Kidney transplants and HIV—the American experience

Researchers at transplant centres across the United States performed kidney transplants in HIV-positive people and subsequently monitored them for three years. At the end of this time, survival rates were about 88%. This rate is relatively high and there were no increased reports of AIDS-related illnesses. However, there were greater-than-expected cases of the immune systems of the transplant recipients attacking or “rejecting” the donated organ.

Study details

Between 2003 and 2009, researchers at 19 clinics enrolled 150 HIV-positive people for kidney transplantation. Prior to transplantation, participants were required to have the following:

- need for a kidney transplant
- at least 200 CD4+ cells
- an HIV viral load of 75 copies/ml or less while on HAART 16 weeks before transplantation

Different transplant centres had additional criteria for participants who wished to receive a transplant. Participants who had the following specific life-threatening infections in the past were excluded from the study:

- PML (progressive multifocal leukoencephalopathy)
- Crypto (Cryptosporidiosis)
- Lymphoma in the brain or spinal cord
- Kaposi’s sarcoma that affected internal organs

At the start of the study, the basic profile of participants was as follows:

- 78% men, 22% women
- common causes of kidney damage – higher-than-normal blood pressure, HIV-related kidney damage, diabetes
- CD4+ count – 524 cells
- HCV co-infection – 19%
- HBV co-infection – 3%

Results

During the first week after transplantation participants received intense immunosuppression with a combination of two or more of the following drugs:

- mycophenolate (CellCept) – 87% of participants
- tacrolimus (Prograf) – 66% of participants
- basiliximab (Simulect) or daclizumab (Zenapax) – 51%
- anti-T-cell antibodies – 32%
- cyclosporine (Neoral, Sandimmune) – 22%

Survival

Transplantation is a major procedure and is often done in patients who are very ill, so there is always a risk of serious complications and not every person is guaranteed survival. In the present study, it is not surprising that some HIV-positive organ recipients eventually passed away. Survival rates after transplantation were as follows:

- at one year – 95% were alive
- at three years – 88% were alive
Researchers described these survival rates as being “generally between those for older [HIV-negative] kidney transplant recipients (those who were 65 years or older) and for all kidney transplant recipients during a similar time frame.”

**Causes of death**

In total, 11 people died from the following causes:

- cardiovascular complications – three people
- blood poisoning from severe infections – two people
- lung infections – two people
- kidney cancer (in the recipients’ original kidneys) – two people
- unknown cause(s) – two people

The researchers noted that the transplanted organs were still working when eight of these 11 people died.

**Grafts**

Transplanted organs and tissues are sometimes called grafts. In 13 people the grafts died mostly because the recipients’ immune systems kept attacking the new kidneys. Analysis of many factors suggested that the following likely played a role in the demise of the grafts:

- needing to treat the recipient for episodes of graft rejection
- using anti-T-cell antibodies during initial immunosuppression following transplantation

Receiving a graft from a living donor was more likely to result in the graft’s survival.

**Rejection**

Transplant centres do their very best to find immunologically similar donors and recipients. Yet the host’s immune system can still attack the new organ, in the case of this study, the kidney. Such attacks are called rejection.

Episodes of rejection that occur during the first three months following a transplant are called acute rejection (though some cases of acute rejection can occur later). Among transplant recipients, 33% had episodes of acute rejection.

A single episode of rejection does not usually lead to the loss of a transplanted organ. However, if not properly controlled by immunosuppressive agents, acute rejection can recur and become chronic rejection.

In total, the proportion of participants who experienced rejection was as follows:

- during the first year after transplant – 31%
- by the third year after transplant – 41%

These rates of rejection puzzled the research team because they are greater than seen in elderly HIV-negative people.

Taking many factors into account, the only statistically significant events associated with an increased risk for rejection were as follows:

- receipt of a kidney from a dead donor
- use of cyclosporine

**Delayed graft functioning**

Even though a new kidney is transplanted and reconnected to blood vessels, it may not immediately begin working; this is called delayed graft function. This problem occurred during the first week after transplant in 15% of people who received an organ from a living donor and in 46% of people who received an organ from a deceased donor. In cases of delayed graft functioning, temporary use of dialysis was necessary.
HIV-related disease and lab tests

After transplantation, because immunosuppressive drugs are used, a few people developed HIV-related illnesses, as follows:

- Kaposi’s sarcoma (KS) tumours on the skin – two people
- yeast infections of the throat – one person
- PCP (Pneumocystis pneumonia) – one person
- Crypto (Cryptosporidiosis) – one person

The researchers found that changes in CD4+ cell counts were “significantly greater in patients who received early therapy with [anti-T-cell antibodies] compared to people who did not.” Overall, three years after transplantation, there were no clinically meaningful differences in CD4+ cell counts between people who had received these particular antibodies and those who had not. And, overall, after three years, CD4+ cell counts had fallen by about 50 cells regardless of exposure to anti-T-cell antibodies.

HIV viral load was suppressed in most participants; in 48 people it became detectable but mostly just once or twice. Only one person had a detectable viral load three years after transplantation.

Serious infections

Of the 150 transplant recipients, nearly 40% developed 140 episodes of infection that required them to be hospitalized. These infections were classified as follows:

- bacterial – 69% of cases
- fungal – 9% of cases
- viral – 6% of cases
- parasitic – 1% of cases

In the remaining cases, researchers weren’t certain about the cause(s) of infection.

Common sites in the body affected by serious infections included the following:

- genitourinary tract
- lungs and throat
- blood

The majority of serious infections occurred within six months of transplantation.

Infections were more common among people co-infected with hepatitis C virus.

Cancers

A total of nine cancers were reported as follows:

- KS – two cases
- kidney cancer – two cases
- oral cancer – two cases
- squamous-cell skin cancer – one case
- basal-cell skin cancer – one case
- thyroid gland cancer – one case

Overall

In this relatively large study, the research team stated that its good results were influenced by the following factors:

- careful selection of participants
- adherence to clinical management protocols
- close coordination among care teams that included surgeons, nephrologists, nurse coordinators,
pharmacologists, social workers, HIV experts and primary care doctors

The team found that its greatest challenge was achieving sufficient immunosuppression so that the graft would survive without causing toxicity. This challenge arose because of what the researchers called the “complicated” interaction between immunosuppressive medicines and some anti-HIV drugs, specifically protease inhibitors. In the future, the transplant team may conduct experiments with relatively new anti-HIV drugs such as the integrase inhibitor raltegravir (Isentress), as this drug has a very low potential for drug-drug interactions.

Although tacrolimus-based maintenance immunosuppression may be used in place of cyclosporine to reduce the risk of rejection, the team notes that cyclosporine has modest anti-HIV and anti-HCV activity and may therefore be useful in cases of co-infection.

Rejection

The researchers were concerned by the “unexpectedly higher rejection rates (by a factor of 2 to 3) in the HIV-infected kidney recipients, as compared with recipients who did not have HIV infection.”

About 50% of these episodes of rejection occurred despite the use of corticosteroids. This resistance to the immunosuppressive properties of steroids is a feature of aggressive rejection. And aggressive rejection often occurred despite low CD4+ cell counts that commonly occur following transplantation. The researchers are not certain about the precise cause(s) driving aggressive episodes of rejection. Several studies are underway to explore possible causes of this problem.

In the future, it is likely that HIV-positive people who will require organ transplants may be very ill with lower CD4+ cell counts and higher viral loads than seen in the present study. Hopefully, transplant protocols will evolve to encompass such people.

REFERENCE:

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