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Short Commentary

Complications of Treatment against SARS-CoV-2: Risk of Hepatitis B Reactivation Associated with Corticosteroids

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The health crisis triggered by the new unknown SARS-CoV-2 has led to using all available resources to curb the disease. As we have learned more about the virus, more targeted drugs have been prescribed. The inflammation phase is perhaps the most worrisome. It requires therapies that slow down the immune system activation [1]. Corticosteroids are the favorite drug. However, dosages and maintenance regime are still uncertain. We have already started to have some results on its effectiveness [2], which were not available at the beginning. We have used a three-day regimen of 125 or 250 mg methylprednisolone pulses according to clinical-analytical severity in our hospital. However, corticosteroids are not without risks. One of the most frequent risks is the reactivation of infections. Reactivation of the hepatitis B virus is especially important because it is frequent and we can prevent it. In addition, a recent study has linked chronic HBV infection with a decreased clearance rate of SARS-CoV-2 [3]. Therefore, we review the recommendations on the prophylaxis of reactivation of HBV infection in patients receiving corticosteroid pulses.

EASL [4] and AGA [5] advise HBV screening in all patients receiving immunosuppressive therapy. They use HBsAg and anti-HBc. The AEMPS [6] published a summary of recommendations based on the results of the screening tests. If the HBsAg is positive, we should request the viral load. If it is greater than 2000, we must start treatment with Entecavir or Tenofovir. If it is less than 2000, universal prophylaxis is performed with Lamivudine. We use a short immunosuppressive regimen so Lamivudine is sufficient. In longer immunosuppressive regimens, other antivirals are preferred because of HBV's ability to develop resistance to Lamivudine.

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When HBsAg is negative, we must look at anti-HBc. If it is positive and the viral load is detectable, the same regimen is used as in patients with HBsAg positive. If anti-HBc is positive and the viral load is undetectable, the approach is more complex and depends on the risk of reactivation. There are three groups according to the annual probability of reactivation of the virus: high (>10%), moderate (1-10%) and low (<1%). Immunosuppressive drugs are classified into one of these three groups [7]. Corticosteroids are difficult to classify because there are many different patterns and clinical trials are lacking. The latest AGA [8] update differentiates two groups. Patients receiving ≤ 20 mg per day of prednisone or equivalent are in the low risk group for reactivation. Doses>20 mg belong to the intermediate risk group. The review does not explain exactly the duration of treatment with corticosteroids. Corticosteroid pulses are not mentioned at any time.

The Journal of Hepatology published a retrospective study in 2020 [9]. It analyzes the risk of outbreaks of hepatitis and HBsAg seroreversion in 12,997 patients receiving at least one dose of systemic corticosteroids. Patients with HBsAg- / anti-HBc +/ anti-HBs- have an annual risk of hepatitis outbreak of 16.2% and resoreversion of 1.8%. This annual risk of seroreversion is included in the intermediate risk group. The investigators concluded that the risk of seroreversionis independent of time and corticosteroid dose. The time of treatment with corticosteroids neither influence outbreaks of hepatitis. But the dose does. Doses higher than 40mg per day increase the risk.

In summary, HBV screening should be performed in all patients with COVID-19 candidate for corticosteroids. We propose a summary of action according to the guidelines of our hospital (Figure 1). There is evidence to recommend prophylactic treatment with Lamivudine in HBsAg- / anti-HBc + / HBV-DNA- patients with high risk of reactivation. If the risk is low, it is not recommended. If the risk is intermediate, prophylaxis can be started or a quarterly control can be done.

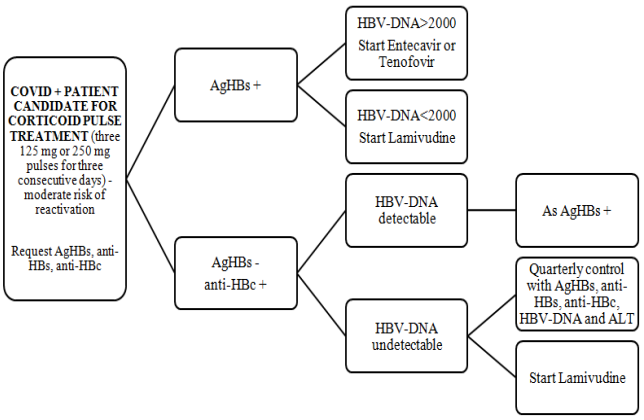

Figure 1: Algorithm of action against COVID+ patients who are candidates for corticosteroid pulses according to serological findings from HBV screening.

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