. 2021 Viguera Editores S.L.U. (2014). *Consenso* nacional sobre dieta cetogénica : Neurología.com. https://www.neurologia.com/articulo/2014277
- 26. McDonald, T. J., & Cervenka, M. C. (2019). Lessons learned from recent clinical trials of

ketogenic diet therapies in adults. *Current Opinion in Clinical Nutrition & Metabolic Care*, 22(6), 418–424.

https://doi.org/10.1097/mco.000000000000596

- 27. Kosinski, C., & Jornayvaz, F. (2017). Effects of Ketogenic Diets on Cardiovascular Risk Factors: Evidence from Animal and Human Studies. *Nutrients*, 9(5), 517. https://doi.org/10.3390/nu9050517
- Hoogeveen, R. C., Gaubatz, J. W., Sun, W., Dodge, R. C., Crosby, J. R., Jiang, J., Couper, D., Virani, S. S., Kathiresan, S., Boerwinkle, E., & Ballantyne, C. M. (2014). Small Dense Low-Density Lipoprotein-Cholesterol Concentrations Predict Risk for Coronary Heart Disease. *Arteriosclerosis, Thrombosis, and Vascular Biology*, *34*(5), 1069– 1077. https://doi.org/10.1161/atvbaha.114.30328
- Rayner, J., D'Arcy, E., Ross, L. J., Hodge, A., & Schoenaker, D. A. (2020). Carbohydrate restriction in midlife is associated with higher risk of type 2 diabetes among Australian women: A cohort study. *Nutrition, Metabolism and Cardiovascular Diseases, 30*(3), 400–409. https://doi.org/10.1016/j.numecd.2019.11.001