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Review

Exploring the Regenerative Potential of Stem Cells for Treating Eye Diseases: A Review of the New Findings

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Abstract

The escalating prevalence of vision loss due to eye diseases has instigated a quest for innovative therapies, given that conventional approaches often fall short in repairing and regenerating damaged eye tissues, particularly the retina. Stem cell-based interventions have emerged as a promising avenue, with numerous studies in animal models and human trials exploring their potential to enhance visual acuity. Beyond addressing conditions like age-related macular degeneration (AMD) and diabetic retinopathy (DR), stem cell therapies demonstrate efficacy in treating genetic disorders such as retinitis pigmentosa (RP). In severe eye damage necessitating regeneration, stem cells play a pivotal role, leveraging their regenerative capabilities. Noteworthy is the transplantation of retinal pigment epithelial (RPE) cells derived from embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs), showcasing promising results in preclinical models and clinical studies, leading to improved retinal function without severe side effects. Mesenchymal stem cells (MSCs) have successfully treated optic neuropathy, RP, DR, and glaucoma, yielding positive clinical outcomes. The safety of adult stem cells, particularly MSCs derived from adipose tissue or bone marrow, has been firmly established. This review highlights significant advancements in utilizing human ESC-derived retinal pigmented epithelium and iPSCs for treating eye injuries. While cell-based therapy is relatively nascent, with numerous clinical trials pending review, stem cells'

regenerative potential and clinical applications in addressing eye diseases offer substantial promise. This study aims to comprehensively examine the applications of stem cells in the context of eye diseases and their potential role in regenerative medicine.

Keywords
Cell-based therapy; eye diseases; mesenchymal stem cells; human embryonic stem cells; inducible pluripotent stem cells

1. Introduction

There is a lack of effective therapies available for certain eye diseases that can cause loss of connectivity within the visual system. As a result, it is crucial to discover a treatment approach that is both safe and effective while minimizing side effects [1]. Stem cells have emerged as a promising technology for treating eye diseases because they can develop into any type of cell within an organism [2]. Their unique capacity for self-renewal and differentiation makes them an ideal candidate for regenerative therapies. Among the most promising stem cells for cell-based therapies are mesenchymal stem cells (MSCs) [3]. MSCs are known for their ability to differentiate into multiple cell types, high migratory and immunomodulatory capacities, and low immunogenicity activity. Recent studies have shown that MSCs could potentially restore certain eye diseases, making them an advanced technology with therapeutic applications [4]. This review study examined different types of stem cells based on their origin and differentiation abilities. Additionally, we will explore the general mechanisms of MSC action in the repair process and investigate the potential of MSCs for treating eye diseases.

2. Various Types of Stem Cells

The classification and developmental potential of stem cells found in human tissues can be segmented into various types. These types include adult stem cells (ASCs), germline stem cells (GSCs), embryonic stem cells (ESCs), and induced pluripotent stem cells (iPSCs). Furthermore, stem cells can be categorized based on their differentiation ability into five distinct groups, which consist of unipotent, oligopotent, multipotent, pluripotent, and totipotent stem cells [5]. Unipotent stem cells, like dermatocytes, can only form one specific cell type. Conversely, totipotent stem cells, such as zygotes, can divide and differentiate into all cell types found in various body organs. Pluripotent stem cells, such as iPSCs and ESCs, can form cells from all three germ layers but cannot differentiate into extraembryonic tissues, such as the placenta [6]. Oligopotent and multipotent stem cells exhibit distinct differentiation potentials, with oligopotent cells capable of differentiating into a limited number of cell types within a specific tissue lineage, such as hematopoietic stem cells (HSCs) in blood-related disorders.

In contrast, multipotent stem cells, like MSCs, have a broader differentiation potential, contributing to tissue regeneration in conditions like osteoarthritis. Typically, oligopotent stem cells are derived from tissues requiring a more limited range of cell types, such as bone marrow. In contrast, bone marrow, adipose tissue, and umbilical cord blood harbor multipotent stem cells. Oligopotent stem cells, known for their high proliferation rate, are widely utilized in clinical

applications like bone marrow transplants. Meanwhile, despite a slower proliferation rate, multipotent stem cells hold promise in therapeutic applications for tissue repair and regeneration [7].

ESCs are pluripotent, but ethical concerns and tumorigenic potential limit their use for therapy. Human iPSCs are an alternative that is generated from somatic cells through reprogramming and offers similar pluripotency without ethical concerns [8, 9]. While the generation of patient-specific iPSCs and their engineered differentiation into target cells is a promising technology for disease modeling and drug screening, the high potential for tumorigenesis is the biggest obstacle to clinical applications of iPSCs [10].

MSCs have high self-renewal and differentiation capacities to produce many specialized body cells such as cardiomyocytes, osteoblasts, hepatocytes, chondroblasts, endothelial cells, lung epithelial cells, adipocytes, and nerve cells [11-13]. Although nearly all tissues or organs can provide isolation for these cells, Ad-MSCs, BM-MSCs, UC-MSCs, and hA-MSCs, originating from adipose tissue, bone marrow, umbilical cord, and human amniotic mesenchymal stromal cells, respectively, are among the most commonly considered forms of stem cells for eye disease treatment [14]. Several main groups can divide these cells, including MSCs, vascular precursor cells (i.e., CD34+ cells, hematopoietic cells, or endothelial progenitor cells), and adipose stromal cells (Figure 1).

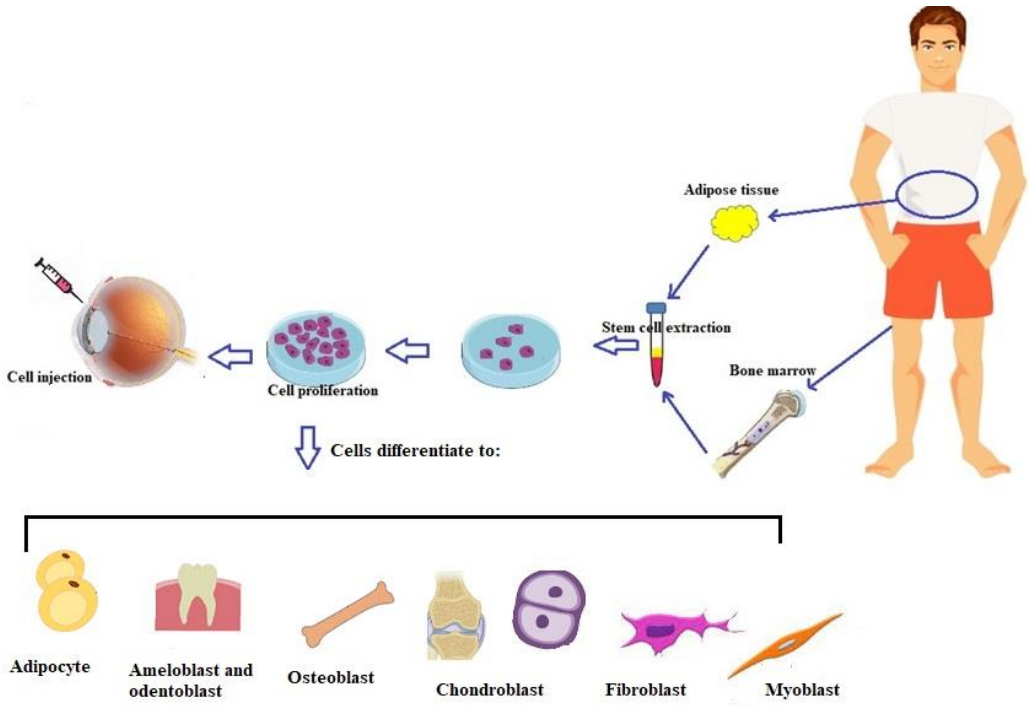

Figure 1 Schematic cell processing for stem cell-based therapy for eye diseases and differentiation to other cells such as adipocyte, dental cells (ameloblast and odontoblast), osteoblast, chondroblast, fibroblast, and myoblast.

BM has been thought to be the only source of stem cells until the 1990s [15]. It is a rich source of MSCs and other stem cell types, such as HSCs. BM-MSCs are the most common cell source that controls hematopoietic stem and progenitor cells (HSPCs) homeostasis and bone tissue regeneration [16]. Recent evidence has revealed that these cells not only play fundamental roles in hematopoiesis regulation but also have the capability of differentiating into a wide variety of cells

such as cardiomyocytes, skeletal muscle cells, chondrocytes, osteoblasts, tenocytes, adipocytes, endothelial cells [17, 18]. Given the high self-renewal and differentiation capacities of BM-MSCs, they are now considered an ideal candidate for eye disease treatment. MSCs sourced from adipose tissues are a reliable option for cell-based therapies. Ad-MSCs exhibit the same typical characteristics as BM-MSCs but have some advantages over BM-MSCs. Firstly, Ad-MSC isolation is easier and cheaper and requires minimal invasive procedures than BM-MSCs [19]. Secondly, obtaining higher yields of Ad-MSCs from subcutaneous sources is possible. Thirdly, Ad-MSCs may be more suitable for allogenic transplantation than BM-MSCs because they can maintain their phenotype longer in culture and exhibit a greater proliferative capacity [20, 21].

Furthermore, autologous Ad-MSCs are not associated with graft rejection after transplantation. Besides, Ad-MSCs can also differentiate into all three developmental germ layers, including endoderm, mesoderm, and ectoderm [22]. For these reasons, Ad-MSCs have become the most attractive source of MSCs for regenerative medicine.

UC is another interesting source of MSCs (UC-MSCs) because the isolation of MSCs from Wharton's Jelly or umbilical cord blood is painless and non-invasive compared to MSCs harvested from other tissues [23]. Furthermore, UC-MSCs can be collected abundantly from discarded UC materials without ethical concerns and harm to the mother or infant. Recent evidence has shown that UC-MSCs have low tumorigenicity or immunogenicity properties and display higher proliferation capacities than other MSC types [24]. These cells can maintain their phenotype and genetic stability even after a long-term in vitro culture. They also have a prolonged survival rate and a high ability to modulate immune responses after transplantation. Some studies demonstrated the long-term safety of UC-MSCs engraftment [25]. For these reasons, human UC-MSCs have become an interesting source of stem cells for treating different diseases. The human placenta, especially the amniotic fluid and amniotic membrane, can be considered a rich and alternative source of MSCs for clinical applications. The process of hA-MSCs collection is easy, safe, and painless, with minimized ethical issues [26]. Similar to UC-MSCs, hA-MSCs are going to be popular in the context of clinical application due to their non-invasive isolation producers, high immunomodulatory potential, large-scale supply, rapidly proliferating and differentiation properties, genome stability, non-tumorigenic behavior and minimized ethical concerns [27-29].

3. Mechanisms of MSC Homing and Regenerative Activities

3.1 Differentiation Properties of MSCs

The remarkable abilities of stem cells to self-renew and differentiate into multiple cell types make them incredibly valuable for tissue regeneration. Stem cells not only directly mature into endothelial cells, contributing to tissue regeneration, but also stimulate resident progenitor cells to multiply and differentiate into mature cells by releasing various growth factors and cytokines [30]. However, the paracrine effect of MSCs in the regeneration process appears to be more significant than their direct differentiation because the MSCs' survival and differentiation capabilities are limited after transplantation at the lesion site or within the ischemic microenvironment [31]. Observations indicate that growth factors derived from MSCs play a crucial role in their therapeutic effects by effectively promoting the proliferation and differentiation of microvascular endothelial cells [17]. To support this hypothesis, researchers in several studies have demonstrated that the

growth factors released by MSCs lead to the regulation of diverse cellular responses, including proliferation, migration, survival, and gene expression, in different cell types [32-34].

3.2 MSCs Migration

MSCs play a crucial role in tissue repair and maintenance, making them an invaluable resource for cell-based therapy in regenerative medicine. They possess diverse growth factors and cytokines, setting them apart as a unique therapeutic option [35]. The migratory capacity, or homing ability, of MSCs, is a vital initial step in the regenerative process. They exhibit a remarkable capability to migrate towards injured sites, where they can differentiate into local components and contribute to tissue regeneration through the secretion of chemokines, cytokines, and growth factors [36]. Recent research has shed light on the involvement of various chemical factors, chemokines, and growth factors in facilitating the delivery of MSCs to injured tissue sites. Of particular importance is the stromal-derived factor-1 (SDF-1)/CXC motif chemokine receptor-4 (CXCR-4) axis, which plays a critical role in recruiting MSCs to the site of injury [37]. Demonstrations have shown the upregulation of CXCR-4 expression in response to increased levels of SDF-1, resulting in enhanced recruitment of MSCs [38].

Furthermore, studies have demonstrated an augmentation in the expression of these proteins following tissue injury [39, 40]. Both in vitro and in vivo investigations have reported that the overexpression of SDF-1 and CXCR-4 proteins significantly stimulates MSC migration and facilitates tissue regeneration [38, 41]. These findings suggest that upregulating SDF-1 and CXCR-4 proteins could potentially serve as a strategy to enhance the migratory capacity of MSCs and expedite tissue regenerative efficiency. In addition to SDF-1 and CXCR-4, there are other factors, such as osteopontin (OPN), C-C chemokine receptors (CCRs), and growth factors, that regulate the migration and homing of MSCs towards the injury site [36, 42]. These factors are known to be upregulated in response to injury and inflammation. Studies have demonstrated that increased OPN expression is associated with enhanced migration and survival ability of MSCs [43]. OPN has also demonstrated the ability to increase the expression of integrin β1 in MSCs, thereby promoting their migration through integrin β1 binding [44]. Growth factors induce MSC migration to the injury site and play a critical role in regulating MSC proliferation and differentiation. Currently, vascular endothelial growth factor (VEGF), primary fibroblast growth factor (bFGF), transforming growth factor β1 (TGF-β1), hepatocyte growth factor (HGF), platelet-derived growth factor (PDGF), and placental growth factor (PGF) are well-known growth factors involved in tissue repair [36]. Moreover, regulators of MSC migration toward the injury site include mechanical factors like matrix stiffness, microgravity, and shear stress. Thus, the microenvironment surrounding MSCs plays a crucial role in their migration [38]. Abnormal changes in the extracellular matrix (ECM) serve as a signal for cellular damage, triggering the recruitment of circulating MSCs [45].

3.3 Angiogenic Properties of MSCs

Angiogenesis, a fundamental process in stem cell activity, is a pivotal factor in tissue healing and regeneration by facilitating the formation of new blood vessels [46]. Expressing angiogenic factors is closely linked to this process, interacting with endothelial cells and stimulating their proliferation. The interaction between stem cells and endothelial cells is crucial in promoting angiogenesis. Recent findings indicate that proangiogenic factors derived from MSCs enhance the angiogenic behavior of

endothelial cells by binding to specific receptors on their surface [47]. Various intracellular signaling pathways are activated or inhibited through this interaction, ultimately promoting angiogenesis [45]. MSCs release extracellular vesicles, multiple cytokines, and growth factors that expedite angiogenesis, promote local cell proliferation, and contribute to tissue repair [48]. Among the significant proangiogenic factors secreted by MSCs, VEGF, fibroblast growth factor (FGF), HGF, monocyte chemotactic protein 1 (MCP1), PGF angiopoietin-1 (Ang1), Ang2, and stromal-derived factor-1 (SDF1) play critical roles in blood vessel formation and the regeneration process. Moreover, these paracrine factors attract and activate resident or circulating stem cells and progenitor cells, thereby facilitating blood vessel formation and supporting the repair of damaged tissues [49].

3.4 Tissue Repairing Properties of MSCs

Following the migration of MSCs into injured tissues, they play a crucial role in promoting the regeneration of damaged tissue through two primary mechanisms: direct differentiation into local cells and paracrine activities. During the repair process, MSCs engage in cell-cell interactions, secrete various angiogenic factors, enhance the survival of resident cells, regulate the tissue microenvironment, modulate immune responses, and activate tissue-specific progenitor cells [50, 51]. These mechanisms, including angiogenesis, differentiation abilities, immunomodulation, anti-apoptotic properties, and anti-fibrotic activities, contribute significantly to the tissue regeneration induced by MSCs. Researchers are exploring stem cells as a potential treatment for retinitis pigmentosa (RP), a degenerative eye disorder. A single-arm trial was conducted at a single center to investigate the safety and effectiveness of purified adult autologous BM-MSCs on RP patients. The trial followed patients for 48 months to assess the long-term outcomes. These stem cells can differentiate into specific functional cell types and potentially regenerate damaged retinal tissue. Furthermore, established clinical methods exist for purifying the cell populations using a clinical-grade purification system [52].

3.5 Anti-apoptotic Properties

In addition to their ability to reduce inflammation and modulate immune response, MSCs also have a protective effect on normal cells at the injury site, preventing early cell death. However, the exact mechanisms behind this anti-apoptotic property of MSCs are not fully understood. Some studies have shown that MSCs inhibit cellular apoptosis and restore tissue balance by secreting specific molecules such as B cell lymphoma 2 (Bcl-2), as well as various growth factors (e.g., VEGF, HGF, IGF, TGF-β, and FGF) and granulocyte-macrophage colony-stimulating factor (GM-CSF) [53-55]. A recent study found that local transplantation of MSCs prevented corneal cell death by increasing the expression of anti-apoptotic molecule Bcl-2 and reducing the expression of pro-apoptotic genes Bcl-2-associated X protein (BAX) and transformation-related protein 53 (TRP53 – p53) [56]. Furthermore, MSC transplantation significantly reduced the production of pro-inflammatory cytokines and molecules related to endoplasmic reticulum stress and apoptosis, such as activating transcription factor 4 (Atf4), binding immunoglobulin protein (Bip), and p21 [56]. Another study demonstrated that treating oligodendrocyte cells with conditioned medium from amniotic epithelial stem cells resulted in decreased expression of apoptosis-related proteins caspase-3, caspase-8, Bax, and Annexin V, as well as an increased ratio of Bcl-2/Bax [57]. Qtani et al. demonstrated that HSCs containing endothelial precursors can effectively stabilize and rescue

retinal blood vessels in mice suffering from retinal degenerative diseases [58]. Additionally, another investigation indicated that the transplantation of BM-MSCs led to a significant reduction in apoptotic outer nuclear layer (photoreceptor cell nuclear layer) cells in mice [59]. These findings suggest that the inhibition of apoptosis may be a primary mechanism through which MSCs exert their therapeutic effects in regenerative therapies.

3.6 Immunomodulatory Properties of MSCs

The ability of stem cells to modulate the immune system is crucial in how they function to regulate inflammation and tissue regeneration. While inflammation is necessary for tissue repair and regeneration, an excessive accumulation of immune cells or leukocytes at the injury site can cause the increased secretion of pro-inflammatory substances, excessive production of reactive oxygen species (ROS), oxidative damage, and apoptosis of nearby cells. So, controlling the immune response at the injury site promotes tissue healing and regeneration. Research suggests that MSCs achieve their immunomodulatory effect through direct cell-to-cell interaction and the release of immunosuppressive substances like prostaglandin E2 (PGE2), indolamine 2,3-dioxygenase (IDO), soluble human leukocyte antigen G5 (sHLA-G5), programmed death-ligand 1 (PDL1), nitric oxide (NO), IL10, IL6, hemeoxygenase-1 (HO1), and growth factors such as TGF-β and HGF. MSCs can interact with various innate and adaptive immune system cells, including natural killer cells, monocytes or macrophages, dendritic cells, neutrophils, and T and B lymphocytes, and modulate their responses [60, 61]. The secretion of cytokines and growth factors by MSCs can suppress immune responses by inhibiting the proliferation and maturation of B and T cells and dendritic cells while promoting the generation of regulatory B and T cells [62, 63].

Moreover, MSCs facilitate the activity and migration of other immunoregulatory cells, like myeloid cells, to the injured site, thus extending the immunosuppressive and immunomodulatory abilities of MSCs over a longer duration. Additionally, MSCs induce the differentiation of macrophages into anti-inflammatory M2 phenotype by secreting metabolic reprogramming factors, such as IDO, upon exposure to IFN-γ [64]. The secretion of PGE2, IL1, and CD40 ligand (CD40L) overexpression on cell surfaces also stimulates M2 macrophage differentiation [65, 66]. M2 macrophages, in turn, produce the anti-inflammatory cytokine IL-10, while the M1 phenotype generates high levels of pro-inflammatory cytokines [IL-6, IL-8, and tumor necrosis factor-alpha (TNF-α)] [67]. Recent research has highlighted the potential of MSC-derived exosomes (MSC-Exos) in treating various eye diseases [68]. These exosomes have gained considerable attention as promising therapeutic options for eye diseases. Just like MSCs, they possess significant immunomodulatory and anti-inflammatory properties. Multiple studies have investigated the potential role of MSC-Exos in treating conditions like glaucoma, retinal injury, optic neuropathy, diabetic retinopathy, and autoimmune uveitis.

Also, MSC-Exos has been recommended for treating other eye diseases, such as large and refractory macular holes (MHs) [69]. For instance, a clinical trial demonstrated that MSC-Exos therapy is effective and safe in improving post-surgical visual outcomes for patients with MH [69]. An example of an eye disease where HSCs have shown potential is autoimmune-related retinopathy (ARRON), an uncommon inflammatory disorder characterized by the immune system attacking proteins within the retina, leading to vision loss and potentially affecting hearing. Recent research has suggested that HSCs may help mitigate the progression of ARRON syndrome [70].

3.7 Anti-fibrotic Effect

Stem cells are known to promote tissue regeneration by suppressing fibrosis. *Fibrosis* is a pathological condition characterized by the excessive proliferation and accumulation of fibroblasts, accompanied by an abnormal extracellular matrix formation. This condition is associated with the overproduction of ROS, oxidative stress, inflammation, morphological damage, and apoptosis of nearby cells [71]. Recent studies have demonstrated that MSCs can migrate to the site of injury or inflammation and reduce collagen deposition and myofibroblast differentiation. They achieve this by inhibiting pro-inflammatory factors and the SMAD/TGF-β and peroxisome proliferator-activated receptor gamma (PPAR-γ)/Wnt/β-catenin signaling pathways [72, 73]. In addition, stem cells release molecules and growth factors that enhance the activity of autophagosomes in accumulated fibroblasts, thereby reducing fibrosis by inhibiting the phosphoinositide 3-kinases (PI3K)/ mammalian target of rapamycin complex 1 (mTORC1) pathway [74]. Notably, transplantation of adipose-derived MSCs limits pulmonary fibrosis. It preserves tissue architecture by increasing the secretion of HGF and prostaglandin E2 (PGE2) while minimizing the expression of TNF-α and TGF-β1 in host cells [75, 76].

Similarly, intravenous injection of muscle-derived MSCs has significantly decreased skeletal muscle fibrosis and the accumulation of calcium/necrotic fibers. The secretion of matrix metalloproteinase-1 primarily mediates this effect as the main anti-fibrotic protein. These findings indicate that MSCs play a critical role in tissue repair and regeneration through various mechanisms, including immunomodulation via their anti-inflammatory properties, attenuation of ROS production and oxidative stress, induction of angiogenesis, suppression of apoptosis and fibrosis, activation of local progenitor stem cells, and direct differentiation into adult cells.

4. *In Vivo* Studies Related to Stem Cells and Regenerative Therapy

Recent experimental and clinical investigations have highlighted the potential of stem cells, particularly MSCs, in the regeneration and treatment of eye diseases. For instance, Collin et al. discovered that HSCs containing endothelial precursors play a crucial role in stabilizing and rescuing retinal blood vessels in mice with retinal degenerative disease [77]. Another study demonstrated a significant reduction in apoptotic outer nuclear layer cells in mice following BM-MSCs transplantation [78]. In a recent study, pluripotent BM-MSCs preserved rod and cone photoreceptors and enhanced visual function in rats with RP disease [79]. Macular Edema associated with ischemic diabetic maculopathy or ischemic central retinal vein occlusion (CRVO) represents another eye disease, and there is no established treatment for this condition. Siqueira et al. demonstrated the safety and effectiveness of intravitreal injection of autologous BM-HSCs in patients with retinal dystrophy. Another clinical trial study indicated that intravitreal injection of BM-HSCs improved Macular Edema in individuals with RP [80]. In a clinical trial, a patient with declining visual acuity underwent a vitrectomy in the right eye involving the injection of BM-MSCs. The procedure included injecting BM-MSCs into the optic nerve of the right eye, retrobulbar, and subtenon, followed by intravitreal injection of BM-MSCs in the left eye. After 15 months, the patient showed improved visual acuity, reaching 20/150 on the right and 20/20 on the left. Bilateral visual fields significantly improved, and there were notable enhancements in macular thickness and fast retinal nerve fiber layer thickness at 3- and 6-months post-cell-based therapy [81]. RP comprises inherited retinal disorders marked by progressive photoreceptor loss, leading to retinal

degeneration and atrophy. A recent non-randomized clinical trial explored the therapeutic impact of hESC RPE transplantation in 12 Stargardt's Macular Dystrophy (SMD) patients.

The trial involved sequential doses of hESC-RPE cells, starting at 50,000 cells and escalating to a maximum of 200,000 cells transplanted. Evaluations are scheduled at 18, 24-, 36-, 48-, and 60-months post-transplant, focusing on ophthalmological findings and predefined Primary Outcome events. After the final visit, whether at 60 months or early discontinuation, patients are invited to partake in a lifelong annual health survey under a separate protocol to ensure ongoing long-term safety monitoring [82]. Research conducted in animal models of RP indicates that subretinal injection of BM-MSCs may delay degenerative changes in photoreceptor cells. A single-arm, single-center trial has explored the safety and efficacy of purified adult autologous BM-MSCs over a 48-month follow-up period in RP patients. These cells possess the potential to differentiate into specific functional cell types, facilitating the regeneration of damaged retinal tissue.

Moreover, a clinical-grade purification system is available to purify these cell populations using clinically approved methods [83]. In a recent non-randomized clinical trial involving 12 patients with SMD, the therapeutic effects of hESC RPE transplantation were investigated. The patients received sequential doses of hESC-RPE cells, starting at 50,000 and reaching a maximum of 200,000 transplanted cells. Planned evaluations are set for 18, 24-, 36-, 48-, and 60-months post-transplant. At 60 months post-transplant or due to early discontinuation, patients will be invited to participate in a lifelong annual health survey. This ongoing survey, conducted under a separate protocol, is designed to monitor the long-term safety of the procedure continuously [84].

4.1 Limitations of Stem Cell-based Therapy

Stem cell-based therapy shows promise in addressing ocular complications, including corneal diseases and retinal degeneration. However, its implementation faces significant challenges. Safety concerns arise from reported cases of adverse effects such as tumor formation, necessitating a focus on minimizing risks. Ethical debates and legal restrictions, particularly regarding ESCs, hinder widespread application. Allogeneic stem cell therapies may encounter rejection, requiring immunosuppressive therapy with associated risks. Limited availability of appropriate stem cell sources, difficulties in procuring specialized cells, and ongoing studies on the long-term efficacy contribute to challenges. Moreover, the high cost of stem cell-based therapy, stemming from complex procedures, poses a barrier to broader accessibility and affordability for patients.

5. Conclusions

The results of both present and previous clinical trials demonstrate that cell-based therapy holds potential and is a safe method to reinstate visual ability in various eye conditions. Adverse effects linked to the eyes, such as tumor development or uncontrolled cell growth, have not been observed. The documented enhancements in visual function are encouraging and show promise. Nevertheless, further extensive studies with extended observation periods are necessary to ascertain this treatment's role in the future.

Author Contributions

Mohsen Akbaribazm participated in performance of the research, research design and writing of the paper.

Competing Interests

Author declares that there is no conflict of interest.

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