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# INTRACAMERAL INJECTION OF LIMBAL MESENCHYMAL STEM CELLS SECRETOME ALLEVIATE INFLAMMATION WITH DELAYED STRUCTURAL RECOVERY ON CORNEAL ENDOTHELIAL CELLS IN PHACOEMULSIFIED RABBIT EYES

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**ABSTRACT : The objective of this research is to investigate the effects of intracameral injection of limbalmesenchymal stem cells (LMSCs) secretomeon corneal endothelial cells density and caspase-3 expression after exposure to phacoemulsification ultrasound energy in rabbits. Twenty-four New Zealand white rabbits (n = 24 eyes) were randomly divided into 2 groups and exposed to phaco ultrasound. The control group was treated with intracameral injection of balanced salt solution (BSS), while intracameral injection of LMSCs secretome was utilized on the treatment group. Thereafter, the endothelial cells density was evaluated with specular microscopy before ultrasound exposure on the 3rd daywith the corneaused to evaluate theexpression of *caspase-3* by immunohistochemistry staining. There were no signs of inflammation in both groups. However, exposure of ultrasound energy significantly reduced the corneal endothelial cell density in the control and treatment groups (-93.69 ± 139.04; p = 0.04 and -119.31 ± 85.41, p = 0.001, respectively). Furthermore, the corneal endothelial cells density (p = 0.592) and caspase 3 expression after treatment for 3 days were indifferent in treatment group compared to control with p = 0.625; 2.17 ± 0.777 and 1.17 ± 0.322, respectively. Intracameral injection of LMSCs secretome tends to alleviate ocular inflammation, improved the profile of endothelial cells density and corneal caspase-3 expression in rabbit eyes after exposure to ultrasound energy-phacoemulsification.**

***Key words :*** Limbal mesenchymal stem cells secretome, endhotelial cells density, phacoemulsification, caspase-3.

## INTRODUCTION

Most cataract extraction are currently performed with phacoemulsification techniques which uses ultrasound energy to fragment and emulsify the lens. With advances in the development of surgical devices and techniques, the safety and efficacy of phacoemulsification has rapidly increased. However, its use has been expanded to include cataracts with hard nucleus, thereby, leading to the need for greater ultrasound energy.This results in greater mechanical and thermal risk of corneal endothelial damage which ultimately triggers cell death through the apoptotic pathway. Some studies report that the endothelial cells loss of between 8.0% and 16.7% has a side effect of phacoemulsification. Damage and loss of corneal endothelial cells at some point tends to disrupte the function of the pump and tight junction which causes corneal edema and irreversible damage (Geffen *et al*, 2008; Bonnano, 2012; Takahashi, 2016; Alarfaj, 2017).

Corneal transplantation is currently the only effective treatment for corneal endotheliopathy due to its low regeneration ability. A national bullous keratopathy survey in Japan reported that cataract surgery was the most common cause of penetrating keratoplasty (PK) by 24.2%. Similarly, various other studies showed cataract surgery was ranked second after Fuchs endothelium dystrophy, thereby, making it the biggest cause of secondary endothelial damage. Keratoplasty has several disadvantages including limited corneal donors and the high level of postoperative endothelial cell damage at 49%. (Zavala *et al*, 2013; Zavala *et al*, 2017).

There are various *in vitro* studies aimed at triggering endothelial cell proliferation which showeda promising result. One of such methods is the secretion factors from stem cells also known as conditioned media, secretome, microvesicles or exosome which are expected to provide new therapeutic alternatives for endothelial damage. Furthermore, the stem cell conditioned mediumswhich