'Mini' transplant may reverse severe sickle cell disease

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Results of a preliminary study by scientists at the National Institutes of Health and Johns Hopkins show that "mini" stem cell transplantation may safely reverse severe sickle cell disease in adults.

The phase I/II study to establish safety of the procedure, published December 10 in the New England Journal of Medicine, describes 10 patients with severe sickle cell disease who received intravenous transplants of blood-forming stem cells. The transplanted stem cells came from the peripheral blood of healthy related donors matched to the patients' tissue types.

Using this procedure, nine of 10 patients treated have normal red blood cells and reversal of organ damage caused by the disease.

Jonathan Powell, M.D., Ph.D., associate professor at the Johns Hopkins Kimmel Cancer Center, says the intravenous transplant approach for sickle cell disease, caused by a single mutation in the hemoglobin gene, does not replace the defective gene, but transplants blood stem cells that carry the normal gene.

Sickle cell disease, named for the "deflated" sickle-shaped appearance of red blood cells in those with the disease, hinders the cells' ability to carry oxygen throughout the body. In severe cases, it causes stroke, severe pain , and damage to multiple organs, including the lungs, kidneys and liver.

All patients in the study, ranging in age from 16 to 45, were treated at

the NIH with what researchers call a non-myeloablative or "mini" transplant, along with an immune-suppressing drug called rapamycin.

Conventional transplant methods use high doses of chemotherapy to wipe out the immune system before the transplanted cells are injected, a process that has many side effects, including serious bacterial and fungal infections, which may kill some patients. In mini-transplants, lower doses of medication and radiation are used to make room for the donor's cells, the new source for healthy red blood cells in the patient.

According to Powell, side effects, including low white blood cell counts, were few and very mild compared with conventional bone marrow transplantation. But in nine of the 10, donor cells now coexist with the patients' own cells. One patient was not able to maintain the transplanted cells long term.

Minitransplants for sickle cell disease were tested in patients almost a decade ago, but were unsuccessful because the patients' immune systems rejected the transplanted cells, according to Powell, but by employing the drug rapamcyin, he says this new approach promotes the coexistence of the host and donor cells.

Powell's earlier research in mice showed that rapamycin inhibits an enzymatic pathway that suppresses the immune system and makes the host and donor cells tolerant to each other.

The NIH/Johns Hopkins team is conducting further studies on immune cells gathered from patients in their study, and looking at a combination of rapamycin with a well-known cancer drug called cyclophosphamide.

Other teams at Johns Hopkins are studying the use of half-matched donors for transplants in sickle cell patients, helping to widen the pool of potential donors for stem cell transplantation.

Source: Johns Hopkins Medical Institutions