Cholesterol-lowering drugs also may protect stem cell transplant patients from GVHD

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Cholesterol-lowering drugs known as statins are among the most prescribed medicines in the U.S. Now a new study by researchers at Fred Hutchinson Cancer Research Center indicates that statins may protect stem cell transplant patients from one of the most serious complications of the life-saving cancer therapy: graft-versus-host disease, or GVHD. The findings are reported in the Nov. 4 first edition of the journal *Blood*.

In a retrospective study of 567 patients who underwent hematopoietic cell transplantation from matched sibling donors between 2001 and 2007, patients whose donors had been taking statins at the time of stem cell donation experienced no severe acute GVHD. About 15 percent of the stem cell donors in the study were taking statins at the time of transplant.

Normally, between 10 percent and 15 percent of transplant patients would be expected to develop severe acute GVHD, according to the study's senior author Marco Mielcarek, M.D., an assistant member of the Hutchinson Center's Clinical Research Division.

No such protection from severe acute GVHD was observed if only the patient was taking a statin, according to the study. There was some indication that protection against severe GVHD was even stronger when both patient and donor had been on statin medications, however the number of patients in this group was too small to be statistically significant.

The researchers also found that only those transplant patients with statin-treated donors who received cyclosporine-based immunosuppression therapy after transplantation were protected from severe GVHD. Patients with statin-treated donors who received a similar drug, tacrolimus, did not experience the same GVHD-protection. The study also found that the greatest statin protection occurred against severe GVHD of the gastrointestinal tract.

GVHD is a common side effect in patients who receive blood stem cell transplants from related or unrelated donors. It occurs when the transplanted cells recognize the recipient's tissues as foreign and attack the tissues. This can cause a variety of problems, including skin rashes, diarrhea and liver inflammation. Acute GVHD often occurs in the first three months after a transplant and can lead to mortality as high as 50 percent if it is severe. It can be deadly because patients require more immunosuppressive drugs to treat it, which can trigger a cascade of complications such as secondary infections.

Mielcarek, first author Marcello Rotta, M.D., a postdoctoral research fellow in the Hutchinson Center's Clinical Research Division, and colleagues undertook the study because previous research showed that statins have anti-inflammatory effects and have been found to improve control of other inflammatory diseases such as rheumatoid arthritis. Recently, studies using mouse models of stem cell transplantation have shown protection against lethal acute GVHD when the donors and recipients had been treated with statins before transplant.

The exact mechanism of how statins protect against GVHD is not known.

"In the literature, a multitude of possible mechanisms are discussed by which statins may influence immune function," Mielcarek said. "One is cell adhesion - the stickiness of cells that influences how donor T cells

that cause GVHD can migrate to certain target tissues. Another is how statins interfere with intracellular signaling in T cells. Statins may dampen the activity of allo-reactive T cells and prevent them from initiating the inflammatory cascade that's required to cause GVHD."

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Source: Fred Hutchinson Cancer Research Center (news : web)