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Letter to the Editor

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Statin Intolerance in Familial Hypercholesterolemia

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To the Editor

Statin therapy is the gold standard for suppressing cardiovascular events in hypercholesterolemic patients. However, we often encounter patients with statin intolerance. Statin intolerance is understood as the inability to continue the statin therapy, due to the development of symptoms or laboratory abnormalities attributable to the initiation or dose escalation of statin [1]. Muscle symptoms are the most commonly observed adverse effect of statin.

Familial hypercholesterolemia (FH) is characterized by severely elevated low-density lipoprotein-cholesterol (LDL-C) levels. Several mutations in genes have been noted in patients with FH: LDL receptor (most common), apolipoprotein B, proprotein convertase subtilin/kexin 9 (PCSK9) and LDL receptor adaptor protein [2]. The prevalence of the heterozygous state has been estimated at 1 in 200 to 1 in 500 and of the homozygous state from 1 in 160,000 to 1 in 1,000,000. FH is common in individuals who had coronary artery disease (CAD) such as myocardial infarction at young age [3]. Therefore, more aggressive cholesterol lowering therapy is required to prevent CAD in FH patients.

In a previous study that analyzed the clinical influence of statins on age at the first clinical onset of CAD in 329 FH patients, the age at onset of CAD in patients on statins at onset was significantly higher than that in patients not on statins by more than 10 years old, suggesting that statins have improved the clinical course of patients with heterozygous FH [4]. In the study which examined possible statin intolerance by using the Japan Medical Data Center database, 10% had possible statin intolerance [5].

Since heterozygous FH is a common inherited metabolic disorder and statin intolerance is also a common medical condition, we are likely to encounter heterozygous FH patients with statin intolerance. What should we do if we encounter such patients? We think that the advent of PCSK9 inhibitors is a gospel for such patients. PCSK9 plays a critical role controlling serum LDL-C levels. Several gain-of-function and loss-of-function mutations in the PCSK9 gene, which occur naturally, have been identified and linked to hypercholesterolemia and hypocholesterolemia, respectively [6]. PCSK9 acts mainly by enhancing degradation of LDL receptor protein in the liver [6]. Inactivation of PCSK9 in mice reduces plasma cholesterol levels primarily by increasing hepatic expression of LDL receptor protein and thereby accelerating clearance of circulating LDL-C.

We experienced a heterozygous FH patient with statin intolerance. This patient showed myalgia and elevation of creatine phosphokinase (CPK) by using atorvastatin and rosuvastatin, and gave up the statin therapy and started to use PCSK9 inhibitor. The monotherapy of PCSK9 inhibitor reduced serum LDL-C from 235 to 80 mg/dL and did not induce myalgia and elevation of CPK.

In conclusion, PCSK9 inhibitor is a promising therapeutic option for heterozygous FH patients with statin intolerance.

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Conflict of Interest

The authors declare that they have no conflict of interest concerning this article.

Informed Consent

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Author Contributions

HK collected data. HY wrote the paper. Both authors read and approved the final paper.

Data Availability

Any inquiries regarding supporting data availability of this

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References

1. Algharably EA, Filler I, Rosenfeld S, Grabowski K, Kreutz R. Statin intolerance - a question of definition. Expert Opin Drug Saf. 2017;16(1):55-63.
2. Singh S, Bittner V. Familial hypercholesterolemia - epidemiology, diagnosis, and screening. Curr Atheroscler Rep. 2015;17(2):482.
3. Santos RD, Gidding SS, Hegele RA, Cuchel MA, Barter PJ, Watts GF, Baum SJ, et al. Defining severe familial hypercholesterolaemia and the implications for clinical management: a consensus statement from the International Atherosclerosis Society Severe Familial Hypercholesterolemia Panel. Lancet Diabetes Endocrinol. 2016;4(10):850-861.
4. Harada-Shiba M, Sugisawa T, Makino H, Abe M, Tsushima M, Yoshimasa Y, Yamashita T, et al. Impact of statin treatment on the clinical fate of heterozygous familial hypercholesterolemia. J Atheroscler Thromb. 2010;17(7):667-674.
5. Nagar SP, Rane PP, Fox KM, Meyers J, Davis K, Beaubrun A, Inomata H, et al. Treatment patterns, statin intolerance, and subsequent cardiovascular events among Japanese patients with high cardiovascular risk initiating statin therapy. Circ J. 2018;82(4):1008-1016.
6. Lopez D. Inhibition of PCSK9 as a novel strategy for the treatment of hypercholesterolemia. Drug News Perspect. 2008;21(6):323-330.