Available online at www.medicinescience.org

ORIGINAL RESEARCH

Medicine Science International Medical Journal

Medicine Science 2019;8(2):260-2

Frequency of lysosomal acid lipase deficiency in patients with primary hyperlipidemia

Bahri Evren[1], Yılmaz Bilgic[2], Feyza Firat Atay[3], Ayse Nuransoy Cengiz[4], Yasir Furkan Cagin[2]

[1]Inonu Universty Faculty of Medicine, Department of Endocrinology Malatya Turkey
[2]Inonu Universty Faculty of Medicine, Department of Gastroenterology Malatya Turkey
[3]Kovancilar State Hospital, Clinic of Internal Medicine, Elazig Turkey
[4]Inonu Universty Faculty of Medicine, Department of Internal Medicine Malatya Turkey

Received 27 January 2019; Accepted 17 February 2019
Available online 10.05.2019 with doi:10.5455/medscience.2019.08.9025

Abstract
The aim of our study was to investigate the prevalence of LAL (lysosomal acid lipase) deficiency in patients with primary hyperlipidemia. Twenty-four patients with primary hyperlipidemia were included in the study. The gender, age, height, weight, body mass index and waist circumference of the patients were recorded. Lipid profiles, glucose, transaminases and LAL enzyme profiles were evaluated. LAL enzyme deficiency was not detected in patients with primary hyperlipidemia. In our study, when we investigated LAL deficiency in primary hyperlipidemic patients, we could not find a relationship between them. As a result of our study, LAL deficiency was not detected in patients with primary hyperlipidemia. However, in this context, there is a need to work with a large number of patients.

Keywords: Primary hyperlipidemia, lysosomal acid lipase deficiency

Introduction

Lysosome is a membrane-associated, acidic organelle found in animal-related cells. Its lead to the breakdown of biological macromolecules (mucopolysaccharides, sphingolipids, glycoproteins, triglycerides, cholesterol esters) which are produced both from the outside and within the cell by the acid hydrolases ıts contain [1]. Lysosomal storage diseases (LSD), which the lack of enzymes involved in the catabolism of macromolecules is a group of diseases caused by the defect of the transports that cause the lysis of the lysosomes to function out of the cell due to the accumulation of specific substrates. Clinical findings vary according to the substance stored. Because the accumulated molecules are highly heterogeneous, clinical presentations are also heterogeneous [2]. Lysosomal Acid Lipase (LAL) deficiency is a rare autosomal recessive, lysosomal lipid storage group. It is characterized by progressive cholesterol ester and triglyceride accumulation in liver, spleen and other organs (central system, gis …) [3].

***Coresponding Author:** Yilmaz Bilgiç, Inonu Universty, Faculty of Medicine Department of Endocrinology Malatya Turkey
E-mail: drybilgic1975@hotmail.com

Material and Methods

Twenty-four patients with primary hyperlipidemia who were admitted to the endocrinology and metabolism outpatient clinic of Inonu University between June 2016 and September 2017 and who were diagnosed with secondary hyperlipidemia such as type 2 diabetes mellitus, nephrotic syndrome, hypothyroidism and primary biliary cirrhosis were included in the study. The gender, age, height, weight, body mass index and waist circumference of the patients were recorded. Lipid profiles, glucose, transaminases and LAL enzyme profiles were evaluated. LAL enzyme deficiency was not detected in patients with primary hyperlipidemia. Exclusion criteria are given in the material method part of our study. LAL activity was measured by using Dried Blood Spot Test (DBS). The results are given in nanomol / punch / hour.

In our study, the mean + standard deviations of the data were given as statistical analysis. Since there was no LAL deficiency in our patients, no specific statistical method was used.

Results

When the laboratory and anthropometric results of the patients with primary hyperlipidemia were evaluated, the mean age was found to be 38.55 ± 10.7 years. The mean weight and body mass index of the patients were 72.42 ± 11.4 kg and 26.72 ± 5.2 kg

/ m2, respectively. The waist circumference of the patients was calculated without gender discrimination and the mean was 84.41 ± 12.8 in both sexes. For the exclusion of diabetes mellitus, a cause of secondary hyperlipidemia, fasting blood glucose was also included in our study and mean fasting glucose was measured as 86 ± 9.5 mg / dl. Liver enzymes were also studied to determine whether there was a high liver enzyme elevation in LAL deficiency. The mean AST 27 ± 7.2 UI / L and ALT 24 ± 6.3 UI / L were determined. In our study, mean blood lipids were 244 ± 54.2 mg / dl for total cholesterol, 121 ± 44.7 mg / dl for triglyceride, 51.4 ± 10.3 mg / dl for HDL cholesterol and 182 ± 39.4 mg / dl for LDL cholesterol (Table 1).

Table 1. Laboratory and anthropometric results of patients with primary hyperlipidemia

Parameters	Patients with primary hyperlipidemia (n = 24)
Age (years)	38.55 ± 10.7
Height (cm)	157.2 ± 6.1
Weight (kg)	72.42 ± 11.4
BMI (kg/m2)	26.72 ± 5.2
Waist circumference	84.41 ± 12.8
Glucose (mg/dl)	86 ± 9.5
AST	27 ± 7.2
ALT	24 ± 6.3
Total cholesterol (mg/dl)	244 ± 54.2
Triglyceride (mg/dl)	121 ± 44.7
HDL cholesterol (mg/dl)	51.4 ± 10.3
LDL cholesterol (mg/dl)	182 ± 39.4
LAL (nmol/punch/h.)	0.74 ± 0.68

Discussion

LAL is a rare lipid storage disease and its prevalence is approximately 1 / 40.000 depolama1 / 350.000 in newborns. Diagnostic images such as liver ultrasound and biopsy are important, which show changes in hepatic morphology such as microvescular steatosis with Kupffer cell involvement, fibrosis and cholesterol-ester-crystal accumulation. These findings should suggest LAL disease. Because the disease is manifested as idiopathic microvesicular hepatosteatosis disease [4]. As the disease progresses in patients with initially indeterminate complaints, some clinical symptoms, such as rough facial, skeletal dysplasia, and developmental delay, stimulate a lysosomal depot disorder. Different lysosomal storage disorders share common symptoms and symptoms [5]. LAL deficiency is a disease associated with progressive hepatic insufficiency accompanied by increased atherosclerosis, cardiovascular disease, hepatomegaly, and increased liver enzyme deficiency, with dyslipidemia frequently associated with. LAL deficiency in adults and children shows very different clinical features and heterogeneous course. While the age at onset may occur in late age as 44 years in men and 68 years in women, the mean age at which onset of symptoms is 5 years in both sexes [3]. Hepatomegaly is the most common clinical manifestation of lysosomal storage disease. High serum total cholesterol, LDL cholesterol, triglyceride high together with hepatomegaly are among the most characteristic findings [6]. Definitive diagnosis is the measurement of enzyme activity in leukocytes, cutaneous fibroblasts or dry blood samples from peripheral blood samples. The values below 0.03 (nmol / punch / h) in LAL activity were inadequate in LAL activity, values in the range of 0.03-0.15 (nmol / punch / hour) were defined as LAL activity at the border. The values between 0.15-0.37 (nmol / punch / hour) with highly reduced LAL activity, 0.37-0.50 (nmol / punch / hour) values are considered as LAL activity in the transition zone [7,8]. In the treatment, cholestyramine and statins can be given. Although hematopoietic stem cell transplantation is potentially curative in patients with LAL deficiency, it is often not a good option because it carries high risks, including fatal complications. The main treatment consists of the enzyme replacement sebelipase alfa, which was approved in 2015. Sebelipase alpha is a recombinant human lysosomal acid lipase that replaces incomplete LAL enzyme activity and thereby reduces hepatic fat content and elevated transaminases [9].

Conclusion

Lysosomal acid lipase deficiency; in patients with high LDL and / or low HDL levels, hepatomegaly and / or high transaminase levels without obesity or metabolic syndrome should be considered.

In our study, the use of lipid electrophoresis in the diagnosis of primary hyperlipidemia is one of the weaknesses of our study.

In our study, we could not find any relationship between these two diseases. As a result of our study, LAL deficiency was not detected in patients with primary hyperlipidemia. However, because the incidence of LAL deficiency is very low, large-volume clinical studies are needed to evaluate the frequency of patients with primary hyperlipidemia.

Competing interests
The authors declare that they have no competing interest.

Financial Disclosure
All authors declare no financial support.

Ethical approval
Ethics committee approval was obtained.

Bahri Evren ORCID: 0000-0001-7490-2937
Yılmaz Bilgic ORCID: 0000-0002-2169-5548
Feyza Firat Atay ORCID 0000-0002-2841-2985
Ayse Nuransoy Cengiz ORCID: 0000-0001-9133-8602
Yasir Furkan Cagin ORCID: 0000-0002-2538-857X

References

1. Zeynep Büşra Aksoy, Ege soydemir. Lizozomal aktivite. Güncel Gastroenteroloji. 2016;4:345-52.
2. Futerman AH, Van Meer G. The cell biology of lysosomal storage disorders. Nat Rev Mol Cell Biol. 2004;5:554-65.
3. Bernstein DL, Hulkova H, Bialer MG, et al. Cholesteryl ester storage disease: review of the findings in 135 reported patients with an underdiagnosed disease. J Hepatol. 2013;58:1230-43.
4. Botero V, Garcia VH, Gomez-Duarte C, et al. Lysosomal acid lipase deficiency, a rare pathology: The first pediatric patient reported in colombia. Am J Case Rep. 2018;19:669-72.
5. Andria, g. & parini, Lysosomal storage diseases early diagnosıs and new treatments edited by: rossella parini, generoso andriat. lysosomal storage d apa (american psychological assoc.). 2010.
6. Lipiński P, Ługowska A, Zakharova EY, et al. Diagnostic algorithm for cholesteryl ester storage disease: Clinical presentation in 19 Polish Patients. J Pediatr Gastroenterol Nutr. 2018;67:452-47.

7. Wierzbicka-Rucińska A, Jańczyk W, Ługowska A, et al. Diagnostic and therapeutic management of children with lysosomal acid lipase deficiency (LAL-D). Review of the literature and own experience. Dev Period Med. 2016;20:212-5.

8. Hamilton J, Jones I, Srivastava R, et al. A new method for the measurement of lysosomal acid lipase in dried blood spots using the inhibitor Lalistat 2. Clin Chim Acta. 2012;413:1207-10.

9. Canbay A, Müller MN, Philippou S, et al. Cholesteryl ester storage disease: fatal outcome without causal therapy in a female patient with the preventable sequelae of progressive liver disease after many years of mild symptoms. Am J Case Rep. 2018;19:577-81.