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Amniotic membrane use for resistant infectious and non-infectious corneal ulcer

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Abstract

In corneal ulcers, amniotic membrane (AM) is utilised for supporting damaged tissues, shield and protect deficiencies from further deterioration or breakdown from external influences and encourage re-cellularization of the cornea. Anti-fibrotic, anti-inflammatory, and anti-angiogenic effects, as well as an antimicrobial impact and the encouragement of epithelial and stromal repair are some of the qualities possessed by amniotic membrane. Surgical grafting to the ocular surface, non-surgical patching with a carriage device, amniotic membrane extract eye drops (AMEED), amniotic membrane with umbilical cord blood, and amniotic membrane with placental fluid are certain uses and techniques for utilising AM in corneal ulcers and corneal epithelial deficiencies.

Keywords: Device, amniotic, membrane

Introduction

Cataracts are the most common cause of blindness, although corneal blindness is also a leading factor. Trauma to the eye, in addition to corneal ulceration, is a main reason of corneal blindness in the majority of instances. Infectious corneal ulcers are a prominent source of ocular morbidity and loss of vision in developing countries. Every year, corneal blindness contributes for between 1.5 and 2 million new instances of monocular blindness^[1]. The cryopreserved amniotic membrane includes a number of beneficial components, the majority of which are found in the extract of the AM. AME includes epithelium-derived growth factors, which may help stimulate epithelial repair and proliferation in contrast to denuded AM. Hepatocyte growth factor (HGF), epidermal growth factor (EGF), along with basic fibroblast growth factor (bFGF), in addition to protease inhibitors and a novel matrix component named HC-HAPTX3 with potent anti-angiogenesis, anti-inflammatory, and anti-scarring features similar to steroid but without the immune-suppressive effects, are all present in remarkable amounts in this substance^[2].

Pathogenesis of Infectious Keratitis

The clinical outcome of keratitis will be based on the pathogenicity and virulence of the organism versus the response of the host. The organisms' pathogenicity is its capability to cause a disease and it is related to its capability for adhering to the base or edge of the ulcer and then invasion of the stroma while Virulence is the relative degree of pathogenicity of the organism^[3].

Risk factors compromising host defense include; Systemic compromising factors (debilitating chronic illness, malnutrition, diabetes, rheumatoid arthritis, etc), local factors that might potentially compromise, such as eyelid and tear defects, a history of keratitis, deficiencies in vitamin A, trauma caused by foreign bodies or the existence of an adnexia with chronic infection^[4].

Resistant infective corneal ulcer

It is a severe ulcer that heals poorly, does not react to the targeted medical therapy, and may potentially become worsened despite receiving therapy continuously for three days to one week^[5].

The causative agents of infective keratitis

- **Bacterial keratitis:** Different types of bacterial species of Gram-positive bacilli, Gram-negative bacilli, Gram-negative cocci, and Gram-positive cocci which can overcome the barrier and toxins that are released by the bacterium and may spread into the surrounding environment, where they can disturb normal tissues.
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- **Fungal keratitis:** Is more prevalent in males and in individuals with a history of outdoor ocular trauma. Its types; Filamentous non-pigmented Moniliaceae family, Filamentous pigmented Dematiaceae family, Yeasts and Dimorphic fungi (rare in keratitis) and its early biomicroscopic features is dry, gray-white colour, and surface of the cornea that is rough and might seem raised and intact, or occasionally, it may be ulcerated, White ring in the cornea [16].
- **Viral keratitis**

Herpes Family include

The family herpes viridae include herpes simplex (HSV), cytomegalovirus (CMV), varicella zoster virus (VZV), and Epstein Barr virus (EBV). Structurally, they are enveloped viruses formed of a double-strand DNA core.

A. Herpes simplex virus (HSV)

One of the most frequent viral causes of adulthood blindness, HSV keratitis is an important component of transplantation of the cornea [7]. The muco-cutaneous spreading of the trigeminal nerve is where primary HSV-I infection most often manifests. It frequently displays no symptoms, although it may also appear as a nonspecific infection of the upper respiratory tract. In order to trigger a lytic infection in ocular tissues, the virus passes from the infected epithelium cells through the axon of the nerve to the cell. Individuals with past stromal involvement have a much greater probability of developing future stromal keratitis, and they also report discomfort, photophobia, impaired vision, lacrimation, and redness. In comparison, individuals with epithelial keratitis only have no higher probability of developing recurring HSV illness [8].

B. Varicella-zoster virus (VZV)

Immunosuppressed individuals or those who have ocular involvement are considered to have complicated herpes zoster infections [9]. The nasociliary branching of the ophthalmic nerve, which feeds the tip of the nose as well, is involved in the eye's condition (Hutchinson's sign). Regardless of whether the eyes are affected, the condition known as herpes zoster ophthalmicus (HZO) affects the ophthalmic division [10]. Ocular symptoms include disciform kerato-uveitis and punctate or dendritic keratitis. Direct viral invasion of cells may potentially cause epithelial keratitis [11].

- **Parasitic keratitis**

Acanthamoeba: They frequently trigger Acanthamoeba keratitis (AK), an eye infection. This corneal infection pains and might impair vision of an otherwise healthy individual that, when identified and managed early in the course of the illness, offers a good prognosis [12].

Acanthamoebic keratitis (AK) is a protracted corneal infection that causes extreme discomfort and remissions and flare-ups [12].

Diagnosis of Infective Keratitis

When treating infective keratitis, it is necessary to take a patient's medical history, make a clinical assessment, conduct a laboratory investigation, and initiate antimicrobial medications depending on the condition's severity, location, associated risks, and clinical signs. The initial plan should include the administration of antibiotics and laboratory tests, and it should be modified depending on the results of the tests [13].

The Recent investigations of infective keratitis besides culture and sensitivity

Cytology of the corneal impression: Since it effectively separates the superficial epithelium from the ocular, it may identify Acanthamoeba cysts and trophozoites in individuals with superficial AK [14].

Confocal microscopy: Is for the early identification of acanthamoeba and fungal keratitis. It can distinguish between various types of microbial keratitis, including fungal keratitis [14].

Electron microscope

Immunofluorescence staining

PCR (polymerase chain reactions): Might be a useful technique for identifying Acanthamoeba and fungal keratitis. It offers benefits like faster diagnosis and a less quantity of clinical materials being needed [15].

Biochemical testing: Such as latex agglutination, immune-diffusion, and counter immune-electrophoresis

Amniotic membrane

In an ophthalmic situation, AM works for supporting injured tissues, conceal deficiencies from further deterioration or breakdown by outside forces, and to encourage re-cellularization. This is made possible by a variety of biological aspects that, used to assist, speed up the healing of wounds, and better control pain while also having antimicrobial effects [16].

Properties of Amniotic membrane

- **Anti-fibrotic, anti-inflammatory, and anti-antigenic effect;** Protease inhibitors of heavy chain 1 of inter- α -trypsin and hyaluronan/pentraxin3 (HC-HA/PTX3) are found in the amnion extracellular matrix (ECM) complex, and mediators from the stromal layer also inhibit the well-known TGF- β signal transduction within fibroblasts, which has additional anti-scarring characteristics. Additionally, IL-10 is present, and IL-10 is known to lower IL-6 and TNF alpha concentrations. By stopping the profibrogenic cytokines from being activated, this prevents the genesis of fibrosis. The amniotic membrane's anti-fibrotic properties work in conjunction with the tissue's anti-inflammatory properties [17].
- Anti-microbial effect of both chorion and amnion, are efficient against certain germs. Progesterone hormones are thought to be bacteriostatic against certain gram-positive pathogens and are found in the amniotic fluid. Both elafin (peptidase-inhibitor 3) and secretory leukocyte proteinase inhibitory agents, which have antibacterial effects and are parts of the innate immune system, are secreted by the amnion [2]. The analogues of the cystine proteinase inhibitor cystatin E is also shown to have antiviral effects [18].

- **Promotion of epithelial and stromal healing:** The conjunctiva and cornea have a similar structure with basement membrane of the AM, particularly in terms of the amount of collagen present. Because of this, it may serve as a substrate for epithelial cells to readily multiplied. AM is claimed to have a variety of impacts on the epithelium of the cornea that is regenerating, including facilitating epithelial cell migration and enhancing basal epithelial cell adhesions. Additionally, it promotes cell differentiation and prevents apoptosis. [17, 19].

Use of amniotic membrane in treating corneal ulcers and epithelial defects: applications and procedures [19]

- **Inlay transplant:** The AM was incorporated into the stromal matrix and keratinocytes from the anchoring attached to it to aid in healing.
- An onlay patch graft covers the entire deficiencies and extends beyond it, creating a physical barrier to protect and a closed chamber below it that is filled with amniotic fluid. It may be fixed with surgical sutures or with a removable carriage equipment like PROKERA, a bandage that fits over the surface of the cornea. With proven effectiveness on resistant infectious keratitis and is used as well established protocol of management in Tanta university hospital in Egypt, also use of cryopreserved amniotic membrane in cases of bacterial keratitis was studied by Yin HY on 2020 with excellent results [20, 21].

Combining the two approaches

Amniotic membrane extract eye drops (AMEED) to make use of advantageous AM growth-factors, protease inhibitors, and antibacterial agents as home therapy, it's been successfully used for ocular surface chemical injury, dry eye, ocular cicatricial pemphigoid and during stem cell cultivation while use in infectious keratitis is still on clinical trial however processing the Amniotic membrane for mass production is the biggest obstacle for routine use.

- AM with umbilical cord blood.
- AM with placental fluid.

Potential dangers of transplanting amniotic membranes

Infection: The use of amnion carries an implied risk of contracting infectious illnesses since it is an allogenic-tissue from a single donor. To reduce this risk, appropriate donors assessment, handling, testing, processing, and storing should be used, along with a subsequent bloodborne infection screening test six months afterwards to adjust for the virus's latent infectious period [19].

Hematoma may develop after surgery, and if they hurt or displace the transplant, they might require to be drained [22].

Granulomas may also develop around stitched membranes, and membranes that are displaced might be annoying. Thicker membranes believed to come from persistent subepithelial membranes that were taken from the umbilical cord [19].

Conflict of Interest

Not available

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Not available

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