Can anti-inflammatory treatment help reduce cardiac risk?

23 August 2010

Results from studies of treatment interruption suggest that cessation of anti-HIV therapy increases the risk for stroke, heart attack and other serious complications related to inflammation. Recent research suggests that HIV infection causes the immune system to remain in an activated state, releasing chemical signals that inflame many organs and tissues. Anti-HIV therapy (commonly called ART or HAART) can only partially reduce levels of inflammatory signals made by the immune system.

Everything old is new again

For some people with circulation problems, doctors can prescribe the drug pentoxifylline (Trental) to help improve the flow of blood. Experiments with cells and HIV-positive people conducted in the time before HAART was available suggested that this drug could do the following:

- suppress excessive levels of the chemical signal (cytokine) tumour necrosis factor-alpha (TNF-a)
- reduce production of HIV
- perhaps strengthen the immune response by increasing production of the cytokines interleukin-2 and interferon-gamma

These effects were seen in short-term clinical trials and the immunologic benefit of pentoxifylline seemed to wane over time. HIV researchers lost interest in pentoxifylline in the mid-to-late 1990s when more potent therapy—HAART—became available.

However, interest in pentoxifylline has recently renewed because of this drug’s anti-inflammatory activity.

Researchers in the United States performed a pilot study of pentoxifylline in HIV-positive people and found that this drug holds promise in reducing the risk for cardiovascular disease.

Study details

The research team recruited nine HIV-positive adults with the following average profile:

- 3 females, 6 males
- age - 40 years
- CD4+ count - 552 cells
- HIV viral load - 32,000 copies/ml
- body mass index (BMI) - 21

All participants received pentoxifylline 400 mg three times daily for eight weeks.

Inside blood vessels

Before the results of the study are presented, a little background information is needed.

Blood vessels have a thin lining called the endothelium. This lining acts as an interface between blood and tissues. But the endothelium is not a passive layer; by alternately relaxing and contracting, the endothelium helps to regulate the flow of blood. The endothelium also helps to control blood pressure and the formation of blood clots. Due to
these capacities, the endothelium can have a major impact on cardiovascular health.

A healthy endothelium can easily expand and contract as needed to help move the blood. However, in cases of cardiovascular disease the endothelium becomes dysfunctional. In such cases, the endothelium can release chemical signals—cytokines—that incite inflammation and stimulate the formation of blood clots, and it becomes less efficient at helping blood flow.

Researchers in the present American study used high-resolution ultrasound scans to assess endothelial dysfunction.

**Results**

Before using pentoxifylline, participants had endothelial dysfunction compared to historical values from healthy HIV-negative people.

After using pentoxifylline, endothelial dysfunction gradually improved over the course of eight weeks. By the eighth week of the study, endothelial dysfunction had decreased by about 4.4%—a significant difference. Although this value seems relatively small, studies in HIV-negative people suggest that such a decrease is associated with a reduced risk for cardiovascular disease.

Pentoxifylline was generally safe, with no laboratory signals of toxicity detected. Six participants reported mild diarrhea, a side effect that has previously been reported.

**Biomarkers**

Technicians tested blood samples from participants for many proteins or biomarkers associated with inflammation. Levels of TNF-α were very low in this group of participants at the start of the study and there was not any measureable change. However, levels of two other biomarkers—IP-10 (interferon-gamma-induced protein 10) and sVCAM-1 (soluble vascular cell adhesion molecule-1)—both decreased significantly during the study. Both of these biomarkers play a role in the development of cardiovascular disease.

As there was no control group of people who were not given pentoxifylline, researchers cannot be certain that the changes detected in their study are due to pentoxifylline. However, the anti-inflammatory changes they observed are what might be expected in people who did receive pentoxifylline.

**What's next?**

Randomized placebo-controlled clinical trials are underway in the United States with pentoxifylline being tested in HIV-positive people—some who use HAART and others who do not. These trials should provide clear answers about the potential of pentoxifylline to help suppress HIV-related inflammation.

—Sean R. Hosein

**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: