Role of stem cells in treatment of Age-Related Macular Degeneration (AMD)

Summary

Age-related macular degeneration is a disease that causes blindness and until now, there is no treatment that restores vision in the end stage of the disease

Age-related macular degeneration (AMD) is a degenerative disorder of the macula for those ages 65 and above. It is a global disease that causes blindness, and it is becoming increasingly prevalent, and has no effective cure. AMD is classified into an early stage and a late stage. Early AMD includes eyes with drusen and eyes with hyperpigmentation or hypopigmentation of the RPE. Late AMD includes eyes with geographic atrophy and pigment epithelial detachment and eyes with neovascular manifestations of the disease.

Laser photocoagulation is one of the methods used in treatment of patient with well demarcted extrafoveal lesions. PDT therapy with verteporfin has proven to slow progressive vision loss in patients with subfoveal and relatively small lesion types, but improvement in visual function may not be achieved with PDT alone.

The development of anti-VEGF agents has introduced an important advance in the therapeutic spectrum of AMD. Pegabtanib, which was approved by FDA for treatment of all subtypes of neovascular AMD just able to slow visual acuity loss. Ranibizumab, however, which blocks all VEGF isoforms, appears to improve visual function in a significant proportion of patients. bevacizumab appears to be a safe and effective substance but still Off-label therapy.

Anti-inflammatory compounds such as steroids have long been used to suppress not only inflammation, but also associated angiogenesis. Unfortunately, profound side effects associated with glucocorticoid activity of many of these compounds make long term administration of effective dosing levels problematic with certain patients.

All the previous treatments don’t restore lost vision so using stem cells in what called regenerative treatment hoping to restore vision. Stem cells are multipotent, self-renewing cells that sit at the top of a lineage hierarchy and proliferate to form differentiated cell types of a given tissue in vivo.

There are multiple sources for stem cells as embryonic, fetal, umbilical cord blood derived cells, bone marrow mesenchymal cells, neural, retinal and limbal stem cells

There are two ways of transplantation: subretinal or intravitreal. Both of them have immune privilege features. The subretinal implantation of stem cells requires a vitrectomy, which is a large and risky procedure. Alternatively, the intravitreal injection is a more popular and much less invasive procedure. Several animal studies show that stem cells integrate well into degenerated retina with expression of the synapse protein, formation of synaptic contacts with bipolar cells after subretinal transplantation.

Transplanted human ESC-derived retinal cells migrate into the appropriate layers in the retina following intravitreal transplantation in newborn mice, express markers consistent with retinal neuronal and rod and cone photoreceptor differentiation, and express a synaptic marker in the outer plexiform layer.

There are multiple problems with stem cell therapy as the possible development of teratomas after transplantation of ESCs, the requirement for adequate homing of cells from the injection site to a desired specific location and ethical and social issues.

Stem cells therapy for eye diseases will face many challenges as safty, application of suitable microenviroment of transplanted cells, stoppage of progression of the original disease, pathfindig of RGCs, remyelination and control of immune response