Unexpected liver damage—is ddl to blame?

Liver damage is not common in the average HIV positive person living in high-income regions who is not co-infected with hepatitis-causing viruses. Yet cases of unexplained liver disease have been reported in this population. To explore this issue, research teams in Spain and Italy collaborated in reviewing the health of their co-infected patients. Their findings suggest that exposure to the anti-HIV drug ddl (didanosine, Videx or Videx EC) may be the culprit.

Study details

Researchers analysed health information, collected from three clinics, of HIV positive patients with unexplained and unexpected liver disease. All patients underwent extensive medical tests to try to find the cause of their problem(s). In total, the teams found 13 patients (2 females and 11 males) who had the following features in common:

- all had higher-than-normal levels of liver enzymes
- there were no obvious causes of liver problems
- no hepatitis-causing viruses were detected
- none of the participants were alcoholics
- swollen blood vessels in the throat and abdomen
- bleeding in the throat or abdomen
- water retention in the abdomen
- unintentional weight loss
- black stools
- exposure to ddl for at least two years

Researchers decided that all 13 patients should discontinue ddl and replace it with another suitable anti-HIV drug. Once this was done, liver enzyme levels fell and symptoms began to resolve.

Why did this happen?

Researchers speculate that ddl may have decreased levels of a protective compound called GSH (glutathione) in cells. GSH is used to make enzymes that help detoxify harmful chemicals. Low levels of GSH may result in liver cells being susceptible to ddl-related toxicity.

Studies in the 1980s and 1990s found less-than-normal levels of GSH in the blood of some HIV positive people not on treatment. It appears that HIV infection may eventually trigger a GSH deficiency, possibly by increasing the body’s need for an amino acid called cysteine that is used to make GSH. It is possible that ddl exposure may intensify the GSH deficit in HIV infection.

Experiments with HIV positive people suggest that supplements of the amino acid cysteine (which is converted into GSH inside cells) can raise GSH levels in the blood. A formulation of cysteine called NAC (N-acetyl-cysteine) is used to help detoxify the liver in cases of overdose with the pain medication acetaminophen (Tylenol). To our knowledge, no clinical trials of NAC have been done in ddl users to assess its impact on GSH and liver health.

The study team did not recommend that ddl be avoided. However, their work does highlight the possible liver-damaging effect of ddl.

REFERENCES:


Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

CATIE provides information resources to help people living with HIV and/or hepatitis C who wish to manage their own health care in partnership with their care providers. Information accessed through or published or provided by CATIE, however, is not to be considered medical advice. We do not recommend or advocate particular treatments and we urge users to consult as broad a range of sources as possible. We strongly urge users to consult with a qualified medical practitioner prior to undertaking any decision, use or action of a medical nature.

CATIE endeavours to provide the most up-to-date and accurate information at the time of publication. However, information changes and users are encouraged to ensure they have the most current information. Users relying solely on this information do so entirely at their own risk. Neither CATIE nor any of its partners or funders, nor any of their employees, directors, officers or volunteers may be held liable for damages of any kind that may result from the use or misuse of any such information. Any opinions expressed herein or in any article or publication accessed or published or provided by CATIE may not reflect the policies or opinions of CATIE or any partners or funders.

Information on safer drug use is presented as a public health service to help people make healthier choices to reduce the spread of HIV, viral hepatitis and other infections. It is not intended to encourage or promote the use or possession of illegal drugs.

Permission to Reproduce

This document is copyrighted. It may be reprinted and distributed in its entirety for non-commercial purposes without prior permission, but permission must be obtained to edit its content. The following credit must appear on any reprint: This information was provided by CATIE (the Canadian AIDS Treatment Information Exchange). For more information, contact CATIE at 1.800.263.1638.

© CATIE

Production of this content has been made possible through a financial contribution from the Public Health Agency of Canada.

Available online at: