ANTIRETROVIRAL THERAPY IN HEPATITIS B VIRUS/HIV COINFECTION

To the Editor:

We commend Drs. Brito and Alhyraba on their thorough review of hepatitis B virus and HIV (HBV/HIV) coinfection.[1] However, we would like to comment on the use of adefovir monotherapy in the HBV/HIV coinfected patient who does not yet meet criteria for initiation of antiretroviral therapy (ART). Although studies of adefovir in HBV/HIV coinfected patients did not demonstrate overt adefovir resistance,[2,3] they did show the development of reverse transcriptase mutations that may be attributable to adefovir. In addition, adefovir monotherapy may produce undetected mutations present only in a subpopulation of HIV species, which could have clinical implications. This scenario was observed with the use of intrapartum nevirapine and the high failure rates of subsequent ART regimens containing nevirapine.[4] The fact remains that there is at least a theoretical risk of developing HIV mutations in a coinfected patient taking adefovir monotherapy.

The natural history of liver disease in HBV/HIV coinfected patients is accelerated as compared with liver disease in those with HBV monoinfection, as was noted in Drs. Brito and Alhyraba's review. Various comorbidities are now considered in the decision-making process for initiation of ART; the accelerated natural history of HBV in HIV patients is a strong indication for initiation of ART earlier than current guidelines suggest. The fact that liver-related mortality is higher in patients with lower CD4 nadirs[5] makes a compelling argument for earlier initiation of ART in coinfected patients. The most recent recommendations for antiretroviral treatment of HIV infection in adults by the International AIDS Society–USA Panel[6] include a category of patients with CD4 cell counts of 350 cells/μL or higher in whom the decision to initiate ART should be individualized and should take into account factors such as high risk of cardiovascular disease and active hepatitis B or C virus coinfections. Based on these newest recommendations, we would argue that the subset of patients with HBV/HIV coinfection who do not meet criteria for initiating ART no longer exists and that the use of adefovir monotherapy should no longer be considered.

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References

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In reply:

We agree that adefovir at high doses (40 mg) has anti-HIV activity and may select for resistance mutations. However, low-dose adefovir has no proven activity against HIV. That is why we specify in our article that the dose of adefovir should be 10 mg. In the nevirapine studies,[1,2] the aim of the treatment strategy was to decrease the levels of HIV viral load, and thus a therapeutic dose of the drug was used. In that scenario, nevirapine exerts enough selective pressure on the virus to induce resistance. For this reason, the comparison of adefovir with nevirapine does not hold. In the absence of further resistance or clinical outcomes data, the risk of having "undetected mutations" remains theoretical, and we are not convinced that adefovir should be discarded as a viable option should it be needed. Regarding the issue of when to start treatment for coinfected patients, we agree that the field is moving toward treating patients at an earlier stage, as some guidelines have begun to suggest. However, there could be special circumstances in which HBV is treated but HIV is not (eg, patient's preference). In those cases, we believe our recommendations are appropriate.

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