Can uridine supplements protect people with HIV/AIDS from drug toxicity?

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For many years a class of drugs called nukes (nucleoside analogues) has been the cornerstone of combination therapy to treat HIV/AIDS. Examples of nukes include the following:

- AZT (zidovudine, Retrovir)
- d4T (stavudine, Zerit)
- 3TC (lamivudine, Epivir)
- ddI (didanosine, Videx)
- ABC (abacavir, Ziagen)
- ddC (zalcitabine, Hivid)

Some nukes have been linked with certain side effects, including:

- damage to the nerves in the hands and feet (peripheral neuropathy)
- painfully swollen pancreas glands (pancreatitis)
- swollen, fatty liver
- loss of subcutaneous fat in the arms, legs, face and buttocks
- higher-than-normal levels of lactic acid in the blood

The underlying reason for this nuke-related damage, at least in test-tube studies, may be because these drugs can damage the energy-producing parts of cells, called mitochondria. When damaged, mitochondria do not produce enough energy, so cells may not work properly and may die.

Treatment for damaged mitochondria can include changing therapy. Also, some doctors have reported that supplements of certain nutrients, including antioxidants, can be helpful, such as:

- L-carnitine
- co-enzyme Q10
- vitamin C
- B-complex vitamins

However, these supplements have not been tested in large controlled trials to assess their potential for rescuing mitochondria from drug toxicity.

Some drugs used for the treatment of cancer may also damage the mitochondria. In the 1980s and 1990s, in clinical trials with cancer patients, researchers found that the natural nucleoside uridine can reduce the toxicity of some forms of chemotherapy. In test-tube studies, uridine also reduces the toxicity of AZT without reducing its anti-HIV effects.

Recently, according to a letter to the editor in the April 30, 2004 issue of the journal AIDS, a research team in Freiburg and Wuerzberg (Germany) conducted further laboratory experiments with liver cells and nukes. They found that uridine protected cells from the toxicity of ddC, d4T, AZT and 3TC but not ddI.

The German team also reported their experience in one case with the use of a supplement called Nucleomaxx. Made
from an extract of sugar cane, Nucleomaxx contains high levels of uridine. This supplement comes in a powdered formulation packaged in sachets and can be taken orally. The researchers were caring for a 54-year-old man with AIDS who had been taking anti-HIV drugs for at least four years. In the past two years he had been taking the following combination:

- 3TC, d4T, ABC and efavirenz (Sustiva, Stocrin)

After he started this regimen, his levels of lactic acid as well as liver and muscle enzymes in the blood gradually started to increase, and eventually muscle pain developed. Ultrasound scans revealed a swollen, fatty liver. No obvious cause of these problems was detected and the medical team speculated that his problems were related to the use of d4T.

They then prescribed Nucleomaxx at a dose of three sachets daily for four days. Two weeks later, lab testing found that his liver and muscle enzyme levels had fallen to near normal levels and his muscle pain had improved. Lactic acid levels also began to fall, and seven weeks after using Nucleomaxx they were within the normal range. The medical team then replaced his d4T with the anti-HIV drug tenofovir (Viread). Blood tests did not detect any further abnormalities and his viral load remained low—at less than 50 copies. Another ultrasound scan showed that his liver had “substantially improved.” No side effects from using the supplement were reported.

Concerns
Readers should bear in mind that this is merely one case report. Results from independently conducted clinical trials are needed before researchers can be certain that uridine supplements can help people with HIV/AIDS (PHAs) who have symptoms of mitochondrial toxicity. Studies are also needed to find out how much uridine enters the blood after a person takes Nucleomaxx. A point to note is that in test-tube studies, Nucleomaxx did not help cells recover from damage due to ddI.

In previous studies in HIV negative subjects there have been some reports of diarrhea and fever with high doses of uridine. In experiments on animals, high doses of uridine have, in some cases, interacted with the nervous system, inducing sleep and reducing anxiety. Uridine levels in the blood appear to be carefully regulated by the liver. It is not clear what effect the long-term use of this supplement might have on the liver, brain and other organs.

In their letter to AIDS, the research team did not state why they decided to test Nucleomaxx over currently available nutrients. One of the researchers appears to have a European patent on the use of the supplement by PHAs.

The cost of nine sachets of Nucleomaxx, not including shipping and taxes, is approximately:

- $133.00 Canadian
- €83
- $99.00 U.S.

Although test-tube studies appear promising, before spending any money readers should be cautious until independent data about the safety and effectiveness of this product in people with HIV/AIDS and other conditions becomes available.

The drug PN401 (triacetyluridine, TAU) is converted to uridine in the body. Testing of PN401 is underway in the United States, sponsored by Wellstat Therapeutics, in HIV negative people with cancers as well as in others with degenerative diseases of the nervous system, such as Alzheimer’s and Parkinson’s diseases. Other companies such as Repligen, also in the United States, are testing TAU for the treatment of conditions such as major depression.

—Sean Hosein

REFERENCES
1. Walker U. Use of pyrimidine nucleosides and/or the prodrugs thereof for combating the side effects of HAART (highly active antiretroviral therapy) and other anti-viral therapies. Patent W002/069943. 12 September, 2002.


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