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Reply to “The Connection between Celiac Disease and Hepatic Steatosis: High Levels of Pigment Epithelium-Derived Factor”

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We read with interest the letter by Dikker and Dağ [1] regarding our article; we thank the authors for their inputs on the relationship between pigment epithelium-derived factor (PEDF) and hepatic steatosis.

In celiac disease (CD), some liver abnormalities, including asymptomatic elevations of transaminases, hepatic steatosis, non-specific hepatitis, autoimmune hepatitis, and cholestatic liver diseases, can occur, especially in the active period [2]. The frequency of CD in hepatic steatosis is 3–7% according to Bardella et al. [3]. After the diagnosis and under a gluten-free diet, the course of hepatic steatosis may improve; however, an increased risk of hepatic steatosis still continues because of weight gain in patients with CD.

The association between CD and hepatic steatosis is not fully understood. In addition to an increased inflammatory load in the intestinal wall, increased intestinal permeability and autoantibodies related to CD are the most suspected pathogenic mechanisms for liver diseases in CD, including hepatic steatosis [4]. It is well known that intestinal permeability increases in active CD. Studies on zonulin suggest that a gluten-containing diet affects the intestinal wall by increasing intestinal permeability. After that, toxins, cytokines, and other unidentified molecules originating from the intestine can reach the liver for further liver damage.

PEDF is synthesized in most organs, including the fetal and adult liver. Some in vitro animal studies have investigated the physiologic role of PEDF in the liver. The main role of PEDF in the liver is lipid homeostasis [5]. PEDF induces adipose lipolysis and, as a result, increases insulin resistance. In contrast with this find-

ing, the PEDF-deficient mouse can also develop hepatic steatosis [6]. Yoshida et al. [7] investigated the effect of intramuscular administration of PEDF on hepatic steatosis in mice and found that PEDF can retard steatohepatitis.

At this point, it is difficult to state that PEDF can induce hepatic steatosis in CD. In addition, measurement of PEDF in CD for assessment of hepatic steatosis is neither feasible nor cost-effective. Further tissue-based studies on PEDF in hepatic steatosis in patients with CD will clarify this issue.

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Author Contributions

Muhammet Yener Akpınar wrote the response; all authors read and approved the response.

References

- 1 Dikker O, Dağ H. The connection between celiac disease and hepatic steatosis: high levels of pigment epithelium-derived factor. *Med Princ Pract*. 2019 Sep, doi: 10.1159/000503633.
- 2 Abdo A, Meddings J, Swain M. Liver abnormalities in celiac disease. *Clin Gastroenterol Hepatol*. 2004 Feb;2(2):107–12.
- 3 Bardella MT, Valenti L, Pagliari C, Peracchi M, Farè M, Fracanzani AL, et al. Searching for coeliac disease in patients with non-alcoholic fatty liver disease. *Dig Liver Dis*. 2004 May;36(5):333–6.
- 4 Rubio-Tapia A, Murray JA. The liver in celiac disease. *Hepatology*. 2007 Nov;46(5):1650–8.
- 5 He X, Cheng R, Benyajati S, Ma JX. PEDF and its roles in physiological and pathological conditions: implication in diabetic and hypoxia-induced angiogenic diseases. *Clin Sci (Lond)*. 2015 Jun;128(11):805–23.
- 6 Chung C, Doll JA, Gattu AK, Shugrue C, Cornwell M, Fitchew P, et al. Anti-angiogenic pigment epithelium-derived factor regulates hepatocyte triglyceride content through adipose triglyceride lipase (ATGL). *J Hepatol*. 2008 Mar;48(3):471–8.
- 7 Yoshida T, Akiba J, Matsui T, Nakamura K, Hisamoto T, Abe M, et al. Pigment Epithelium-Derived Factor (PEDF) Prevents Hepatic Fat Storage, Inflammation, and Fibrosis in Dietary Steatohepatitis of Mice. *Dig Dis Sci*. 2017 Jun;62(6):1527–36.