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Stem Cell Therapy in Cardiovascular Diseases

Kardiyovasküler Hastalıklarda Kök Hücre Tedavisi

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Abstract

The majority of heart diseases, especially myocardial infarction, have high mortality and morbidity. Surgical operation and transplantation are common treatment methods for these diseases. Stem cells are specialised cells with high regenerative ability and the ability to transform into different cells and tissues. In the past years, it was argued that there was no regeneration in the heart, but stem cell therapy has emerged as a new hope in cardiovascular system diseases with the discovery that cardiomyocytes renew themselves and that there are cells with telomerase activity that show c-Kit, Sca-1 stem cell markers. Experimental studies show that especially in myocardial infarction model regeneration is observed in the damaged area after stem cell transplantation. As a result, stem cell therapy has started to be used for therapeutic purposes in our country, but since it is a new method, it has not yet gained widespread use. In addition, it is thought that more scientific studies on cardiac stem cells are needed both experimentally and clinically.

Keywords: Cardiovascular, Diseases, Stem Cell.

Özet

Başta myokart enfarktüsü olmak üzere kalp hastalıklarının büyük bir kısmı, Yüksek mortalite ve morbiditeye sahiptir. Bu hastalıklar için cerrahi operasyon ve transplantasyon yaygın tedavi yöntemlerindendir. Kök hücre, yenilenme yeteneği yüksek olmasının yanı sıra farklı hücre ve dokulara dönüşebilme yeteneğine sahip özelleşebilir hücrelerdir. Geçmiş yıllarda, kalpte yenilenme olmadığı savunulan görüş, kardiyomiyositlerin kendilerini yeniledikleri ve bünyesinde c-Kit, Sca-1 kök hücre markırlarını gösteren, telomeraz aktivesine sahip hücreler olduğunun bulunmasıyla kardiyovasküler sistem hastalıklarında kök hücre tedavisi yeni bir umut olarak belirmiştir. Yapılan deneysel çalışmalar, özellikle myokart enfarktüsü modelinde kök hücre nakli sonrasında oluşan hasarlı bölgede yenilenmelerin gözlendiğini göstermektedir. Sonuç olarak kök hücre tedavisi ülkemizde de tedavi amaçlı kullanılmaya başlanmış olmakta, fakat yeni bir yöntem olduğundan henüz yaygınlık kazanmamıştır. Ayrıca kalp kök hücreleri üzerine gerek deneysel gerekse klinik olarak daha bilimsel çalışmalara ihtiyaç bulunduğu düşünülmektedir.

Anahtar Kelimeler: Kardiyovasküler, Hastalıklar, Kök Hücre.

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INTRODUCTION

The cardiovascular system (circulatory system) originates from the mesoderm and blood cells from primitive blood cells in the splanchnic mesoderm of the vitellus sac. These blood cells that start to form form blood islets. Mesenchyme cells around these blood islets turn into endothelial cells to form vessels and short tubes begin to form, then these short tubes form vessels (1). The cardiovascular system is a closed system in which the blood is distributed throughout the body. Thanks to this system, clean blood is taken to all tissues and organs and the dirty blood used is brought back to the heart to be cleaned. (2).

Cardiovascular system diseases are one of the most common causes of death worldwide. Even if it does not result in death, arrhythmias in this system disorder are among the important reasons affecting the quality of life (3).

What is a Stem Cell?

Stem cells are specialised cells with high regenerative ability and the ability to transform into different cells and tissues. These cells are first formed in the embryonic period and then contribute to the formation of our tissues and organs. In other words, embryonic stem cells, which form the basis of the living body, are the first known stem cells. Stem cells have high telomerase capacity, as in cancer cells (4,5). At birth, embryonic stem cells transform into adult stem cells. Adult stem cells don't regenerate the tissue or organ like embryonic stem cells, but undertake tasks such as renewal and repair (4). The most important characteristics of stem cells are their ability to specialise and differentiate, and because of this ability they can transform into more than one cell type (6,7). According to these differentiation abilities, stem cells are classified as totipotent, pluripotent, multipotent, oligopotent and unipotent (8). In general, there are three types of stem cells. These are totipotent, pluripotent and multipotent stem cells. Cells that can differentiate into all tissues and organs of the body and also have the ability to differentiate into non-embryo tissues such as placenta and amniotic sac membranes are called totipotent cells. These cells are obtained from blastomere cells in the pre-blastocyst stage (9). In mammals, the two-celled, four-celled, eight-celled and morula stage cells that are formed by early cleavage divisions of the embryo from the zygote are examples of totipotent cells capable of forming a complete organism. Fertilised oocytes and blastomeres can't be defined as stem cells. Because their formation is limited during early cleavage division. As a result, although they have the capacity to form a complete organism, they are unable to regenerate themselves.(10). Pluripotent cells are embryonic stem cells that can develop into tissues and organs of the foetus but have lost their ability to form extra embryonic tissues (9). They are obtained from the inner cell mass of the 5-6 day old blastocyst. Although these cells can be the source of all tissues in the body and cells that support pregnancy, they are not capable of forming a new individual (6). Multipotent cells are cells from a more advanced stage of development and can differentiate into specialised cell types. Cord blood cells and adult stem cells are multipotent cells (9). Pluripotent or multipotent stem cells give rise to progenitor cells that will later differentiate into specific cell lines (7). Transitional cells in different stages of differentiation between stem cells and differentiated cells are called differentiating transitional cells (11).

Stem Cell Treatment

Stem cell therapy started in 1878 with egg cell fertilisation, which is the first steps of invitro fertilisation, which is widely used today, and continued to develop rapidly in the following years as studies revealing the embryonic development of cells in invitro cultures (12). In the late 90s, the first embryonic stem cells were obtained from animals (12,13). Stem cells were

initially used in cancer patients for treatment purposes, and their effectiveness was investigated in studies to destroy cancer cells with differentiated cells obtained from stem cells (14). Today, stem cells are being used to treat rheumatoid arthritis, diabetes, Graft versus Host Disease, muscular dystrophy, autoimmune diseases (15, 16).

In order to obtain an effective result in stem cell therapies, the number of cells to be used should be well calculated, the minimum number of cells required for treatment and the criteria for determining this number should be well known (17).

Stem Cell Usage in Cardiovascular Diseases

Although the mechanisms of cardiovascular diseases have been rapidly elucidated with the development of science and technology, the search for alternative treatments other than medical and organ transplantation for these diseases continues (18).

Cardiomyocytes, vascular endothelial cells and vascular muscle cells are the cells responsible for cardiac function. Whether the mammalian heart is capable of regeneration or not, and if so, whether this ability may be limited, has been a subject of debate in the past years. However, recent studies have cleared the question marks in this direction (4, 19, 20). Although regeneration is not as rapid as in other tissue types, it has been reported that cardiomyocytes regenerate themselves in an adult heart and are telomerase-activated cells that show c-Kit, Sca-1 stem cell markers (19). In parallel with these developments, stem cells have started to be used in the treatment of heart diseases, and the prognosis of diseases has started to be evaluated by applying appropriate number of cells to appropriate patient profiles (21, 22). Mesenchymal stem cells, embryonic stem cells, pluripotent stem cells and cardiac stem cells can be used in the treatment of myocardial infarction (23,24). Stem cells can be applied directly to the damaged area, or when administered intravenously, they go to the target area and stop hypertrophic and thickened cell death and repair the damaged area (25). Yerebakan ve ark. (22) reported that stem cell therapy was applied to patients with myocardial infarction in coronary artery bypass surgery and reliable results were obtained in the long term. There are studies suggesting that mesenchymal stem cells administered after myocardial infarction reduce the area of scar tissue and the number of apoptotic cells (26, 27, 28, 29).

Orlic ve ark (30), experimentally applied haematopoietic stem cells for scar tissue healing in mice with myocardial infarction and observed that a new myocardium was formed as a result of this application. It has been reported that more than half of the scar tissue is regenerated in nine days after application.

CONCLUSION

Although not as much as in other organs and tissues, studies have recognised that the heart also has renewable and specialisable cells. The alternative of treatment with differentiated cells derived from stem cells in patients with myocardial infarction and heart failure will provide an advantage over surgical operations and organ transplantation in these diseases. It is thought that stem cell therapies may be possible as an alternative and more effective treatment for cardiovascular system diseases with high mortality and morbidity rates in recent years, but since these methods are very new, more experimental and clinical studies are needed.

Conflict of interest and funding disclosure

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Author Contributions

Working Concept / Design	**:** ÖG, MD
Data collecting	**:** ÖG, MD
Data Analysis / Interpretation	**:** ÖG, MD
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