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Research Article

**ANALYSIS OF NEURO DEGENERATION IN GLAUCOMA
PATIENTS BY TRANSPLANTED DIFFERENT CELL
PRECURSORS**Muhammad Adnan Sarwar¹, Khalida Qasim², Muhammad Adil Nawaz³¹District Headquarter South City Hospital Okara, ²District Headquarter Hospital Vehari, ³Rural Health Centre Tibbi Qaisrani District Dera Ghazi Khan.**Article Received:** August 2019**Accepted:** September 2019**Published:** October 2019**Abstract:**

Objectives of the study: Glaucoma is a common neurodegenerative disease for which current therapies are often insufficient. The purpose of our investigation was to determine whether oligodendrocyte precursor cells (OPCs), a type of neural stem cell, can protect retinal ganglion cells (RGCs) from glaucomatous damage in vivo.

Methods: This descriptive study was conducted in DHQ South City Hospital Okara during 2018 to 2019. Intraocular pressure was chronically increased by trabecular laser treatment delivered unilaterally to adult rat eyes. OPCs were isolated in vitro and then transplanted intravitreally either before, or concurrent with, injury induction.

Results: Transplanted OPCs were found to survive within the eye for at least 12 weeks and to localize close to the RGCs. Moreover, OPCs significantly enhanced the survival of RGCs in the glaucomatous eye, but only when concomitantly activated by inflammation. Amelioration of RGC death was not attributable to inflammation but relied on an interaction between inflammatory cells and OPCs. Engrafted cells also displayed multipotentiality in vivo.

Corresponding author:**Muhammad Adnan Sarwar,**

District Headquarter South City Hospital Okara

QR code



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INTRODUCTION:

Glaucoma is still one of the leading causes of blindness worldwide. In England and Wales glaucoma is a major or contributing factor in 12-14 % of all registrations for blindness and partial sight, only to macular degeneration [1]. The worldwide burden is greater with glaucoma is the second leading cause of global blindness after cataract [2]. It has been estimated that almost 60.5 million people worldwide affected by glaucoma in 2010, with the figure expected to rise to 80 million by 2020 [3].

A neurodegenerative disease known as glaucoma, which is caused by the gradual occurring death of retinal ganglion cells (rGCS). The pathophysiological changes can share with other neurodegenerative diseases, including axonal transport dysfunction, oxidative stress [4] increased the level of intraocular pressure (IOP) is the main risk factor and depression in the level of IOP is the only cure for this particular disease. Whereas decreased levels of IOP cannot suppress RGC degeneration in some patients with glaucoma, so there may be a new method of treatment to protect RGC. Stem cell technology is a newer tool in the treatment of neuroprotective treatment in the degeneration of CNS disease, then the increases neurodegeneration in the supply of neurotrophic factors (Corti et al. 2007), (Madhavan et al. 2008), (Yasuhara et al. 2006). There is abundance oligodendrocyte precursor cells (OPCs) in the central nervous system (CNS) of adult individuals, where they are the most widely used type of proliferative cell⁵. OPCs hold great responsibility for the generation of oligo dendrocytes in the developmental stage, whereas in adult individuals, they play a vital role in demyelinating pathologies and remyelinating of axon [6].

MATERIAL AND METHODS:

Preparation of Culture Medium:

This descriptive study was conducted in DHQ South City Hospital Okara during 2018 to 2019. First of all, primary mixed glial cultures generated from the cortex dissected from postnatal day 0 Lewis rat pups and grown on poly-D - lysine - coated tissue culture flasks in DMEM and 1% penicillin / streptomycin. OPC was isolated from the mixed glial cultures by a series of mechanical shaking steps and then kept in OPC expansion medium and analyzed directly after isolation.

Experimental Design:

Transplantation of naive OPCs were performed either at the time of glaucoma induction (acute group), or 8 weeks prior to (chronic group). A group experienced transplantation of activated OPCs 8 weeks before glaucoma induction and the OPC acute transplant experiment, the animals received one unioocular 3UL intra- vitreous injection of PBS alone.

RESULTS:

According to Figure 1 oligo dendrocyte progenitor cell (OPC) culture were analyzed for expression of A2B5 explaining the purity of the culture prior to transplantation. A2B5 is a cell surface antigen expressed by immature OPCs in culture (23). Immuno- cytochemical analysis showed that $93.9 \% \pm 2.9 \%$ (mean \pm SD, $n = 7$) of the transplanted cells was OPCs. In addition, the OPC cell cultures show appropriate morphology in culture. Immuno- cytochemical labeling of either ED1 or GFAP in OPC cultures showed a $2.37 \% \pm 1.9 \%$ (mean \pm SD) contamination of microglia and $2.34 \% \pm 0.9%$ (mean \pm SD) contamination of astrocytes, respectively. Parallel staining in microglial cultures showed $1.15 \% \pm 1.2%$ (mean \pm SD) contamination of OPCs and $0.84 \% \pm 0.6 \%$ (mean \pm SD) contamination of astrocytes.

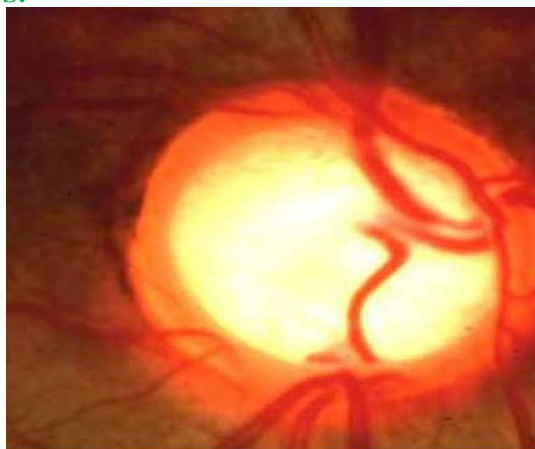


Figure1. Characterization of OPCs cultured for transplantation.



Figure 2: Intravitreal transplantation of OPCs did not affect intraocular pressure changes following ocular hypertension induction.

Table 2: Experimental Glaucoma Group

Group	Peak (mmHg)
Acute transplant	23±1.8
Chronic transplant	28±2.3

DISCUSSION:

In the present study, we found that intra-vitreous transplantation of OPCs protected rGCS from glaucoma-induced death *in vivo*, but not until the engrafted cells had been activated by co-stimulation of inflammatory cells. Thus, we can deduce that the grafted OPCs were responsible for reducing RGC loss, rather than neuroprotection occurs as a side effect of inflammatory processes [6].

This is a key point that cytokine activated astrocyte can support injured neurons. However, the inflammatory stimulus was needed to induce OPC mediated neuroprotection as we also found that OPCs injected into the eye does not remedy glaucomatous neuronal degeneration. These results indicate that neuroprotection was mediated by the engrafted OPCs and it was triggered by a signal or signals transmitted by reactive immune cells. It seems unlikely that OPCs responded directly to zymosan, where they seem to lack TLR2, the innate receptor responsible for detecting zymosan, and failed to respond to zymosan exposure *in vitro* [7].

As previously reported, the throat also been shown to increase expression of MBP by OPCs *in vivo* and optionally OPC-mediated myelination of RGC axons normally unmyelinated retinal. We observed less OPC differentiation into MBP-expressing cells in the retina than previously reported. It is not clear why this difference in myelin production was detected, but it may be due to the use of different breeds of rats which strain differences in the inflammatory response and protective autoimmunity has been documented [8-9].

OPCs were injected into the vitreous of both injured and glaucomatous eye were found to survive well in all experiments. In addition, the grafted OPCs observed to spread across the inner retinal surface, which puts them in the ideal location for mediating the observed neuroprotection [10].

CONCLUSION:

We have demonstrated that transplantation of OPCs may relieve RGC death *in vivo* and that this neuroprotective capacity depends on inflammatory cell activation of OPCs. Such long-term relief of RGC death in glaucoma at an experimental intervention is rarely seen, suggesting a new approach to the development of neuroprotective strategy.

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