Putting heart attack risk into perspective

In the 1980s, people in high-income countries who became HIV positive had about 10 years before succumbing to dreadful AIDS-related infections and eventual death. But in 1996, HAART became available and the spectre of many AIDS-related deaths gradually receded. Today, HIV positive people who have minimal co-existing health conditions and who are engaged in their care and treatment will likely have near-normal life spans. This benefit should not be overlooked in the race to find the cause of heart attacks in some HIV positive people. Moreover, the numerous benefits of HAART continue to outweigh side effects.

This immense benefit of HAART sometimes gets tarnished by unwelcome news, such as reports of an increased risk of heart attacks if certain treatments are used. The news about heart attacks and the use of HAART is disturbing to both physicians and HIV positive people. However, it is important to bear in mind several points when reading about such news. These points may help place some perspective on the news and limit the development of anxiety.

Don’t forget HIV

Emerging research suggests that HIV can infect the lining of blood vessels and that infection with this virus triggers inflammation. Also, research suggests that this inflammation may, in some cases, be linked to heart attack and stroke.

Heart attack numbers—DAD

While the increase in risk for heart attacks does sound large, depending on which study is examined, the actual number of people affected by this problem is relatively low. Indeed, in the DAD study, there were a total of 33,308 people, of whom 580 developed a heart attack while on HAART, about 2%. What’s more, 20% of these 580 people had previously experienced a heart attack. That DAD did not take into account these prior heart attacks may have weakened its conclusions.

Heart attack numbers—French database

In the French Hospital Database (FHDB), there were 289 cases of confirmed heart attacks among at least 60,000 people taking HAART. This means that less than about 0.5% of people in this database developed a heart attack. This is very low and is reassuring about the overall safety of HAART when it comes to heart health.

The FHDB found an increased risk for heart attack of 16% for each year a PI-ritonavir was used. But since the baseline risk of a heart attack for most people is low, this increased risk still remains low and that is why the number of people who developed a heart attack is low in the Cohort studies.

Lipid-lowering therapy

What is clear from the DAD study is that only 36% of 580 people who developed a heart attack received lipid-lowering therapy. Given that 75% of the these 580 people had higher-than-normal levels of lipids in the blood, and that just over one-third of them received lipid-lowering medicines, this raises questions about the quality of care that European HIV positive patients receive. Lipid-lowering therapy, particularly the group of drugs called statins, has a number of protective benefits, including anti-inflammatory activity. In North America, physicians who are experienced in the care and treatment of HIV infection would have been much more likely to have prescribed a statin or other lipid-lowering medication in the same situation. It is possible that better management of cardiovascular risk factors in Europe might reduce the risk of heart attacks in HIV positive people. Certainly, data on decreasing rates of heart attacks in HIV positive people in California, reported earlier in this issue of TreatmentUpdate, support this
possibility.

**DAD vs. the French database**

There are differences in the results of both of these databases and it is important to bear these differences in mind when considering their findings about heart attacks.

The DAD did not exclude people who already had a heart attack. This could have affected researchers’ ability to reduce bias when interpreting their results.

On the other hand, the FHDB did exclude people who had previous heart attacks. This could strengthen the conclusions drawn by the FHDB.

Another difference between the two data sets is that people in France tend to be at lower cardiovascular risk than people in Northern Europe. This difference could have affected the outcomes of the French study.

The FHDB found an increased risk of heart attack with fosamprenavir. The DAD study is unable to reach conclusions about fosamprenavir at this time because it does not have enough people enrolled who are using this drug.

**DAD vs. other data sets**

Some analyses (at least four, including the DAD) have found that the use of abacavir is associated with an increased risk of heart attacks (though the actual proportion of people who experienced these heart attacks is very low). Most of these studies have had people who have been taking anti-HIV medicines for years. In contrast, there have been at least three analyses that found no increased risk of heart attacks in abacavir users. These latter analyses have been done mostly in people who have been new to HAART. Thus, there may be a reasonable explanation for the different findings of various studies. This difference is worthy of further investigation.

**Balancing risk**

Since there are different findings depending on which data set is analysed, it is not likely that broad recommendations about which therapy to use (or not) can be made with high levels of confidence. So physicians and their patients will have to weigh the various risks of each anti-HIV drug before starting or switching therapy.

Observational studies such as DAD and the FHDB are good at finding associations but cannot conclusively prove cause and effect. But if the results from these observational studies are correct (and not based on incorrect analyses), then for a very small proportion of HIV positive people the use of abacavir can cause a heart attack. In such cases, it may be prudent for people at high risk for cardiovascular disease to not use abacavir. Some physicians, such as Dr. Peter Reiss, a member of DAD’s steering committee, have suggested that even HIV positive people who have moderate cardiovascular disease risk factors should avoid abacavir. Unfortunately, there does not seem to be widespread international consensus or clarity about exactly what to do about abacavir and its potential for causing heart attacks.

Bear in mind that other anti-HIV drugs could also have side effects. For instance, tenofovir could be used to replace abacavir. Tenofovir can cause kidney dysfunction, which in turn reduces the ability of this organ to retain the body’s calcium. Over the long term, reduced calcium could lead to thinning bones. This has been the case in another study presented at the 16th CROI.

The above example shows the complexity of decision-making that people with HIV and their physicians are grappling with now and in the future.

There are trends in DAD that suggest the possibility of finding of an increased risk of heart attack with other anti-HIV drugs in the future, if these trends continue. As DAD, the FHDB and other studies accumulate more participants over longer periods of time their conclusions will be closely watched in the years ahead.

**Dangerous liaisons**

Although researchers may disagree about the importance of findings from observational studies about HAART and heart attacks, what nearly every leading HIV researcher who studies cardiovascular disease in people with HIV
agrees upon is this: Traditional risk factors for heart attacks and stroke play a huge role in causing these problems. So rather than rushing to dump HAART, a good first step would be to reduce or eliminate traditional risk factors for heart attack, at least the ones that can be changed, such as:

- smoking tobacco
- abnormal cholesterol levels – high concentrations of bad cholesterol (LDL) and low concentrations of good cholesterol (HDL)
- excess weight
- excessive levels of belly fat
- diabetes
- higher-than-normal blood pressure
- not enough exercise
- poor diet

As mentioned earlier in this issue of TreatmentUpdate, that researchers in California have found that heart attack rates can fall to near-normal levels in HIV positive people shows that the risk of heart attacks can be reduced despite the use of protease inhibitors.

REFERENCES:


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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.

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