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# Role of Mesenchymal Stem Cell Therapy on Healing of Corneal Wound Induced by Alkali Burn in Rats

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***Author's contribution***

*The sole author designed, analysed, interpreted and prepared the manuscript.*

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***Mini-review Article***

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## ABSTRACT

**Background:** Chemical injury is the common cause of corneal damage. Alkali exposure cause defective clarity and impaired vision with lack of satisfactory therapy. Bone marrow mesenchymal stem cells (BM-MSCs) are multipotent self-renewal cells and they give a hope for better treatment of many diseases.
**Aim of the Review:** This review aimed to show the role of subconjunctival administered BM-MSCs therapy on alkali-induced corneal burn in rats, and its effect on the damaged corneal epithelium and the area of corneal neovascularization (CNV).
**Conclusion:** Subconjunctival injection of MSC transplantation could accelerate corneal wound healing attenuates inflammation and reduces CNV in alkaline-burned corneas.

*Keywords: Mesenchymal stem cell; corneal injury healing; rats.*

## 1. INTRODUCTION

The cornea is a highly specialized organ, so in the event of a corneal injury characterized by healing fibrosis, [1]. Blood vessels [2] which is bad for corneal transparency and leads to permanent visual impairment is a common complication of burning alkalis [3] more than 7.7%. of eye, injury is the cause of burns and occurs more at an early age [4].

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Corneal injury stimulates the release of progenitor cells such as neutrophils, epithelial cells, [5] fibroblasts, [6] endothelial cells, [7] and neurons [8] from the bone marrow. Also, stimulate the cyclic epithelial stem cells (LSCs) that are able to differentiate into mature endothelial cells, so re-lining of blood vessels and blood vessels occurred [9]. Therefore, treatment depends on the inhibition of inflammation to reconstruct the damaged cornea, but available anti-inflammatory drugs are not enough to inhibit blood vessels. Also, transplant LSCs are not readily available and have high immune rejection rates [10].

Mesenchymal stem cells (MSC) have attraction repair therapy because they have less or no immunogenic potential and are easy to isolate from bone marrow, expanded in vitro and have the potential to differentiate into epithelial cells and utilized for transplantation so they used in cell-based tissue engineering [11].

Mesenchymal stem cells (MSCs) are undifferentiated cells that can multiply, regenerate, and transform into differentiated cells [12,13]. The bone marrow is a major source of tissue-derived MS [14].

When MSCs transplanted systematically, they have the ability to identify and move to infection sites and ultimately differentiate into the cells of the tissue itself and act as a single member of this tissue [15]. Stem cell markers allow the identification of embryonic, hematopoietic, mesenchymal / stromal stem cells, and neurons.

## 2. LITERATURE REVIEW

Deterioration of visual acuity caused by corneal surface diseases such as chemical injuries accompanied by delayed re-epithelial corneal epithelium. These conditions are difficult to treat and cause a serious medical problem. Continued failure to heal wounds in the corneal epithelium may lead to corneal ulceration or in severe cases to puncture [16].

Corneal epithelial wound healing is a multi-step process that begins with the migration of surface cells to cover the twisted surface, cell proliferation, apoptosis, adhesion and cell differentiation. This complex chain mediated by autocracy and paracrine interactions of cytokines and growth factors produced by corneal epithelial cells, stromal cells, conjunctival cells, and lacrimal glands [17].

Few studies that systematically implanted MSCs have shown the effect after removing the alkaline immersed application stick from the eye, the affected central corneal stroma appeared opaque with a distinct edematous margin. Stem cells transplanted systematically develop highly localized cornea. These pluripotent stem cells can harbor specific tissues, differentiate in response to the local microenvironment, stimulate local repair response, and promote healing of corneal wounds after alkaline burns [18].

Undifferentiated MSCs can respond to local cues in vivo to differentiate into endothelial cells, contributing to neovascularization in the setting of wound healing but CD34-positive endothelial and hematopoietic progenitors and stem cells from bone marrow are most important during stress angiogenesis Also decreased CD34-positive HSCs account for the delayed and malformed corneal neovascularization. Engrafted MSCs in the bone marrow microenvironment, which express various hematopoietic cytokines, including interleukin (IL)-6, IL-11, thrombopoietin (TPO), stem cell factor (SCF), and other molecules, could provide the appropriate milieu for efficient stimulation of quiescent HSCs.24–26 These activated HSCs released into the circulation, migrate to the wound site, thereby accelerating neovascularization [19].

Implantation caused by tissue injury from systematically transplanted cancer stem cells to specific locations with subsequent differentiation in response to the microenvironment of tissues promotes wound healing. In healthy bone marrow, MSCs support and potentiate the response of HSCs to vascular stimuli and then HSCs can migrate to local sites, where they contribute to corneal blood vessels and promote wound healing [20].

Further studies needed to illustrate the exact differential ability of local engrafted MSCs. Severe alkaline burns in the cornea infiltrate a large amount of inflammatory cells and mediators, which can lead to corneal formation. In intact corneas, corneal epithelial stem cells are located in the limb region. When these stem cells migrate from the limbus to the center of the cornea, they differentiate into mature corneal epithelial cells [6].

Cornea, with severe injury showed that the borderline and mesothelioma are absent, adjacent conjunctival epithelial cells invade the

surface of the cornea and become covered with an abnormal conjunctiva. This process is accompanied by persistent epithelial defects and scarring of vascular tissue [7,8].

## 3. DISCUSSION

Corneal chemical burn is a common ophthalmologic emergency. It often cause sever corneal damage and permanent visual impairment. In general healing of corneal injury divided into 4 phases: immediate, acute, early repair and late repair phases. In the last 15 years, Subconjunctival injection of MSC transplantation could enhance the healing [21]. Other studies deny this issue and refer the benefits related to inhibition of angiogenesis and inflammation [22,23]. The result from [6], support by previous studies [21], and both suggest that MSCs treatment can accelerate the wound healing of a chemically burned cornea via anti-inflammatory and antiangiogenic activity. In addition, other previous study found that MSCs might decrease macrophage infiltration maybe by suppressing the expression of the macrophage chemokine MIP-1a [24].

## 4. CONCLUSION

This mini-review suggests that topical subconjunctival injection of MSCs accelerates the corneal epithelial recovery and can inhibit the neovascularization process in case of a corneal alkali burn in rat model. The findings of this review confirms the anti-inflammatory mechanism of MSCs in the acute phase of a corneal chemical burn, and it is suggested that the sub conjunctival administration of MSCs could be used as a good alternative treatment for clinical management of corneal chemical burn.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Author has declared that no competing interests exist.

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