Sirolimus monotherapy after liver transplants

Sirolimus (rapamycin, Rapamune) is an immunosuppressive drug with additional but modest activity against some tumours and HIV. Unlike many other drugs used to suppress the immune system, sirolimus does not damage the kidneys or increase the risk of developing diabetes. Researchers in Italy performed a pilot study of sirolimus as the sole immunosuppressive treatment in HIV-positive people who received organ transplants. Their results are promising but require confirmation in a well-designed clinical trial.

Study details

Researchers enrolled 14 participants (12 men, 2 women), 10 of whom were co-infected with hepatitis B or C viruses. On average, their CD4+ count was 275 cells and HIV viral load was less than 50 copies/ml. On average, they had been on the waiting list for a liver transplant for about eight months. Half of the participants had liver cancer. Using the MELD scoring system, these participants had a 20% chance of dying within three months if they did not receive a liver transplant. HAART was discontinued just before the transplant and resumed about two weeks later.

Results

Immediately following transplantation, immunosuppression with cyclosporine or tacrolimus (Prograf) together with prednisone was prescribed.

In six cases, researchers replaced cyclosporine with sirolimus an average of 67 days after transplantation because of kidney dysfunction (five cases) and the emergence of Kaposi’s sarcoma (KS) lesions on the skin (one case).

In all cases, participants who were switched to sirolimus improved as kidney function returned to normal and KS skin lesions cleared. Moreover, in the person whose KS lesions faded, technicians could no longer detect the virus that causes KS (HHV8; human herpes virus 8) in his blood.

One case of mild acute rejection occurred in a person who was switched to sirolimus but this resolved when additional immunosuppression with methylprednisone was used for 10 days. In contrast, three cases of acute rejection occurred in people who continued to receive cyclosporine or tacrolimus.

After transplantation, hepatitis C virus (HCV) infection became reactivated in seven people, all of whom were taking cyclosporine or tacrolimus. Two other people who had HCV and were taking sirolimus had this co-infection clear.

Survival

Four people died—two taking cyclosporine or tacrolimus and two taking sirolimus. In the latter cases, death ensued because of complications from severe fungal and bacterial infections. Among people who died while taking cyclosporine or tacrolimus, heart failure and severe bacterial infections were the causes of death. After 50 months of observation, survival rates of participants on sirolimus or tacrolimus/cyclosporine were similar—about 68%.

Side effects

Sirolimus can cause side effects such as elevated levels of cholesterol and triglycerides in the blood. Ultimately these can increase the risk for cardiovascular disease. In all cases, treatment with lipid-lowering medications resolved this issue.

The findings from this study should be treated with caution, as this was not a randomized controlled trial, so inadvertent confounding when interpreting the data is a possibility. As a result, researchers cannot be certain that sirolimus provided additional benefits to people.

REFERENCES:


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