

(AEGiS) Transplanted livers and kidneys for HIV+ people

(from the 8th Conference on Retroviruses and Opportunistic Infections)

Although use of highly active antiretroviral therapy (HAART) has reduced death rates from many of the infections associated with AIDS in North America, Western Europe and Australia, people with HIV/AIDS (PHAs) are dying in increasing numbers from complications due to severe liver and kidney damage. Some of this damage may be due to the long-term toxicities of HAART, long-term hepatitis B or C infection and/or substance use, including alcohol.

PHAs with severely damaged liver and kidneys have not historically been given high priority for scarce transplant-ready organs. In part, this is because PHAs have been viewed as having a shorter-than-average lifespan because of their weakened immune systems. Another reason is that in order for transplanted organs to survive, recipients have to use drugs such as cyclosporine (Neoral, Sandimmune), tacrolimus (FK 506, Prograf) and CellCept (mycophenolate mofetil). These drugs prevent the immune system from attacking or "rejecting" the transplanted organs. In doing so, transplant drugs also weaken the immune system's ability to fight infections and cancers. Researchers therefore thought that transplant drug would increase the damage caused by HIV infection and speed up the decline of the immune system.

The availability of HAART has clearly prolonged survival in PHAs who are able to tolerate and adhere to such treatment, removing one possible barrier to transplants for such people. There are still issues of safety around the interaction between transplant drugs and HAART that need to be considered. To study these issues, researchers in San Francisco have begun a clinical trial of transplanted organs into PHAs.

Research in San Francisco

PHAs who wish to be considered for a liver transplant must have a CD4+ count of at least 100 cells. Those who wish to be considered for a kidney transplant must have at least 200 CD4+ cells. As well as having low viral loads (fewer than 50 copies), subjects cannot have had life-threatening infections/cancers in the past. Researchers reported results on five PHAs who have received organs for the following reasons:

- ◆ livers -- damage due to hepatitis C infection
- ◆ kidneys -- damage due to complications from high blood pressure, diabetes and HIV infection

A total of seven organs (two livers, five kidneys) have been transplanted into five PHAs. In two subjects, their immune systems attacked the new kidneys, and transplant drugs other than cyclosporine were needed. One of these subjects later developed diabetes.

Before the transplants, the average CD4+ count of the group was 510 cells. Five months after transplantation, their counts have fallen on average to 314 cells. These changes in CD4+ cell counts are interesting because results from other experiments on PHAs who did not receive transplants but did get cyclosporine suggest that this drug does, at least in the short term, raise CD4+ cell counts.

Viral loads have all remained below the 50 copy mark and stayed low, even when HAART was temporarily interrupted.

Five months after receiving their transplants, all subjects remain alive. No life-threatening infections/cancers have developed. In one subject who had a liver transplant, hepatitis C recurred and a new liver had to be transplanted as well as a kidney.

Notes on cyclosporine

The most commonly used transplant drug was cyclosporine. The doctors found that PHAs using protease inhibitors have had less-than-normal levels of cyclosporine in their blood. PHAs using non-nukes, such as efavirenz (Sustiva), nevirapine (Viramune) or delavirdine (Rescriptor), tend to have normal cyclosporine levels.

A number of previous studies in HIV negative people have found that in black subjects, particularly women, the body eliminates cyclosporine faster than in white subjects. The reason(s) this happens is not clear but may prompt physicians to carefully monitor and adjust cyclosporine levels in black women.

The drugs lovastatin (Mevacor) and pravastatin (Pravachol) are used to help lower levels of fatty substances - cholesterol and triglycerides -- in the blood and thus reduce the risk of cardiovascular disease. In experiments of HIV negative people using cyclosporine, researchers have found that levels of lovastatin quickly build up, a situation that could lead to serious side effects. Pravastatin levels do not appear to be significantly affected by cyclosporine.

There are recent reports that the herb St. John's wort lowers levels of cyclosporine in the blood. Therefore, people using cyclosporine should not take St. John's wort.

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