Review paper

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Pharmacological considerations in pharmacotherapy of rheumatology patients with liver disease: a brief narrative review

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Abstract

The presence of chronic liver diseases such as metabolic dysfunction-associated steatosis liver disease, viral hepatitis, and cirrhosis may affect the treatment plan in patients with rheumatologic disorders, with concern about the adverse effects of the rheumatic medications on the course of liver disease. Advanced liver disease can change the elimination and activation of many drugs. In addition, there are concerns about the risk of viral reactivation after using biologics and immunosuppressants in patients with chronic viral hepatitis. This narrative review will assess the considerations that should be made before starting the most frequently used drugs in all common rheumatic diseases and patients with chronic liver diseases including chronic viral hepatitis.

Key words: antirheumatic agents, osteoporosis, liver diseases, viral hepatitis.

Introduction

Several factors should be considered in pharmacotherapy in rheumatology patients with concomitant chronic liver diseases. These include drug toxicity, etiology of the liver disease, severity of liver disease, presence of fatty liver, chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infection, and other infections [1]. The risk of viral reactivation can also be increased in patients receiving immunosuppressive and biologic treatments based on the type and duration of these medications, the levels of liver enzymes, and the status of HBV infection (serum HBV DNA level) and the severity of the liver disease. The risk of HBV reactivation (HBVr) is divided into low (< 1%), moderate (1–10%), and high (> 10%) [2]. For example, among the most important high-risk drugs are rituximab (RTX) and high-dose glucocorticosteroid (GC; prednisolone ≥ 20 mg/day for ≥ 4 weeks); moderate-risk drugs include tumor necrosis factor inhibitors (TNFi); and low-risk drugs include azathioprine (AZA), methotrexate (MTX) and any dose of oral GCs for ≤ 1 week or low dose (< 10 mg daily) for ≥ 4 weeks [3]. All patients undergoing treatment with a biologic or immunosuppressant with high or moderate risk of HBVr should be subjected to screening (serum evaluation of HBsAg, anti-HBc, and anti-HBs). The prevalence of chronic liver disease and cirrhosis is increasing worldwide, especially metabolic dysfunction-associated steatotic liver disease (MASLD) and alcohol-related liver disease [4, 5]. Metabolic dysfunction-associated steatotic liver disease has been reported in 25% of the general population, 30% of patients with rheumatoid arthritis (RA), and in an even higher percentage of patients with psoriatic arthritis [6].

Liver metabolism accounts for the elimination of many drugs. The liver has a high functional reserve, and a significant hepatic impairment must occur before the metabolism of the drug is affected. There is, however, no readily available marker to estimate the degree of hepatic impairment and guide drug dose adjustment in liver disease. There are multiple interacting factors in patients with liver cirrhosis including impaired hepatic metabolism of drugs, liver blood flow, binding to plasma proteins,

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plasma half-life in patients with chronic hepatic impairment, compared to healthy subjects [68]. The main route of elimination of colchicine is hepatobiliary excretion, so the risk of toxicity is increased in patients with cirrhosis, and in moderate liver dysfunction dose reduction is recommended [69].

Medications used in osteoporosis

Bisphosphonates

There is no need for dose adjustment in patients with liver disease [70]. In a study, 57 patients with liver cirrhosis and esophageal varices received oral risedronate at 35 mg weekly plus daily calcium and vitamin D supplementation for the treatment of osteoporosis. The improvement in T score with low bleeding risk under endoscopic surveillance was not significantly different from the control group [71].

Denosumab and parathormone

There is no need for dosage adjustment in patients with liver disease, as described in the manufacturer's recommendations. Denosumab treatment was found to be safe and effective in 60 patients with chronic liver disease diagnosed with osteoporosis [72]. Teriparatide has not been studied in patients with liver disease.

Conclusions

Treatment of patients with rheumatic disease and severe hepatobiliary disease may be challenging. In addition, there are concerns about viral reactivation during treatment with immunosuppressants and biologic medications in patients with chronic viral hepatitis. Therefore, many precautions should be considered; in most cases, collaboration with a hepatologist is required.

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