Hypothesis

Are Endometrial Stem Cells Novel Tools against Ischemic Heart Failure in Women? A Hypothesis

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Abstract

Recently stem cell therapy has suggested novel therapeutic strategies for management of heart failure and myocardial infarction. Our aim was to show that endometrial stromal cells produce a higher overall clonogenicity with a high angiogenesis potential. In addition, they may be converted into osteoblasts, odentoblasts, chindroblasts, neuroblasts and myoblasts and can be used for cell therapy as autologous and heterologous transplantations in future studies.

Keywords: Endometrium; Stem cell; Ischemic heart disease

Introduction

Ischemic heart disease or myocardial ischemia is a disease characterized by reduced blood supply to the heart muscle, usually due to coronary artery disease. Therapeutic approaches mostly aim to restore blood flow to a localized segment by angioplasty or bypass surgery.[1] Therapeutic angiogenesis and/or arteriogenesis describe a strategy where blood vessel formation is induced for the purposes of treatment and/or prevention of ischemic disease.[2] Previously, it was believed that the heart lacked the capacity to renew itself but recently new insights into the mechanisms of cardiac repair have provided evidence that the adult heart can repair itself through intricate mechanisms that include proliferation of cardiac precursor cells and recruitment and engraftment of bone marrow-derived precursor cells.[3] The current investigations demonstrate that transplantation of autologous bone marrow stem cells can improve cardiac function.[4] Some studies did not show higher angiogenesis in the bone marrow stem cells transplantation group but combined autologous cellular therapy induced both myogenesis and angiogenesis with enhancement of cardiac performance and reduction of cardiac remodelling, suggesting a capable strategy for treatment of severe ischemic cardiomyopathy.[5] Autologous bone marrow therapy for ischemic heart failure appears to be a promising solution to the current lack of treatment in patients ineligible for endovascular/surgical interventions.[6] However, this is limited by the need for anesthesia during the bone marrow extraction procedure, which is dangerous in the ischemic heart failure people.

Angiogenesis occurs regularly in the endometrium throughout the reproductive life of females as part of the rapid growth and regression of this tissue occurring during the menstrual cycle. It is now clearly evident that angiogenesis plays a key role in the reproductive processes such as embryo implantation, and endometrial regeneration after menstruation. Evidence is reviewed for the hypothesis that the endometrium in women has a high capacity of cell proliferation, and angiogenesis.[7] Endometrial layers contain a population of stromal (stem) cells and these would exhibit stem-cell activity.[8] CD146 is a marker of colony-forming human endometrial stromal cells, supporting the concept that human endometrium contains a population of candidate stromal stem/progenitor

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cells.[9] Recently, the induction of an angiogenic phenotype in human endometriotic cells has been shown by the establishment of their ability to implant.[10] 3-D culture allows the quantification of cell proliferation and angiogenesis from endometrial stromal cells.[11]

In addition, recent investigations demonstrated that some stem cells such as CD117, CD34 and Oct-4, a transcription factor crucial for stem cell pluripotency, are expressed throughout the menstrual cycle in human endometrial stroma[12,13]. On the other hand, some degree of similarity exists between endometrial stem cells and bone marrow derived mesenchymal stem cells, for example, expression of CD90, CD105 and lack of CD45 and CD34.[14]

Hypothesis

Recently, stem cell therapy has offered novel therapeutic strategy for the management of heart failure and myocardial infarction. Although cell therapy via bone marrow stem cell transplantation is promising, there are some concerns about the outcome and complication of this method. Based on the mentioned points, it can be postulated that stem cell therapy through application of endometrial stem cells can open a new horizon for the treatment of such cardiac disorders with lesser degree of complications and better efficacy and outcome.

Discussion and future directions

Evaluation of Hypothesis

The hypothesis can be evaluated by using flow cytometery for counting endometrial stem cells that are isolated from endometrium and immunohistichemistry staining for the detection of stem cell markers such as STRO-1, CD146, CD90, CD133, CD117, and Oct-4. The next step in this case would be comparing the treatment process in ischemic heart failure patients receiving endometrial stem cells as autologus with ischemic heart failure patients receiving bone marrow stem cells as autologus transplantation.

Endometrial Stem Cell vs. Bone Marrow Stem Cell

Theoretically, the application of endometrial stem cells in the treatment of ischemic heart failure can be more beneficial than that of bone marrow stem cells due to some reasons.

First, it is limited by the need for anesthesia during the bone marrow extraction procedure, which is dangerous in the ischemic heart failure people.[6] Second, endometrial stromal cells produce a higher overall clonogenicity of 1.25%, only 1 in 1400–5000 formed large colonies, similar to endometrial epithelial cells. In comparison with the bone marrow stem cell clonogenic activity, this is quite substantial, as only 1 in 10,000 is clonogenic.[15]

The next reason is that purification of bone marrow stem cells is notoriously difficult since there are no stem cell-specific markers. Various markers or combinations of markers are used to isolate [the] bone marrow stem cells. However, none has been able to isolate a pure bone marrow stem cell population. Hence, the precise phenotypic identity of bone marrow stem cells remains unknown.[16]

Finally, the application of endometrial stromal cells for this indication is the possibility of administering allogeneic, standardized cell populations.[16] To explain this process, it was proposed that progenitor cells are present in the basal layer of human endometrial layer and endometrial stem cells have been isolated from samples consisting of both functional and basal layers of the endometrial layer,[17] showing that these cells can be used as cell therapy even in post-menstrual women.

Previous studies involving long term follow up of animals treated with endometrial stromal cells, as well as karyotypic normality of these cells after extended passage (68 doublings) have demonstrated lack of tumorogenicity. Endometrial stromal cells represent a unique population and their proliferation rate is approximately once every 19 hours.[18]

Future Direction

Endometrial stromal cells produce a higher clonogenicity with a higher angiogenetic potential. In addition, they can be converted into osteoblast, odentoblast, chondroblast, neuroblast and myoblast to be used in autologus and heterologus cell therapies in future.

Conflict of interest: None declared.

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