Unexpected liver damage—is ddI 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 ddI (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 ddI for at least two years

Researchers decided that all 13 patients should discontinue ddI 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 ddI 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 ddI-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 ddI 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 ddI users to assess its impact on GSH and liver health.

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

REFERENCES:


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