

Letter to Editor

Allopurinol and Liver Cirrhosis Complications: A Call for Further Investigation

Key words: Liver Cirrhosis, Allopurinol, liver disease, Patients

To the Editor,

Cirrhosis signifies the final stage of liver disease, defined by unalterable widespread liver fibrosis and the development of regenerative nodules. As it advances, complications such as jaundice, ascites, encephalopathy, and variceal bleeding become apparent, signifying a more advanced stage and a worse prognosis.¹ The phrase 'decompensated liver disease' is frequently used to describe the occurrence of any of these symptoms, which together indicate a substantial deterioration in liver function, often requiring immediate medical attention.

Cirrhosis remains a significant global health burden, ranking as the 15th leading cause of disability-adjusted life-years (DALYs) and among the top ten causes of death in regions such as Africa, Southeast Asia, and the Eastern Mediterranean. Furthermore, liver-related healthcare costs in the United States alone reached \$32.5 billion in 2016, underscoring cirrhosis's substantial financial and public health impact.² Liver transplantation is regarded as the optimal treatment for advanced cirrhosis; however, access is limited by high costs and donor shortages, meeting less than 10% of the global demand.³ These barriers highlight the urgent need for alternative, affordable therapies that could delay progression and alleviate complications in cirrhosis patients.

Patients with cirrhosis exhibit elevated oxidative stress in their intestinal mucosa, which can be traced back to heightened xanthine oxidase (XOR) activity. This increase in XOR activity, especially prominent during active liver disease phases, closely aligns with liver transaminase levels, particularly serum ALT. These findings suggest an intensified state of oxidative stress and inflammation. Furthermore, the elevated plasma XOR activity likely mirrors damage to hepatocytes and bile duct epithelial cells, thereby exacerbating liver injury.⁴ Moreover, the induction of hepatic fibrosis by reactive oxygen species (ROS) occurs through the activation of hepatic stellate cells, leading to an exaggerated production of extracellular matrix proteins, consequently contributing to the progression of fibrosis, cirrhosis, and ultimately hepatocellular carcinoma.⁵ Hence allopurinol, a xanthine oxidase inhibitor, could potentially be a life-changing protocol in cirrhosis patients.

In a recent 2023 study, one hundred patients with hepatic decompensation were randomly assigned in a 1:1 ratio to receive either allopurinol 300 mg or placebo tablets once daily for 6 months. The results demonstrated that after six months of treatment, allopurinol significantly reduced the risk of experiencing any first complication by 56% (hazard ratio

[HR] 0.44; 95% confidence interval [CI], 0.27-0.62; $p < 0.001$). Moreover, allopurinol notably decreased the risk of overt ascites by 67% (HR 0.33; 95% CI, 0.0098-0.94; $p = 0.039$), spontaneous bacterial peritonitis by approximately 75% (HR 0.25; 95% CI, 0.05-0.76; $p = 0.01$), and hepatorenal syndrome by 80% (HR 0.2; 95% CI, 0.04-0.87; $p = 0.033$).⁶

Conclusion

Allopurinol, a cost-effective remedy, presents a promising opportunity to extend the time before complications arise and enhance the overall quality of life for cirrhosis patients. Despite ongoing research efforts, progress has been slower than anticipated, necessitating further clinical trials involving larger cohorts and more comprehensive investigations. Additionally, exploring potential synergies between allopurinol and existing cirrhosis therapies could offer significant benefits. Further research endeavors could also delve into identifying specific patient subgroups, such as those with distinct etiologies or comorbidities, to learn whether they stand to gain greater advantages from allopurinol treatment, thus guiding targeted therapeutic approaches.

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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