

Lurking Dangers Behind Overuse of Lamivudine to Treat Non-HIV Hepatitis B Patients in Africa

Sir,

The potent nucleoside analog reverse transcriptase antiretroviral drug lamivudine, which is also called 3TC, is a vital tool in the treatment and management of HIV and acquired immunodeficiency syndrome (AIDS)-related diseases. Using 3TC in combination with other antiretrovirals to treat HIV-positive patients ensures that the viral load is kept at a beneficially low level thus preventing the advent of opportunistic infections like tuberculosis and *Pneumocystis carinii* pneumonia (PCP).

However, the continuous use of 3TC in the treatment of non-HIV hepatitis B in poor countries will invariably counteract all the good intentions behind the creation of the drug in the first place. 3TC was created primarily to help reduce HIV-related morbidity and mortality by keeping the viral load minimal, lowering the healthcare cost for HIV-positive patients obtaining treatment as a result of comorbidity with other infections and to help reduce the treatment time for HIV-infected patients.

There are many biomedical problems associated with the overuse of 3TC in the treatment of hepatitis B. The pharmaceutical world is populated with cases in which the overuse of one drug to treat a disease has led to different types of drug resistances, including that of cross-resistance, whereby there emerges a tolerance to a toxic drug as a result of exposure to a similarly acting drug. Hepatitis B is now being recorded to show resistance to 3TC. Cross-resistance is well documented for

many non-antiretroviral drugs such as colistin and polymyxin,^[1] as well as for antiretroviral like 3TC^[2] and zidovudine that are used to treat HIV and AIDS-related diseases.

One of the main reasons offered for the overuse of a particular drug for the treatment of a disease for which it was not originally designed is the unavailability of the appropriate medicine for the disease under consideration due to its high cost. 3TC was initially approved for use as part of a combination of HIV treatment by the Food and Drug Administration (FDA) in 1995, but was subsequently approved for chronic hepatitis B treatment in December 1998^[3] after researches showed that the drug was successful in preventing the hepatitis B virus from reproducing itself.

In many underdeveloped countries, the overprescription and hence the overdependence on a clinically approved drug for the treatment of a different disease for which it was not originally designed is almost of a daily practice these days. For example, patients diagnosed with chronic hepatitis B in Sierra Leone nowadays are treated with 3TC treatment immediately: A practice that is common even among medical practitioners with better clinical experience.

This situation is also similar to other third world countries, where hepatitis B prevalence is on the increase in the presence of high HIV/AIDS prevalence. Most local physicians in these countries, due to the non-availability and high cost of conventional hepatitis B drugs such as interferon alpha, entecavir, adefovir dipivoxil and telbivudine, often prescribed 3TC as the drug of choice. But, while entecavir^[4] and the other drugs that are also used to treat hepatitis B are said to have little or no effect on HIV infection, 3TC does.

Treating hepatitis B using 3TC seems reasonable. After all, there are striking similarities between viruses that have the same mode of transmission and use the same methods of prevention and control.

Studies have also shown that there is a direct correlation between the prevalence of HIV-induced immunodeficiency and the prevalence of hepatitis B antigen HBeAg in certain subpopulations.^[5] A high prevalence of HIV/AIDS in a population is often associated with a high prevalence of hepatitis B within the same population. This is quite understandable because many viral infections like hepatitis B are as a result of T-cell immunodeficiency, of which HIV is the primary cause for immune deficiency. However, what is lacking in such studies is the fact that correlation does not necessarily imply causation.

There is a high prevalence of hepatitis B among HIV/AIDS patients nowadays, especially in many developing countries, which will have an influence in the treatment option for these patients. It is possible that the over-reliance on 3TC for the treatment of hepatitis B, particularly in Sub-Saharan African, is due to medics prescribing 3TC on the assumption that

patients with hepatitis B infection are generally suffering from HIV-induced T-cell immunodeficiency.

In most third world countries, one important factor leading to immunodeficiency of which AIDS is a product is malnutrition. Malnutrition in and of itself, although a major cause of death, also helps in the onset and progression of HIV,^[5] which can lead to immunodeficiency and, subsequently, AIDS. This implies that tackling hepatitis B using the 3TC therapy alone on the basis that it is immunodeficiency induced is thus insufficient as there are many other important factors leading to immunodeficiency.

Other possible problems that will be associated with the use of 3TC include the increase in the treatment cost for HIV/AIDS, stigmatization of hepatitis B patients and the concurrent increase in the prevalence of HIV/AIDS-related morbidity and mortality.

With the continuous and overprescription of 3TC for the treatment of hepatitis B, there will be a corresponding increase in the treatment cost of HIV/AIDS-related diseases that requires the use of 3TC because of the competing force of demand for the drug. In most parts of Africa, 3TC still remains the best drug for chronic hepatitis B treatment, irrespective of the fact that other drugs such as tenofovir, interferon and telbivudine are now being considered as the drug of choice outside Africa. Adefovir is the drug of choice for patients with lamivudine resistance.

In Sierra Leone, and presumably also in other developing countries, this new demand curve has resulted in a shortage of the life prolonging 3TC drug for the treatment of HIV/AIDS-related morbidities. The future thus look bleak for HIV/AIDS patients considering the overconsumption of 3TC.

The issue of stigmatization in relation to HIV/AIDS still remains a contentious issue, which tends to blight every effort to curb the spread and management of the epidemic. In Africa, where there is a high HIV/AIDS and hepatitis B burden, most patients for these infections are barely consulted about the various treatment options that exist for the treatment of their infection simply because of their financial status and the modicum of their medical education. Even when these patients are sometimes informed about the availability of alternative healthcare interventions for their health problem, majority cannot afford it as they often rely on free healthcare service provided by the States, in which case they are unable to make any choice. Majority of the HIV-infected patients in Africa still rely on the free supply of antiretroviral drugs for their HIV infection. Drugs associated directly with HIV/AIDS treatment and management are mostly frowned at for fear of stigmatization on the healthcare recipient.

It is a common scenario in Africa for HIV/AIDS patient to waste away and subsequently die rather than show up for antiretroviral treatment involving 3TC, AZT and others. Unlike hepatitis B,

which is still relatively new in the African settings in terms of its health impact on the population, the problem of treatment compliance with respect to HIV/AIDS treatment, at least in the African context, has to do with the stigma that HIV/AIDS is incurable and untreatable. It will thus take a lot of education and sensitization to convince 3TC-treated hepatitis B patients that the preference use of the drug does not imply that the stigma that is being applied to HIV/AIDS is also applicable to hepatitis B. This problem can be solved by explaining to HIV-negative hepatitis B patients that using 3TC for treating their infection is similar to using an antibiotic to treat different infections.

Because of the low socioeconomic status of the majority of chronic hepatitis B patients in most developing countries, most physicians see the disclosure of the other alternative courses of treatment alongside the relationship between 3TC and HIV/AIDS as simply unnecessary because 3TC in most third world countries is the most affordable drug for such class of patients in the first place.

This failure to disclose the alternate treatment drug for non-HIV hepatitis B patients is also a bioethical issue. It is clear that the ready use of 3TC in the treatment of hepatitis B, especially in third world countries, is to save life, but failure to completely disclose the other ailment for which the drug can be put into use, especially within the context of HIV/AIDS, is a total disrespect for the autonomy of those patients in making a decision toward the treatment of their infection. Also, it is not an acceptable bioethical reason not to treat chronic hepatitis B patients with the only available drug (e.g., 3TC) on the grounds that majority of the treatment population are unaware of the alternative use to which the drug can be put to use. The non-disclosure of the alternate use of 3TC in the treatment of HIV/AIDS can best be appreciated and understood on ethical grounds if it is the only drug available to the physician within the treatment area. This bioethical issue can further be addressed by physicians through educating and raising awareness about 3TC use to non-HIV hepatitis B patients living in HIV-endemic African countries.

Most of the hepatitis B patients in third world countries are poor, with a modicum of medical education. The right of these patients to decide which form of treatment drug they receive is mostly abused because of asymmetrical information to the advantage of medical practitioners, especially if there are alternate treatment drugs. For these medics, informed consent for the use of 3TC for hepatitis B treatment is implied. It is thus expected of the physician to explain to the patient as much as he or she can understand before embarking on the use of such drug.

Acting on patients' wishes has medical implications for resource allocation and costing. Implied consent is no justification to embark on a particular treatment course. To tackle the growing problems of drug resistance and shortages with respect to 3TC and other antiretrovirals in HIV/AIDS treatment, healthcare resources should be prescribed with

caution, irrespective of whether implied or explicit informed consent has been sought.


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