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Clinical Applications of Blood-Derived and Marrow-Derived Stem Cells for Nonmalignant Diseases

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Context Stem cell therapy is rapidly developing and has generated excitement and promise as well as confusion and at times contradictory results in the lay and scientific literature. Many types of stem cells show great promise, but clinical application has lagged due to ethical concerns or difficulties in harvesting or safely and efficiently expanding sufficient quantities. In contrast, clinical indications for blood-derived (from peripheral or umbilical cord blood) and bone marrow–derived stem cells, which can be easily and safely harvested, are rapidly increasing.

Objective To summarize new, nonmalignant, nonhematologic clinical indications for use of blood- and bone marrow–derived stem cells.

Evidence Acquisition Search of multiple electronic databases (MEDLINE, EMBASE, Science Citation Index), US Food and Drug Administration [FDA] Drug Site, and National Institutes of Health Web site to identify studies published from January 1997 to December 2007 on use of hematopoietic stem cells (HSCs) in autoimmune, cardiac, or vascular diseases. The search was augmented by hand searching of reference lists in clinical trials, review articles, proceedings booklets, FDA reports, and contact with study authors and device and pharmaceutical companies.

Evidence Synthesis Of 926 reports identified, 323 were examined for feasibility and toxicity, including those with small numbers of patients, interim or substudy reports, and reports on multiple diseases, treatment of relapse, toxicity, mechanism of action, or stem cell mobilization. Another 69 were evaluated for outcomes. For autoimmune diseases, 26 reports representing 854 patients reported treatment-related mortality of less than 1% (2/220 patients) for nonmyeloablative, less than 2% (3/197) for dose-reduced myeloablative, and 13% (13/100) for intense myeloablative regimens, ie, those including total body irradiation or high-dose busulfan. While all trials performed during the inflammatory stage of autoimmune disease suggested that transplantation of HSCs may have a potent disease-remitting effect, remission duration remains unclear, and no randomized trials have been published. For reports involving cardiovascular diseases, including 17 reports involving 1002 patients with acute myocardial infarction, 16 involving 493 patients with chronic coronary artery disease, and 3 meta-analyses, the evidence suggests that stem cell transplantation performed in patients with coronary artery disease may contribute to modest improvement in cardiac function.

Conclusions Stem cells harvested from blood or marrow, whether administered as purified HSCs or mesenchymal stem cells or as an unmanipulated or unpurified product can, under appropriate conditions in select patients, provide disease-ameliorating effects in some autoimmune diseases and cardiovascular disorders. Clinical trials are needed to determine the most appropriate cell type, dose, method, timing of delivery, and adverse effects of adult HSCs for these and other nonmalignant disorders.

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