

Lactic Acidosis

WHAT IS LACTIC ACIDOSIS?

Some <u>antiretroviral medicines (ARVs)</u> in the <u>nucleoside reverse transcriptase inhibitor (NRTI)</u> drug class have negative side effects that may lead to liver and other problems. One such side effect is damage to the mitochondria inside your cells, or mitochondrial toxicity. When mitochondria are damaged, lactic acid production is increased. This can cause levels of lactic acid (lactate) in your blood to rise. If levels of lactic acid become too high, a rare but serious condition called lactic acidosis can occur.

NRTIs that may cause lactic acidosis include:

- <u>abacavir (Ziagen)</u>
- emtricitabine (Emtriva)
- lamivudine (3TC, Epivir)
- tenofovir AF (Vitekta)
- tenofovir DF (Viread)
- zidovudine (AZT, Retrovir)

WHAT CAUSES LACTIC ACIDOSIS?

Lactic acidosis is one of several conditions which are believed to be caused by damage to mitochondria.

Mitochondria are small organs inside your cells. They help convert energy in the food you eat into energy that your body uses to function. Like solar cells that convert sunlight into electricity, mitochondria are power plants inside your cells that create energy. The more energy a cell needs, the more mitochondria it contains. One cell can have anywhere from a few mitochondria to up to thousands. The highest numbers are found in nerve, muscle, and liver cells.

Mitochondria use oxygen, fat, and sugar to produce adenosine triphosphate (ATP) in a process called cellular respiration. When the cell needs energy, it breaks down molecules of ATP to release the stored energy. Your body makes lactic acid as a waste product (unwanted substance) in this process. Normally, the body breaks down lactic acid and gets rid of it.

Mitochondria have an enzyme that helps them multiply. This enzyme is called DNA polymerase gamma or pol gamma. It is very similar to HIV's reverse transcriptase enzyme. Unfortunately, this also means that some ARVs we use to inhibit reverse transcriptase can also inhibit pol gamma. When this happens, fewer new mitochondria may be produced.

Long-term usage of NRTIs therefore increases some people's risk of developing lactic acidosis. Obesity is another risk factor. In addition, people assigned female at birth (AFAB) may be at greater risk than people assigned male at birth (AMAB), and there is some evidence of a link with severe infection and <u>malnutrition</u>.

Lactic acidosis may occur at any time during <u>antiretroviral therapy (ART)</u>, but it tends to develop after several months of treatment. Fortunately, lactic acidosis is rare – even with stavudine and didanosine, fewer than one person in a hundred develops it. With newer NRTIs, it is even less common, with estimates of one person in a thousand, or one person in ten thousand for some drugs.

SYMPTOMS OF LACTIC ACIDOSIS

Lactate is usually processed by the liver. If lactate begins to build up in the blood, symptoms increase very gradually over a long period of time. Therefore, it can be difficult to diagnose. The symptoms of lactic acidosis include:

- Persistent nausea, vomiting, and abdominal (belly) pain
- Unexplained tiredness
- Shortness of breath
- Rapid breathing
- Enlarged or tender liver (area just under the right ribcage)
- $\circ~$ Cold or blue hands and feet
- Abnormal heartbeat
- Weight loss

It is important to get in touch with your healthcare provider right away if you experience these symptoms. Because lactic acidosis can be fatal, it is best to identify and treat it early.

TREATMENT OF LACTIC ACIDOSIS

If your healthcare provider suspects that you have lactic acidosis, they will perform a physical exam to check for an enlarged liver and may order a CT scan or ultrasound of your liver. You will probably also have some blood tests done to measure:

- Liver enzymes
- Electrolyte levels
- Blood pH (the level of acid in your blood)
- Lactic acid or lactate level

There is no proven treatment for lactic acidosis other than stopping the NRTIs that are causing it. In serious cases, hospitalization and supportive care, such as intravenous (IV) fluids and a machine to help you breathe, may also be needed.

Some healthcare providers recommend giving thiamine (vitamin B1), riboflavin (vitamin B2), L-carnitine, coenzyme Q, or vitamins C, E, and K to people with lactic acidosis. While some of these vitamins and supplements have shown encouraging results in small studies, they have not yet been proven to be effective.

It is important that you not stop taking any ARVs without talking with your healthcare provider. If you are diagnosed with lactic acidosis, your healthcare provider can help you decide how to stop your ARVs, when to restart, and which ones to take when you go back on treatment. If you have only slightly elevated lactic acid levels and no symptoms, you may not need to change your HIV treatment regimen.

THE BOTTOM LINE

Lactic acidosis is a rare side effect of some HIV medications, especially the older NRTIs.

People with HIV and their healthcare providers need to recognize the symptoms of lactic acidosis. If ignored, lactic acidosis can be fatal.

Although lactic acidosis can be life-threatening, it is also very rare. The point of learning about lactic acidosis is not to scare you. Rather, it is to help you be aware of important signs in your body that may indicate a serious problem. In this way, you will be better able to recognize symptoms of lactic acidosis, tell your healthcare provider right away, and get treatment if necessary.

MORE INFORMATION

HIVInfo.NIH.gov: <u>HIV and Lactic Acidosis</u>

nam aidsmap: Lactic acidosis

TheBody: HIV and Lactic Acidosis

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