International Journal of Contemporary Pediatrics
Eiras I et al. Int J Contemp Pediatr. 2026 Sep;13(9):1841-1843
https://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20262978

Case Report

Glucagon-like peptide-1 analog in the treatment of metabolic dysfunction-associated steatotic liver disease

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Received: 15 July 2026
Accepted: 14 August 2026

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ABSTRACT

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common chronic liver disease in children with obesity. No pharmacological therapies are currently approved specifically for paediatric MASLD. A 12-year-old boy with obesity presented with persistent hypertransaminasemia and ultrasound-confirmed hepatic steatosis. After lifestyle interventions failed to improve liver enzymes, a glucagon-like peptide 1 (GLP-1) analog was initiated and titrated to 1.8 mg/day. Six months later, transaminases improved, accompanied by a 4 kg weight loss. After one year, liver enzymes normalized without adverse effects. This case supports the potential role of GLP-1 analog as a therapeutic option for paediatric MASLD, warranting further study.

Keywords: Metabolic dysfunction-associated steatotic liver disease, Obesity, Glucagon-like peptide 1 analog

INTRODUCTION

The previous non-alcoholic fatty liver disease (NAFLD) definition emphasized chronically elevated liver enzymes in the context of hepatic steatosis, after exclusion of other causes. The new metabolic dysfunction-associated steatotic liver disease (MASLD) definition requires confirmation of hepatic steatosis (by imaging or histology) plus at leat one of five cardiometabolic risk factor (obesity, type 2 diabetes mellitus [T2DM], hypertension, hypertriglyceridemia, and low high-density colesterol), regardless of liver enzyme values.[1,2] MASLD can progress to metabolic dysfunction-associated steatohepatitis (MASH), fibrosis, and, in severe cases, cirrhosis.[2,3] There is also a strong association between MASLD, obesity, insulin resistance, and T2DM.[2]

The treatment of this entity has become an active area of research.[2] One of the most promising advances involves the use of glucagon-like peptide 1 (GLP-1) analogs, which are substances that mimic the action of the GLP-1 hormone, playing an important role in regulating blood glucose levels, stimulating insulin secretion, inhibiting glucagon secretion, slowing gastric emptying and promoting satiety.[2] Therefore, GLP-1 analogs are drugs designed for the treatment of T2DM, as they stimulate insulin secretion and reduce blood glucose. Furthermore, they have demonstrated beneficial effects on lipid metabolism and weight control, and are currently approved as pharmacological treatment for obesity in adolescentes, representing a key adjuntive option alongside lifestyle intervention in this age group.[2] These drugs also have the potential to treat MASLD by increasing insulin sensitivity, reducing liver inflammation, decreasing lipogenesis, and increasing fat oxidation, thus contributing to the reduction of hepatic steatosis.[2] However, no pharmacotherapies are currently approved specifically for MASLD in children.[2,4]

The authors aim to demonstrate a clinical case of MASLD associated with hypertransaminasemia and its normalization associated with the use of a GLP-1 analog.

CASE REPORT

A 12-year-old male adolescent, followed in Pediatric consultation for obesity (BMI at the 98th percentile) and cyclic vomiting syndrome. On physical examination, he presented with central obesity, without hepatomegaly or

splenomegaly on palpation, and no signs of chronic liver disease. During screening for comorbidities associated with obesity, hypertransaminemia (AST 42 IU/l; ALT 83 IU/l) was detected, with normal gamma-glutamyl transferase, alkaline phosphatase, and total bilirubin levels. Abdominal ultrasound demonstrated diffuse hyperechogenicity, suggestive of moderate hepatic steatosis. Dietary counseling and increased physical activity were initiated, and he was reevaluated after 5 months, with an increase in transaminase levels (maximum AST value of 56 IU/l; maximum ALT value of 151 IU/l), and BMI at the 98th percentile. Given this deterioration, further investigation was conducted to exclude other underlying causes, including viral hepatitis, celiac disease, Wilson's disease, autoimmune hepatitis and hypothyroidism. Amitriptyline, given in the context of cyclic vomiting syndrome, was also discontinued due to rare hepatotoxic effects, without improvement in transaminase levels. Treatment with liraglutide, a GLP-1 analog, was initiated, with a progressive dose increase up to 1.8 mg/day, with a favorable response. The patient maintainded good adherence to pharmacological therapy and dietary recommendations throughout the follow-up period. After 6 months, there was an improvement in transaminase levels (AST 45 IU/l and ALT 74 IU/l) and a weight loss of 4 kg. After one year, resolution of hypertransaminemia was achieved (AST 25 IU/l and ALT 44 IU/l), with no adverse effects related to liraglutide reported throught the treatment period.

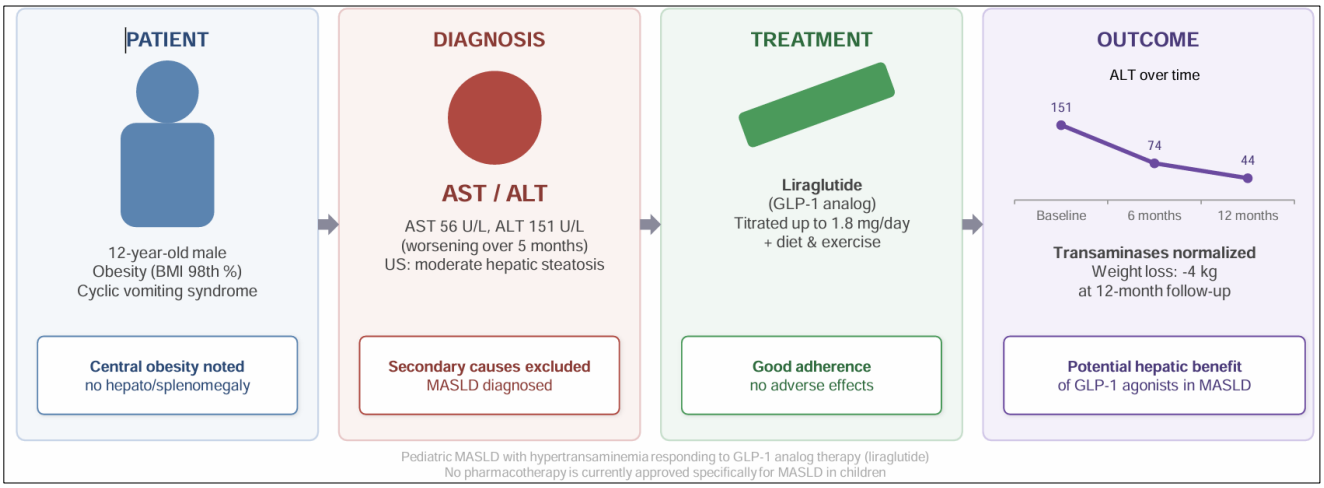

Figure 1: GLP-1 analog therapy for pediatric MASLD.

DISCUSSION

The differential diagnosis of hypertransaminemia is extremely broad and includes viral hepatitis, autoimmune hepatitis, metabolic causes, Wilson's disease, Celiac disease, hepatotoxicity, alcoholic liver disease, MASLD, ischemic hepatitis, and hepatic malignancy.[4,5] The clinical context (obesity), moderate elevation of transaminases (less than 4 times the upper limit for age) with a preferential increase in ALT, and ultrasound findings, suggested MASLD. This entity is estimated to affect 7,6% of children globally and up to 26% of those with obesity, making it the most common cause of chronic liver disease in paediatric population worldwide.[2-4]

Its onset is usually silent, with diagnosis often made in the context of screening for obesity-related complications. Not innocuous, it can ultimately lead to liver cirrhosis, making its evaluation and treatment essential.[2,3]

Treatment is essentially based on lifestyle modifications, including diet and exercise, with weight loss being the primary goal.[2-4] Pharmacologically, there are currently no specific recommendations for MASLD in children.[2,4] Although GLP-1 agonists, such as liraglutide, are approved for the treatment of T2DM from age 10 and obesity from age 6, no pharmacotherapy is currently approved specifically for MASLD in children.[4] Nevertheless, the favourable response observed in this case, along with weight loss, is consistent with emerging evidence suggesting potential hepatic benefit of GLP-1 receptor agonists in children with MASLD.

CONCLUSION

GLP-1 analogs represent a promising approach in the treatment of MASLD, aiming to improve insulin sensitivity, reduce liver inflammation, and decrease fat accumulation in the liver. However, their use should be carefully considered and monitored by specialized healthcare professionals. Dedicated paediatric trials are urgently needed.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Eiras I, Magalhães I, Martins S. Glucagon-like peptide-1 analog in the treatment of metabolic dysfunction-associated steatotic liver disease. Int J Contemp Pediatr 2026;13:1841-3.