Clinical trial demonstrates safety of pre-transplant expansion of umbilical cord blood stem cells

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Taking blood stem cells collected from an umbilical cord into the lab and expanding their number before transplanting them to replace a patient's blood supply is as safe as a standard cord blood transplant, researchers reported today at the 50th Annual Meeting of the American Society of Hematology.

In a first-of-its-kind randomized clinical trial, researchers at The University of Texas M. D. Anderson Cancer Center are addressing the critical challenge to successful "standard" cord blood transplants for adult patients - low doses of stem cells that lead to longer recovery times, leaving patients more vulnerable to bleeding, infection and transplant failure.

"The major determinant of success in a cord blood transplant is cell dose. A higher dose minimizes early complications and speeds establishment of the new blood supply," said study presenter Marcos de Lima, M.D., associate professor in M. D. Anderson's Department of Stem Cell Transplantation and Cell Biology.

The clinical trial randomized 71 patients with advanced leukemias or lymphomas into either a standard cord blood transplant, in which a patient receives blood stem cells from two umbilical cords, or to a second group that receives regular cells from one cord plus cells from a second cord that were exposed to growth factors in the lab to expand

their number.

"So far, we've shown that this expanded stem cell technique is safe and comparable to the usual double-cord transplant," de Lima said.

"There are some interesting trends pointing toward possible improved engraftment and survival in the patients who receive the expanded cord blood cells, but these are preliminary and not statistically significant at this point," de Lima said.

Patients with recurrent, high-risk acute myeloid leukemia, acute lymphocytic leukemia, chronic myelogenous leukemia, many types of lymphoma, aplastic anemia and other genetic and immunologic disorders require blood stem cell transplants to rebuild their blood supply after intense chemotherapy or as a therapeutic attack on their disease.

A transplant of bone marrow-derived stem cells from a perfectly matched donor is the optimum course of treatment because a large volume of cells is transplanted, leading to rapid engraftment and fewer side effects. Finding a required perfect match of six human leukocyte antigen (HLA) genes between donor and patient can be prohibitively difficult.

Cord blood stem cells are easily collected, readily available, and do not require a perfect HLA gene match due to their immaturity. "Clinical trials have shown that cord blood transplants are most effective in pediatric patients and small adults, because the number of stem cells provided by two cords is limited," de Lima said.

Previous research has shown that adding stem cells from a third umbilical cord not only doesn't help, but increases the likelihood of transplant failure.

In all double-cord blood transplants, one of the two blood types ultimately becomes the patient's sole blood supply. In half the patients who received expanded cord blood cells in the trial, de Lima noted, the expanded stem cells were predominant for the first 2-12 months after transplant, but by 14 months, the cells from the unexpanded cord become dominant.

"We hypothesize that expanding cord blood stem cells in this way gives them greater short-term capacity to grow quickly but also makes them differentiate so they start to lose their stem cell profile," de Lima explained. The expanded cells may help initially while the cells from the other unit slowly but surely take over.

Expanding stem cells by exposing them to growth-promoting cytokines led to a median 23-fold expansion of cells, however, the range of fold-expansion varied greatly, from a .44 increase to a 275-fold increase. "Some cords expand very well and others don't. That remains a challenge," de Lima said. The clinical trial will enroll up to 100 patients.

The study's senior scientist, Elizabeth Shpall, M.D., professor in Stem Cell Transplantation and Cell Biology, has opened a new phase II study that involves growing the cord blood stem cells on a framework of supportive mesenchymal stromal cells while exposing them to growth-promoting cytokines. This approach might more closely simulate the bone marrow microenvironment where stem cells are produced, de Lima said.

Source: University of Texas M. D. Anderson Cancer Center