FPIN's Clinical Inquiries

Metformin for Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis

Samira Farah, MD; Thu Nguyen, PharmD; and Gary Kelsberg, MD
Valley Family Medicine Residency, Renton, Washington
Sarah Safranek, MLIS, University of Washington Health Sciences Library, Seattle, Washington

Clinical Question

How effective is metformin in the treatment of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis?

Evidence-Based Answer

Metformin does not seem to be an effective treatment for nonalcoholic steatohepatitis. There are no studies evaluating whether metformin improves long-term patient-oriented outcomes such as progression from NAFLD to nonalcoholic steatohepatitis, cirrhosis, hepatocellular carcinoma, or death from liver failure. Metformin does not improve anatomic outcomes (histologic or ultrasound features of the liver) or biochemical outcomes (alanine transaminase [ALT] and aspartate transaminase [AST] levels, or insulin resistance) in adults. Metformin does not improve liver histologic or biochemical outcomes, or body mass index (BMI) in adults with nonalcoholic steatohepatitis. (Strength of Recommendation: C, based on a meta-analysis of randomized, controlled trials [RCTs] evaluating laboratory parameters.) Similarly, metformin does not improve histologic or biochemical outcomes, or BMI in children and adolescents with NAFLD. (Strength of Recommendation: C, based on RCTs evaluating laboratory parameters.)

Evidence Summary

ADULTS WITH NAFLD

No studies have evaluated patient-oriented outcomes of metformin therapy for NAFLD or nonalcoholic steatohepatitis. An RCT found no improvement in liver histology on biopsy.[1,2] Two placebo-controlled RCTs (N = 113) evaluating the effect of metformin (850 to 1,700 mg per day) on ALT and AST levels, insulin resistance, and BMI found no differences. One RCT (n = 48) found a small decrease in BMI. Another RCT (n = 2,153) found no improvement in ALT levels after treatment with metformin (850 mg twice per day) vs. placebo.[2]

ADULTS WITH NONALCOHOLIC STEATOHEPATITIS

Two RCTs (N = 52) evaluating metformin (500 to 1,000 mg per day) in patients with nonalcoholic steatohepatitis found that it did not improve liver histology, ALT and AST levels, BMI, or insulin resistance.[1,3]

CHILDREN WITH NAFLD

Two RCTs (N = 172) evaluating metformin (1,000 to 1,500 mg per day) vs. placebo in children with obesity and NAFLD found no improvement in liver histology on biopsy, ALT and AST

Clinical Inquiries provides answers to questions submitted by practicing family physicians to the Family Physicians Inquiries Network (FPIN). Members of the network select questions based on their relevance to family medicine. Answers are drawn from an approved set of evidence-based resources and undergo peer review. The strength of recommendations and the level of evidence for individual studies are rated using criteria developed by the Evidence-Based Medicine Working Group (http://www.cebm.net).

A collection of FPIN's Clinical Inquiries published in *AFP* is available at https://www.aafp.org/afp/fpin.

Author disclosure: No relevant financial affiliations.

levels, BMI, or insulin resistance.[4,5] A smaller RCT (n = 50; mean age: 15 years) found that metformin (850 mg twice per day) improved ultrasound scores for fatty liver but did not improve ALT and AST levels.[6]

Recommendations from Others

An evidence-based guideline from the American Association for the Study of Liver Diseases, the American College of Gastroenterology, and the American Gastroenterological Association states that metformin has no significant effect on liver histology and is not recommended as a treatment for liver disease in adults with nonalcoholic steatohepatitis.[7]

Address correspondence to Gary Kelsberg, MD, at Gary_Kelsberg@valleymed.org. Reprints are not available from the authors.

References

1. Li Y, et al. Metformin in non-alcoholic fatty liver disease: a systematic review and meta-analysis. *Biomed Rep*. 2013;(1):57-64.
2. Krakoff J, et al. Effects of metformin and weight loss on serum alanine aminotransferase activity in the Diabetes Prevention Program. *Obesity (Silver Spring)*. 2010;18(9):1762-1767.
3. Kazemi R, et al. Metformin in nonalcoholic steatohepatitis: a randomized controlled trial. *Middle East J Dig Dis*. 2012;4(1):16-22.
4. Lavine JE, et al. Effect of vitamin E or metformin for treatment of nonalcoholic fatty liver disease in children and adolescents: the TONIC randomized controlled trial. *JAMA*. 2011;305(16):1659-1668.
5. Nobili V, et al. Metformin use in children with nonalcoholic fatty liver disease: an open-label, 24-month, observational pilot study. *Clin Ther*. 2008;30(6):1168-1176.
6. Nadeau KJ, et al. Treatment of non-alcoholic fatty liver disease with metformin versus lifestyle intervention in insulin-resistant adolescents. *Pediatr Diabetes*. 2009;10(1):5-13.
7. Chalasani N, et al. The diagnosis and management of non-alcoholic fatty liver disease: practice guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. *Hepatology*. 2012;55(6):2005-2023. ■