

## FRESH NON-PRESERVED HUMAN AMNIOTIC MEMBRANE TRANSPLANTATION IN THE TREATMENT OF DEEP CORNEAL ULCERS IN A DEVELOPING COUNTRY (NIGERIA): CASE REPORTS ON INITIAL EXPERIENCE

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### ABSTRACT

**Aim:** To demonstrate the use of Fresh non-preserved human amniotic membrane in treating deep corneal ulcers.

**Methods:** Three patients who had deep corneal ulcers following traditional medicine instillation had amniotic membrane transplantation at the University of Benin Teaching Hospital, Benin City. Appropriately cut pieces of amniotic membrane were layered in the centre of the of the corneal ulcers, epithelial surface up and the top one or two pieces were anchored with sutures.

**Results:** There was dramatic improvement in all the cases with the ulcers healing within 3 weeks.

**Conclusion:** Fresh non-preserved amniotic membrane is very useful in the management of severe deep corneal ulcers in the absence of preserved amniotic membrane. This will be of value in developing countries.

**Key Words:** Corneal ulcer, Amniotic membrane transplant.

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### INTRODUCTION

Amniotic membrane (AM) is the innermost layer of the foetal membranes. It has a stromal matrix, a thick collagen layer and an overlying basement membrane with a single layer epithelium. AM was first used in human transplantation in 1910 by Davis;<sup>1</sup> and first used in the eye in 1940 by De Roth<sup>2</sup> for scarring and adhesions between palpebral and bulbar conjunctiva. AM is said to have some unique properties that make them suitable for eye transplant such as promotion of epithelial cell migration and healing, production of various growth factors, bacteriostatic properties, suppression of fibrosis<sup>3-5</sup> and also lacks immunogenicity<sup>3</sup>. Reasons for lack of interest in amniotic membrane transplant (AMT) in treating eye conditions was not really known but interest in AMT was awakened after the publication by Kim and Tseng<sup>6</sup> in 1995. Presently AMT is used in the management of variety of external ocular conditions such as corneal epithelial and stromal defects, leaking filtering blebs in glaucoma surgery, pterygium surgery and also alkali and acid burns<sup>3,7-12</sup>. There are various surgical techniques in AMT such as “inlay”, “overlay” and “filler” techniques. The “inlay” technique involves placing the AM graft in the ulcer and holding it down

with sutures<sup>13</sup>. The “overlay” technique involves the whole cornea defect including at times the limbus being covered by AM graft functioning like a biological contact lens<sup>14</sup>. The “filler” technique involves layering of AM strips in the crater of the corneal ulcer until filled to the level of the corneal epithelium. The “filler” technique provides substitute for collagen in deep corneal ulcers<sup>15</sup>. These techniques have been used singly or in combination in treatment of corneal ulcers and ocular surface abnormalities of the eye. Letko et al<sup>14</sup> considered inlay and overlay AMT and found no difference in terms of healing time and recurrence rate. Use of native traditional medicines (cocktail of herbal extracts and such substances as breast milk, cow urine, cow dung, kerosene and gasoline) on the eye is fairly widespread in our environment. The major factor responsible for the use of these harmful substances for treating minor eye ailments and trivial eye injuries is ignorance and such other factors as poverty and lack of access to Ophthalmic health facilities in developing countries. There is also widespread use of various native traditional medicines for treatment of other common disorders like malaria, abdominal pains and bone fractures. These other forms treatment may have other side effects, but they are not as severe as in the eye where native medications often lead to blindness and ocular surface abnormalities. Many of the corneal ulcers from these native medicines lead to

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anterior staphyloma or perforation and may progress to panophthalmitis. Conjunctival autograft is for now the best effort in developing countries. The success rate is fairly satisfactory, but the results are usually not as satisfactory cosmetically. Preserved AM are usually beyond many in the developing world because of cost and availability<sup>16</sup>. In this case report series we describe our initial experience at the University of Benin Teaching Hospital (UBTH), Nigeria with non preserved fresh AM in treating deep corneal ulcers where impending perforation was evident in very poorly sighted eyes following instillation of harmful native medicines to treat ocular ailments.

## PATIENTS AND METHODS

AMT in our centre (UBTH) was usually an elective procedure. On the day of the surgery a senior resident from the Ophthalmology department obtained the AM from the labour ward after delivery by women who have been screened for HIV and hepatitis B. The AM was separated from the chorion by blunt dissection and rinsed in Normal saline. It was then cut into small sizes of about 3cm by 4cm and transferred to balanced salt solution (BSS) containing gentamycin antibiotics, and then kept in the refrigerator at 4<sup>o</sup>c. The cornea surface to be transplanted was debrided adequately and bathed in fortified gentamycin antibiotic solution. Then a 360 degree peritomy of the limbal conjunctiva was made and reflected for about 4-5mm. The stromal side of the AM was usually identified with the aid of a cotton tip applicator, which usually sticks to the stromal side but not the basement epithelial surface. Appropriately cut pieces of AM were layered in the crater of the corneal ulcer, epithelial surface up until the crater is filled to the level of the corneal epithelium. The top 1 or 2 pieces were anchored to the cornea with 9/0 nylon. Then a large piece of AM, epithelial side up was used to overlay the layered AM covering the whole cornea defect. It was also our usual practice to extend the overlay 1-2mm under the conjunctiva at the limbus and then anchored with 9/0 nylon sutures at the limbo-scleral junction. Fortified antibiotics drops and ointments are applied and the eye padded. The patients were admitted for about seven to ten days and the cornea observed and examined daily.

### PATIENT 1

This was a 52-year-old woman that treated an ailment in her left eye {LE} with herbal extracts and kerosene mixture. She had been on antibiotic medication for 2 weeks and was referred to us because of persistent tearing, redness, ptosis and pains. On examination, the visual acuity {VA}LE

was light perception {LP} and the Right Eye {RE} 6/6. She had a large corneal ulcer in the LE that stained very strongly with fluorescein. Culture and sensitivity yielded no significant growth as patient had been on antibiotic medication for 2 weeks. The patient had AMT {the overlay technique}, which was anchored with 9/0 nylon sutures. We inadvertently grafted the stromal surface up. The initial AMT which was the overlay technique was not successful. The AM dissolved by the 8<sup>th</sup> day. Before it dissolved, the patient felt much better and the tearing much less. We were determined and we convinced the patient to have the procedure repeated. In the repeat surgery, we layered the ulcer {filler technique} with about 4 pieces of AM and thereafter covered with the overlay. The repeat surgery was successful and the eye healed after 2 weeks {no staining with fluorescein}, the LP vision was maintained and the eye was saved from perforation.

### PATIENT 2

This was a 42-year-old woman who instilled native medicines to treat her left eye that became red because of foreign body. She would not tell us the constituents of the herbal cocktail. She also had deep corneal ulcer that stained strongly with fluorescein. Her VA was LP and the culture revealed no organisms as she was already on various antibiotics with some containing topical steroids. She told us the problem started under a week, but we were convinced it had been on for much longer. Patient had inlay layering (filler) and then the overlay graft on top anchored at the limbus. The patient had dramatic improvement in her eye condition. She could open her eye by the 4<sup>th</sup> day and the ulcer was healed by the 18<sup>th</sup> day. The VA was still LP but with very good light projections.

### PATIENT 3

This was a 48-year-old man who instilled herbal extract and alcohol mixture into his left eye following splash of car battery water into his eye. His company brought him on the 3rd day when the eye got much worse with severe tearing.

Ulcer was still clean and no growth of organisms because he was on antibiotic eye drops dispensed by the company nurse. The VA was hand movement (HM). Patient had inlay layering (filler) and overlay techniques. The transplant was successful and patient retained a count fingers vision at 1 meter.

## DISCUSSION

Amniotic membrane transplant (AMT) in Ophthalmology was neglected between 1946 and the close of the last century for reasons not quite clear. The rediscovery of the ophthalmic use of AM has greatly improved the ability to treat debilitating ocular surface disease. In the developing countries,

minor eye ailments and trivial injuries that would have healed spontaneously or responded to orthodox treatment usually result in infections, corneal ulcers and ocular surface abnormalities because of use of harmful native traditional eye medicines. The best treatment options for these corneal ulcers had been conjunctiva flap surgery and fortified antibiotics. These usually lead to the cornea being vascularised and causing pseudo-pterygium, which are usually cosmetically unpleasant. Cost and non-availability of preserved AMT prohibit wide use of AMT in treating ocular surface problem in developing countries<sup>17</sup>. Some authors<sup>16,17</sup> have described the use of fresh non-preserved human AM in treating ocular surface problems when preserved AM was not available. They recommended that developing countries should take advantage of the possibilities AM offer in treatment of external ocular disease by using fresh non-preserved human AM. In this case series we used fresh non-preserved human AM to treat deep corneal ulcers in three patients with very poor vision where preventing corneal perforation was our major concern. Our experience was that use of fresh non-preserved AM was very successful for treating deep corneal ulcers and the comfort of the patients improved rapidly immediately following the AMT. The case that failed initially was our first case. We performed the overlay technique alone that was perhaps not adequate for a very deep corneal ulcer and we also inadvertently grafted the AM with the epithelial stromal surface facing down instead of facing up. The repeat surgery on this patient and the surgeries for the two other patients had inlay-filler techniques and the overlay techniques and the results were very satisfactory. HIV and Hepatitis B screening were negative for the women that produced the AM. We also deliberately allowed the conjunctiva to overlap the AMT after the overlay for it to provide a basement membrane for the conjunctival epithelium to epithelise the AM graft. The cornea surface is strengthened further by the additional layer of conjunctival epithelium and there is less chance of anterior staphyloma occurring. It is our hope the successful outcome of our initial experience will encourage Ophthalmologists in developing countries who are unable to obtain persevered AM to use fresh non-preserved AM to treat deep corneal ulcers to reduce corneal perforation and staphyloma and also give their patients more cosmetically acceptable eyes.

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