

lactic acidosis

Lactic acidosis is a serious side-effect of the nucleoside analogue class of anti-HIV drugs. This class includes AZT, 3TC, d4T, ddI, ddC and abacavir. The drugs most linked with lactic acidosis are d4T and ddI. Lactic acidosis is very rare. Nevertheless, it is an important subject to understand because people who develop the condition can become dangerously ill.

The term lactic acidosis is used to describe high levels of a substance called lactate in the blood. Lactate is a by-product of the processing of sugar within the body.

Causes

Lactic acidosis is one of several conditions which are believed to be caused by damage to mitochondria. Mitochondria are found in all human cells and are involved in the production of energy. Other side-effects of nucleoside analogues which may also be associated with damage to mitochondria include peripheral neuropathy (numbness or pain in the feet and hands); bone marrow suppression; pancreatitis (inflammation of the pancreas); hepatic steatosis (accumulation of fat in the liver); and myopathy (muscle damage).

As well as attacking HIV, nucleoside analogues disrupt an enzyme (polymerase gamma) which mitochondria need to reproduce. This reduces the number of functioning mitochondria. Long-term usage of nucleoside analogues therefore increases some people's risk of developing lactic acidosis. Obesity is another risk factor. In addition, women may be at greater risk than men, and there is some evidence of a link with severe infection and malnutrition.

Lactic acidosis has been recognised as a problem in HIV infection only relatively recently. Because it has emerged around the same time as body fat and metabolic changes seen amongst people on anti-HIV therapy (also called the lipodystrophy syndrome), some people suggest these conditions may be linked. However, this has not been proven.

A review of cases in the US found that the average time at which the condition occurred was nine months after anti-HIV therapy was begun. However, it may occur at any time. The incidence is believed to be less than one in one hundred people per year.

Signs and symptoms

Initial signs and symptoms of lactic acidosis include general gastrointestinal symptoms such as nausea (feeling sick), vomiting, bloating, abdominal pain and lack of appetite, as well as malaise, and difficulty in breathing. Of course, these symptoms can also occur for many other reasons. In people who have lactic acidosis, the liver may be swollen and tender (hepatomegaly), and liver enzymes, which are measured by a liver function test, may be abnormally high. Other signs which may be detected on laboratory tests include low bicarbonate, raised lactate, and deteriorating kidney function.

Monitoring

At present there are no laboratory tests which clearly predict who is at risk of lactic acidosis. A number of tests have been proposed, such as measuring lactate, the ratio of lactate to pyruvate, monitoring serum bicarbonate anion gap, and measuring liver function. However, although these tests may be important in diagnosis, their relevance as monitoring tools for lactic acidosis risk is not established.

There are also several practical issues which seem likely to prevent some of these tests being used routinely. For example, testing lactate levels may be more reliable if blood is taken from an artery rather than from a vein. However, this is an unpleasant procedure, which most people would probably not wish to undergo regularly.

Potential treatments

What to do with raised lactate levels in the blood is uncertain, but if there is evidence of lactic acidosis, then treatment with nucleoside analogues should be stopped immediately. A number of agents have been proposed as treatments for lactic acidosis, including riboflavin and acetyl L-carnitine. It has also been suggested that vitamins C and E, and co-enzyme Q10 may protect against damage to the mitochondria, although this remains speculative. There is no evidence at present that supplementation with these products would have any effect on preventing the condition.

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