Successful treatment with lomitapide in a patient with homozygous familial hypercholesterolemia and severe fatty liver disease

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Introduction and Aims: Homozygous-familial hypercholesterolemia (Ho-FH) is a rare condition due to biallelic mutations in low-density lipoprotein-receptor (LDL-R) genes characterized by high level of LDL-cholesterol (LDL-c) and huge risk of premature atherosclerotic cardiovascular disease (ASCVD), determining low quality of life and life expectancy.
Lomitapide represents a therapeutic option for Ho-FH, but caution should be observed when used in fatty liver disease (FLD) and hypertransaminasemia since it is associated with onset/worsening of liver steatosis. We present a case of safe lomitapide therapy in an adult Ho-FH patient with pre-existing FLD.
Case presentation: A 39-year-old man with severe hypercholesterolemia since childhood (LDL-c 405 mg/dl) and premature coronary heart disease history, was referred to our Modena Lipid Clinic. He presented an overt metabolic syndrome, FLD with hypertransaminasemia and elastosonographic significant liver fibrosis. Lipid-lowering-therapy (LLT) included rosuvastatin 20 mg, ezetimibe and evolocumab 140 mg twice a month without reaching LDL-c goal. Genetic analysis revealed homozygous pathogenic LDL-R gene mutation. Evolocumab was increased up to 420 mg twice a month and LDL-apheresis was started with quality of life worsening. Therefore, lomitapide 5 mg daily and low-fat diet were started, obtaining weight loss and lipid profile improvement. However, liver enzymes elevation higher than 5-fold was observed, leading to lomitapide discontinuation and baseline liver enzymes values restoration. After one-month wash-out, lomitapide was gradually reintroduced up to 5 mg daily without significant hypertransaminasemia recurrence, leading to LDL-c target achievement and LDL-apheresis discontinuation. Adherence to low-fat diet and weight loss resulted in FLD and fibrosis improvement.
Conclusion: Ho-FH requires complex, combined treatment. Metabolic comorbidities co-existence makes Ho-FH management more difficult. Lomitapide can be safely used in Ho-FH patients with FLD and hypertransaminasemia, but strict follow-up of liver disease and a multidisciplinary approach are needed. Before lomitapide introduction, low-fat diet should be started advantageously and weight stabilization should be obtained.

Optimization of glucose control drives improvement of NAFLD independent of weight loss in people with T2D

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Aim: The mainstays for the treatment of non-alcoholic fatty liver disease (NAFLD) are lifestyle intervention with the aim of significant weight loss alongside aggressive cardiovascular risk reduction. NAFLD is tightly associated with both obesity and type 2 diabetes (T2D). In people with T2D, glucose lowering agents that promote weight loss have shown a beneficial impact on NAFLD based on histological features. However, it remains unclear as to whether glucose lowering can improve NALFD in patients with T2D, independent of weight loss.
Methods: In a consecutively recruited population of 637 patients with T2D with HbA1c levels above treatment targets, DPP-IV inhibition, GLP-1RA therapy or SGLT2 inhibition was initiated, alongside lifestyle education with maintenance of exiting background glucose lowering treatment. We examined the longitudinal impact of the optimization of glycaemic control on fatty liver index (FLI) and Fibrosis score 4 (Fib-4) adjusting for changes in BMI and choice of glucose lowering regimen over a 12-month period.
Results: Change in HbA1c and change in FLI correlated significantly in a linear regression analysis after adjustment for change in BMI, age, sex, and drug class ($R=0.467$, $p=0.031$). The greatest reduction in FLI was observed in patients with the largest reduction in HbA1c ($p<0.0001$). The probability of improvements in FLI with optimization of glycaemic control was similar with all 3 glucose lowering agents, despite differences in weight reduction. Similar relationships were observed examining the changes in glycaemic control and Fib-4.
Conclusions: Significant reductions of HbA1c are associated with improvement in NAFLD independently from weight loss. These results suggest a prominent role for the optimization of glucose control in the management of coexistent NAFLD and T2D, especially in the 'lean' NAFLD and where significant weight loss may not be achieved.