International Journal of Medical Science and Clinical Research Studies

ISSN(print): 2767-8326, ISSN(online): 2767-8342

Volume 04 Issue 04 April 2024

Page No: 699-703

DOI: https://doi.org/10.47191/ijmscrs/v4-i04-16, Impact Factor: 7.949

Tendinopathies Associated with Statin Therapy in Patients with Dyslipidemia: Case Study

Denisse Eugenia Aguilar Domínguez*[1], Erika Palacios Rosas[1], Jorge Luis León Álvarez[2]

[1]Universidad de las Américas Puebla.

[2]Clinica Fixen

ABSTRACT

Statins are considered the initial and first-line treatment in cardiovascular and atherosclerotic diseases, characterized by inhibiting HMG-CoA reductase. Some adverse effects associated with these drugs are injuries to the tendon structure including tenosynovitis, tendon and tendon rupture.

The aim of this article is to evaluate the tendon structure by musculoskeletal ultrasound and to raise the question of whether chronic statin consumption in this patient with dyslipidemia is related to the appearance of tendinopathies.

Methodology A cross-sectional descriptive observational study was carried out, focused on the evaluation of the incidence of tendinopathies in patients who have been using statins chronically. A case study approach was used, analysing in detail a female patient selected according to the established inclusion and exclusion criteria.

The sample consisted of a patient who met the inclusion criteria: age between 45-60 years, chronic use of statins for more than 12 months, presentation of symptoms suggestive of tendinopathy.

Patients with a history of musculoskeletal diseases prior to the start of treatment were excluded, and anyone with arthritis, chronic septic inflammatory processes, athletes, young patients, and those who did not want to participate in the study and did not agree to give informed consent were excluded.

For data collection, 7 patients were selected, of which 1 only met the inclusion and acceptance criteria for the study, a clinical history was taken with exhaustive clinical evaluations of the selected patients, focused on the identification of tendinopathy symptoms and other possible risk factors, at the end a musculoskeletal ultrasound was carried out where possible tendon injuries were identified and characterized. evaluating tendon structure and its relationship to statin use. This methodology provides a detailed and structured approach to conducting research on the incidence of tendinopathies associated with statin use.

Results During the clinical evaluation of this patient, symptoms associated with tendinopathy of the long portion of the biceps brachii on the right side were identified. The results of the musculoskeletal ultrasound confirmed the alterations in the structure of the tendon, finding tenosynovitis, significant peritendinous effusion and microruptures of the long portion of the biceps brachii not only on the affected side, but also on the contralateral side, which was asymptomatic for tendon pathology. In addition, not only was the biceps tendon modified, micro ruptures in the supraspinatus tendon and subacromial bursitis were observed. This patient had been taking atorvastatin 20mg every 24 hours in the mornings for 9 years and was not attributed with any mechanism of overuse injury that triggered multiple tendinopathies at the rotator cuff level.

KEYWORDS: Statins, Tendinopathy, dyslipidemia.

ARTICLE DETAILS

Published On:
18 April 2024

Available on:
https://ijmscr.org/

INTRODUCTION

Statins are lipid-lowering drugs par excellence, they are considered the first-line treatment for atherosclerotic and cardiovascular diseases, and dyslipidemia is no exception.

Dyslipidemia is characterized by an elevation of total cholesterol (TC), low-density cholesterol (LDL-C), or triglycerides (TG) and a decrease in serum high-density cholesterol (HDL-C) levels. The prevalence of dyslipidemia can vary geographically, however, it has been estimated that more than 50% of the adult population worldwide has this condition. (Hedayatnia et al., 2020).

Statins have the mechanism of action to inhibit 3-Hydroxy-3-Methylglutaryl coenzyme A reductase, also known as HMG-CoA, which plays an important role in cholesterol production. These drugs are commonly used for the treatment of patients with dyslipidemia to prevent cardiovascular events such as CVD, acute myocardial infarction, and atherosclerotic processes. These drugs have been established as the first line of treatment in cardiovascular diseases, preventing, eliminating and reducing the formation of thrombotic and embolic plaques, however, they help us improve endothelial function and reduce the inflammatory activity produced by high cholesterol levels. (Jaschke, 2023).

Defining tendinopathy we can say that it is a spectrum of changes that lead to tendon disease and damage, it is characterized by abnormalities in the microstructure, composition and modifications of tendon cells. (Cook et al., 2017)

A normal tendon is composed mostly of collagen fibers with dispersed cells, mostly by tenocytes, aligned along the entire length path of the collagen fibers, however an altered or damaged tendon consists of the fragmentation of collagen fibers, the disorganization of collagen fibers, accumulation of glycosaminoglycans and an increase in microvascularity associated with neo-innervation, causing various changes in the material properties of the tendon, (Cook et al., 2017).

Statins are commonly used to lower blood cholesterol levels, which helps prevent cardiovascular disease. Although they are generally believed to be safe drugs, there is considered to be some toxicity to muscle tissue and even greater attention has been paid to the possible harmful effects on tendons, which often lead to tendinopathy or rupture. (Elliason, 2019, p.1).

It is important to mention that currently it has not been possible to establish a mechanism of action of statins on tendon cells, some in vitro case studies show that the extracellular matrix is reduced after treatment with statins, but surprisingly collagen levels are not altered.

CASE REPORT

Anamnesis

This is a 55-year-old female patient who comes to the rehabilitation clinic for manifesting pain in the right shoulder radiating in the anterior region of the shoulder, posterior region of the shoulder and scapular region with more than 6 months of evolution, the patient does not remember having any mechanism of injury that has led her to manifest any injury.

AHF: Mother with hypertension and mixed dyslipidemia, diabetic father, dyslipidemic, diabetes mellitus 2 and 2 thrombotic events that led to hemiplegia.

APP: Dyslipidemia diagnosed 9 years ago treated with atorvastatin and bezafibrate, patient with insulin resistance treated with metformin 850 mg by ISSSTEP doctors for 6 years and diagnosed with hypothyroidism for 5 years treated with levothyroxine sodium 100 mcg taking half a tablet daily on an empty stomach, rest denied.

A. surgical: two cesarean sections more than 20 years ago, complete hysterectomy in 2010 due to uterine myomatosis, release of the first extensor compartment due to tenosynovitis of Quevain.

APNP: A patient who has been teaching for 34 years, performs regular cardiovascular exercise approximately 5 times a week for 50 minutes at moderate intensity.

AGYO: Menarche at 10 years, regular cycles of 28x8, IVSA at 18 years, G6,A2,C4, two live births currently, LMP: does not remember it.

Physical Exam

Patient who reports pain in the right shoulder, which radiates to the anterior and lateral region of the shoulder, in addition to mentioning that it radiates to the scapular region of more than 6 months of evolution, predominantly nocturnal, reports that the pain is accompanied by burning in the anterior region of the shoulder and is located in the supraspinatus region. In the palmar region and in the lateral region of the right shoulder, he currently comments that he recurrently attends physical rehabilitation sessions where the muscles involved are treated, however he reports that the pain appears after 3 weeks.

Manual examination is performed to assess muscles and passive structures (ligaments and tendons) and the following results are obtained. The patient is asked to perform arcs of motion in which no limitation of 60° to 90° of shoulder flexion, abduction and adduction is observed. The patient is asked to perform abduction with resistance and at 60° she reports pain at the level of the middle and anterior deltoids that worsens with increasing ranges of motion, the pain decreases when resistance is removed.

Muscle exploration was performed for anterior deltoids, patient with normal ranges of motion, without pain, at resistance the patient manifested pain at counterresistance of 5/10 on the VAS scale.

A detailed examination of this muscle complex is performed with manual muscle examination, first the patient performs extension, abduction and internal rotation actively without pain, when resistance is applied, pain manifests in the posterior region of the shoulder. 4/10 EVA.

Physical examination of the middle deltoid was performed: arc of motion up to 90° without pain, the pain manifested when resistance is applied to the patient and reaches 60° of abduction.

Maneuver	Result
Speed Maneuver It is an exploratory maneuver for the tendon of the long portion of the biceps.	**Positive**
Yegarson's manoeuvre The bicipital region is evaluated and indicates involvement of the biceps tendon in its long portion or tendon sheath.	**Positive**
Jobe's Maneuver Assesses supraspinatus tendon injuries Weakness: rupture of the supraspinatus	**Negative**
Drop Arm Test Assesses supraspinatus muscle tears	**Negative**
Lift Off Sing It assesses the existence of tendinopathy or injury to the subscapularis.	**Negative.**
Test de Eiichoff It values the slippage of the first extensor compartment, it is positive when performing the flexion of the thumb.	**Positive**

A patient who was diagnosed with biceps brachii long tendinopathy underwent musculoskeletal ultrasound with a 7.5 MHz linear transducer musculoskeletal ultrasound, where the following were evident.

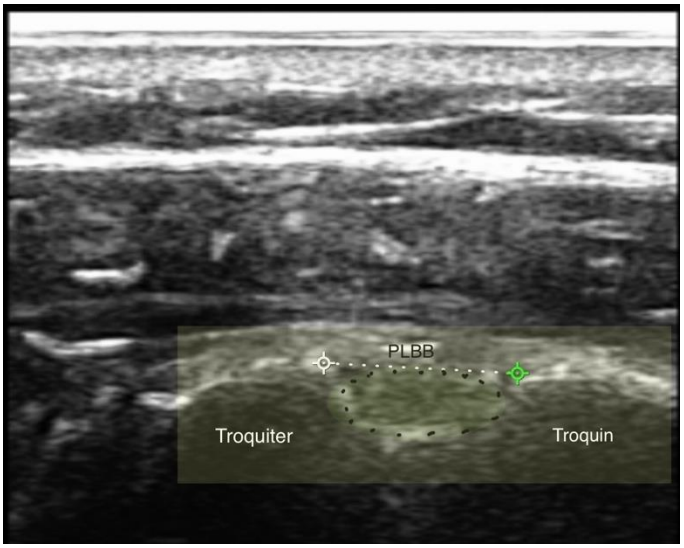

Figure 1. On the short axis, the tendon of the long portion of the biceps is evident, on the left side with the presence of synovitis.

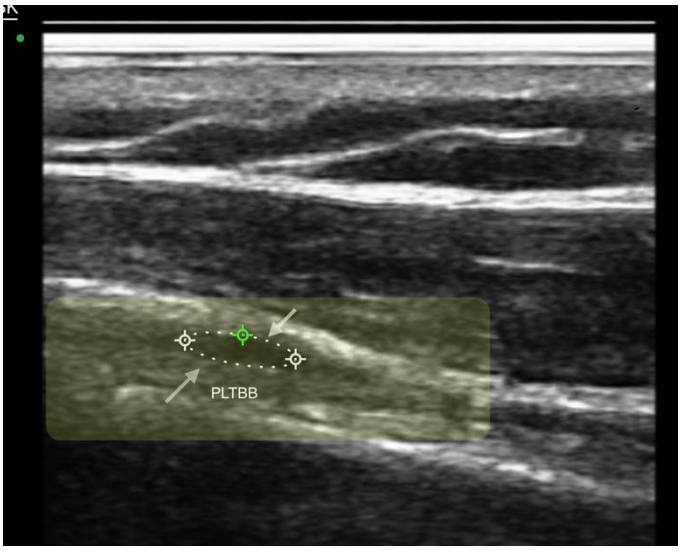

Figure 2. On the long axis, the tendon of the long portion of the biceps is evident, on the left side, with the presence of an anechoic zone suggestive of synovitis, with little relevance of peritendinous effusion.

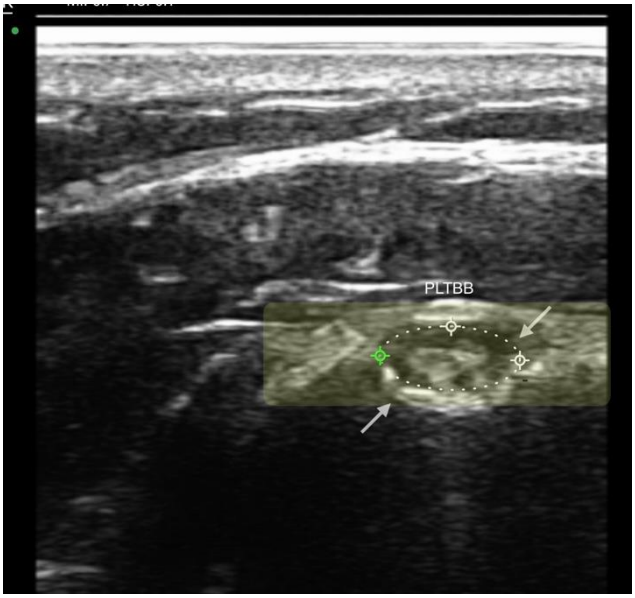

Figure 3. In the short axis of the musculoskeletal ultrasonography technique, the tendon of the long portion of the biceps on the right side was evidenced with the presence of an anechoic region suggestive of fluid in the synovial sheath and significant peritendinous effusion.

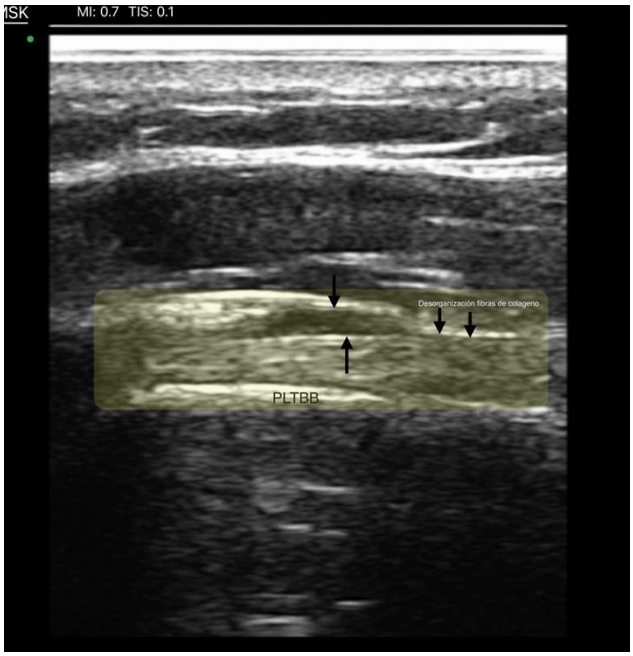

Figure 4. In the long axis of the musculoskeletal ultrasonography technique, the tendon of the long portion of the biceps on the right side is evidenced with the presence of an anechoic region suggestive of fluid in the synovial sheath, disorganization of the collagen fibers and microruptures in the area of tendon insertion.

DISCUSSION

Tendinopathy can be of multifactorial etiology since it can occur in active and inactive individuals, this pathology can be accompanied by pain, inflammation and loss of functionality of basic activities of daily living and even sports activities of people who suffer from it. Various studies used for this review article have suggested that several common side effects of statins can manifest as muscle weakness and pain, actually increasing the risk of tendinopathy, tendon rupture, and complications in the viscoelastic characteristics of the tendons.

However, in the study conducted by Chandog Jeon, entitled *Exploring the In Vivo Anti-Inflammatory Actions of Simvastatin-Loaded Porous Microspheres on Inflamed Tenocytes in a Collagenase-Induced Animal Model of Achilles Tendonitis,* he mentions that tendon ruptures and tendon injuries cause local inflammatory responses by inducing pro-inflammatory cells, these substances are responsible for generating inflammation that affects directly on the biomechanical properties of the tendon tissues. Based on the reports they obtained in their published studies, they suggest that statins already listed as inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase, have pleiotropic effects including anti-inflammatory, antioxidant, and immunomodulatory effects. The drug that gave an exponential result in their studies was simvastatin, as it may have a protective function in tendinopathies in patients with severe hyperlipidemia.

Statin treatment can also improve tendon healing, as well as improve the healing of various musculoskeletal structures through their angiogenic and osteogenic effects.

Not all the benefits of statins can be manifested in individuals who are on therapy with these drugs, according to the results of the research carried out by Wen Chung, Tung Yang, Li-pin and Cheng-Lung (2016), emphasize that simvastatin reduces the number of viable tendon cells, alters the tendon cell cycle in addition to altering the expression of kinase-dependent cyclins.

Several hypotheses could explain the relationship between the use of statins and tendon injury, although the exact cause is not yet known, it is believed that their effects may be suppressors on the metalloproteinase enzyme of the extracellular matrix of the tendon, this enzyme is present in the process of tissue remodeling where it is believed that when it does not perform its proper function it could cause the weakening or even rupture of the tendon.

CONCLUSION

Tendon complications attributed to statins are very rare considering the large number of prescriptions for these drugs. In cohort studies carried out by various authors, it has not been ruled out that the use of statins in dyslipidemic patients increases or enhances the inflammatory effect at the cellular level and that this has an impact on musculoskeletal tissue.

In conclusion, the study highlights the importance of active surveillance and careful evaluation of patients on statin therapy, especially in those with dyslipidemia. It is essential to note that while the exact mechanism behind this association is not yet fully elucidated, our results support the need for an individualized risk-benefit assessment when prescribing statins. To conclude the topic, more research is required to fully understand the relationship between statin use and tendinopathies, in order to improve clinical care and quality of life for patients.

REFERENCES

I. Bard, H. (2012). *Tendinopathies: etiopathogenesis, diagnosis and treatment*. CME Musculoskeletal System; 45(3):1-20 [Article E – 14-469]. Retrieved from: https://sci hub.se/https://doi.org/10.1016/S1286-935X(12)62764-6.

II. Bolon, B. (2017). Mini-Review: *Toxic Tendinopathy*. *Toxicologic Pathology*, *45*(7), 834-837. doi: 10.1177/0192623317711614. https://journals.sagepub.com/doi/10.1177/0192623317711614?url_ver=Z39.88-

2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed

III. Cook, J., Eboni, R., Purdam, C., & Ortega-Cebrian, S. (2017). The Continuum of Tendon Pathology: Current Concept and Clinical Implications. *Apunts Med Esport*, *52*, 63,64,65. doi: doi.org/10.1016/j.apunts.2017.05.002. Retrieved from: https://www.apunts.org/en-pdf X0213371717613161

IV. Delgado, L., Alvarez, B., De la Cruz, J., & Ramirez S, A. (2012). Statin Rhabdomyolysis: A Fatal Case Report and Review of the Literature. *Mexican Journal of Cardiology*, *23*(1), 27-30. Retrieved from https://www.medigraphic.com/pdfs/cardio/h-2012/h121f.pdf

V. Eliasson, P., Dietrich-Zagonel, F., Lundin, A., Aspenberg, P., Wolk, A., & Michaëlsson,

VI. K. (2019). *Statin treatment increases the clinical risk of tendinopathy through matrix*

VII. *metalloproteinase release – a cohort study design combined with an experimental study*. *Scientific Reports*, *9*(1). doi: 10.1038/s41598-019-53238-7. https://pubmed.ncbi.nlm.nih.gov/31784541/

VIII. Goodman & Gilman 1906-, Blengio Pinto, J., Rivera Muñoz, B., & Girolamo, G. (2007). *The pharmacological basis of therapeutics* (p. 780). Mexico: McGraw-Hill Interamericana.

IX. Guerra FR, V. (2013). Statin Therapy and Tendon Disorders. *Journal Of Glycomics & Lipidomics*, *03*(01). doi: 10.4172/2153-0637.1000e115. Retrieved from: Guillen, J.F. (2005). Terminology and classification of tendinopathies. Spanish Society of Sports Medicine. Retrieved from: http://www.femede.es

X. Jeong, C., Kim, S., Shim, K., Kim, H., Song, M., Park, K., & Song, H. (2018). *Exploring the In Vivo Anti-Inflammatory Actions of Simvastatin-Loaded Porous Microspheres on Inflamed Tenocytes in a Collagenase-Induced Animal Model of Achilles Tendinitis. International Journal Of Molecular Sciences*, *19*(3), 820. doi: 10.3390/ijms19030820. Hatps://vv.nakbi.nalam.nih.gov/pmc/articles/pmc5877681/pdf/ijms-19-00820.pdf

XI. Kaleağasıoğlu, F., Olcay, E., & Olgaç, V. (2015). Statin-induced calcific Achilles tendinopathy in rats: comparison of biomechanical and histopathological effects of simvastatin, atorvastatin and rosuvastatin. *Knee Surgery, Sports Traumatology, Arthroscopy*, *25*(6), 1884-1891. doi: 10.1007/s00167-015-3728-z. https://pubmed.ncbi.nlm.nih.gov/26275370/

XII. Knobloch, K. (2016). Drug-Induced Tendon Disorders. *Metabolic Influences on Risk For Tendon Disorders*, 229-238. doi: 10.1007/978-3-319-33943-6_22.

XIII. Liao, X., Falcon, N., Mohammed, A., Paterson, Y., Mayes, A., Guest, D., & Saeed, A. (2020). Synthesis and Formulation of Four-Arm PolyDMAEA-siRNA Polyplex for Transient Downregulation of Collagen Type III Gene Expression in TGF-β1 Stimulated Tenocyte Culture. *ACS Omega*, *5*(3), 1496-1505. doi: 10.1021/acsomega.9b03216 https://pubs.acs.org/doi/10.1021/acsomega.9b03216

XIV. Mennickent, S. (2008). *Pleiotropic effects of statins.* Medical journal of chile. (136), 775-782. https://scielo.conicyt.cl/pdf/rmc/v136n6/art14.pdf

XV. Muhammad, Z., Ahmad, T., & Baloch, N. (2019). Can alternate-day Statin regimen minimize its adverse effects on muscle and tendon? A systematic review. *J Pak Med Assoc*, *69*(07), 1006-1008. Retrieved from https://jpma.org.pk/PdfDownload/9237.

XVI. Ramos, P. (2015). From the concept of high-potency statins to the extralipidic effects of statins. *Spanish Journal of Cardiology Supplements*, *15*, 22-27. doi: 10.1016/s1131-3587(15)70121-4. Retrieved from: https://www.revespcardiol.org/es of-the-statin-concept-high-potency-article-S1131358715701214

XVII. Soslowsky, L., & Fryhofer, G. (2016). Tendon Homeostasis in Hypercholesterolemia. *Metabolic Influences On Risk For Tendon Disorders*, 151- 165. doi: 10.1007/978-3-319-33943-6_14. Recuperado de: https://link.springer.com/article/10.1007%2Fs11926-017-0704-2

XVIII. Tsai, W., Yu, T., Lin, L., Cheng, M., Chen, C., & Pang, J. (2015). *Prevention of Simvastatin Induced Inhibition of Tendon Cell Proliferation and Cell Cycle Progression by Geranylgeranyl Pyrophosphate. Toxicological Sciences*, *149*(2), 326-334. doi: 10.1093/toxsci/kfv239. Recuperado de: https://academic.oup.com/toxsci/article/149/2/326/2461515