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Acceleration of Donor Site Healing of Skin Graft by Application of Amniotic Membrane

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ABSTRACT

The usefulness of (Human Amniotic Membrane) HAM as a dressing biomaterial for split-thickness skin-graft (STSG) donor sites has not been investigated yet. The purpose of this study has been to evaluate the usefulness of HAM as an alternative biomaterial for STSG-donor site coverage and to compare the results with the commonly used wound dressings in order to test the null-hypothesis that HAM exhibits superior qualities as a wound dressing when compared with other dressings. This hypothesis is based on the positive results obtained in previous clinical studies that demonstrated the qualities of HAM in the treatment of burn wounds and in ophthalmologic surgery and for the treatment of full-thickness skin-graft donor sites.

INTRODUCTION

Human amniotic membrane (HAM) is the inner layer of the fetal membranes (the outer layer being formed by the chorion) and has been investigated as an alternative biomaterial for various purposes in reconstructive surgery and wound-healing research since its initial description as a transplantable material by Davis in 1910 **[1]**. In the 20th century, it offered new perspectives, for example, in the treatment of burn wounds, as shown in a 1977 clinical study in which it was used as a dressing for second and third degree burns in children, exhibiting superior qualities when compared with conventional dressings **[2]**. In another exemplary study in 1982, amniotic membranes were used for the coverage of facial dermabrasions in thirty-three patients. The results "were excellent" and revealed "advantages of amniotic membranes over the other employed dressing techniques" **[3]**. However, interest in HAM research and clinical investigations diminished as a consequence of the emerging awareness of AIDS and the consequent fear of virus transmission in the 1980s. It was not before the end of the 1990s that new methods for the processing and long-term storage (cryopreservation) of HAM were established, and its use in wound care and reconstructive surgery became a target of scientific interest again **[4]**.

MATERIAL AND METHODS

The wound-healing process was evaluated on postoperative days 5, 7, 10, 20, 40, and 60 by photodocumentation with a digital camera in 20 patients.

All patients gave written informed consent. In the context of reconstructive procedures, a standardized STSG of 0.4mm (0.016 inch) thickness was harvested from the thigh with a dermatome from 20 patients. The STSG-donor sites of the study group 10 patients were covered with allogenic HAM (group A), with at least 3mm overlapping and with the chorion site of HAM toward the wound ground HAM was covered by vaslein gauze. This procedure ensured sufficient stability of the HAM-dressing. In the control group 10 patients vaslein gauze served as a cover of the STSG-donor site.

The following clinical parameters were evaluated: Exudation/dryness degree, number of dressing changes, pain sensation through dressing changes, pruritus, and dressing comfort.

RESULTS

During postoperative progress, the two groups showed no differences with regard to bleeding, inflammation, infection, or chronological sequence of wound-healing. Wound contraction measurements revealed no contraction in either group. In the HAM group, seven wounds (70%) showed a final skin-like color on day 60 (the remaining wound exhibited a pink color).

Whereas four wounds (50%) exhibited a skin-like color in the Vaseline gauze group (of the remaining wounds, 3 were pink, 1 was white).

In the study group A, 93.3% of the wounds were completely epithelialized on postoperative day 8, whereas 86.7% were epithelialized in control group B at 8th day.

Significantly less wound exudation was found in HAM-treated wounds (group A) compared with the control group of wounds covered with Vaseline gauze.

Groups A required fewer dressing changes compared with group B.

Pain sensation during dressing changes was significantly less in study group A compared with group B.

HAM-treated wounds (group A) showed the slightest pruritus during the initial phase of wound-healing.

Regarding the comfort of the wound dressings as reported by the patients, the HAM-dressing exceeded the comfort of the control group.

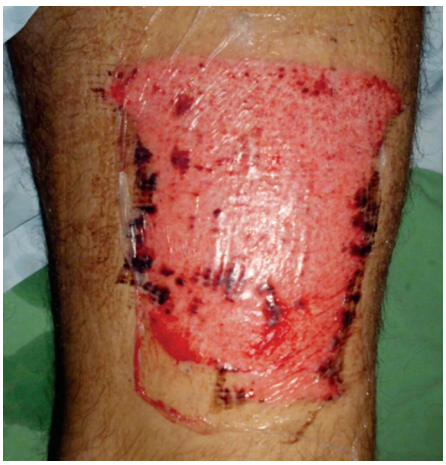

Fig. (1): 3 days after.

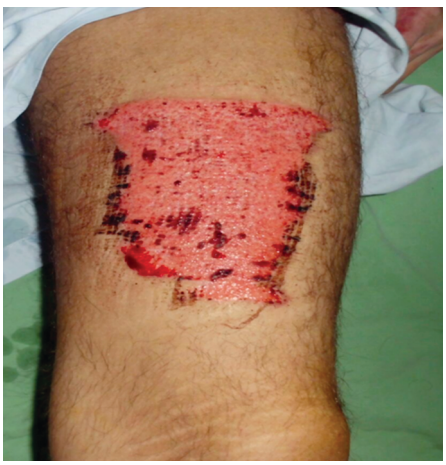

Fig. (2): 8 days after.

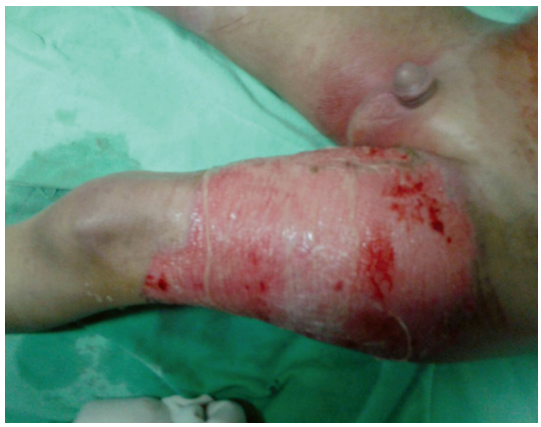

Fig. (3): 3 days after.

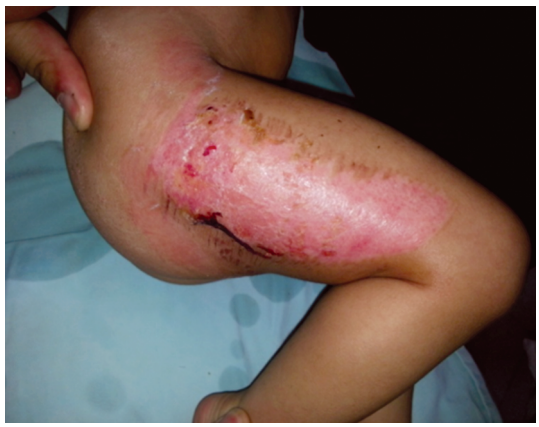

Fig. (4): 8 days after.

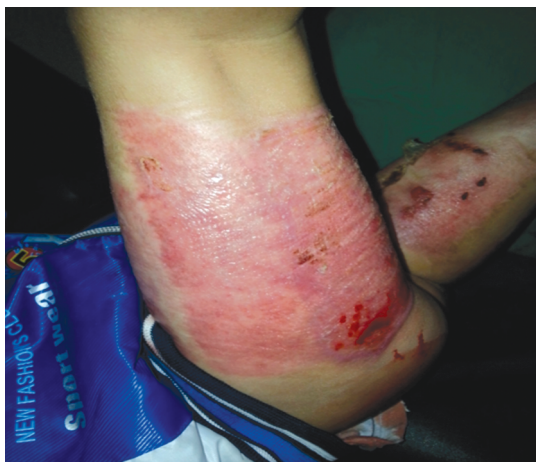

Fig. (5): 8 days after.

DISCUSSION

STSG are widely applied in all fields of reconstructive surgery such as skin cancers, burns, and extensive wounding. Under normal conditions, the donor site heals by reepithelialization from the dermis (epithelium grows out from hair follicles) and from surrounding skin but requires dressings for the first two to three weeks. The ideal dressing for an STSG-donor site should promote the rate

of reepithelialization, control the exudation to a physiological level, avoid leakages, and be comfortable for the patient with regard to pain and pruritus and the number of dressing changes. The postoperative course of wound-healing significantly depends on the degree of inflammation and infections. An anti-infective effect of HAM has been reported **[6,7]**. This seems to be a result of the synthesis of anti-inflammatory proteins and of a reduction of the expression of transforming growth factor-b (TGF-b) and proinflammatory cytokines, such as interleukin-10 (IL-10) **[6,8]**. Amnion cells synthesize peptides of the innate immunity system, such as ß-defensins, elastase-inhibitors, elafin, lactoferrin, or IL-1-RA; these factors might be the effectors of the antimicrobial capacities of HAM **[9,10]**. In the present study, split-thickness wounds treated with HAM showed almost no infections, which is in accordance with the above-mentioned reports demonstrating the anti-infective capacities of HAM. In addition to its endogenous factors, another reason responsible for the low rate of infections in defects covered with HAM might be its capacity of wound adherence **[11]**.

In this study, measurement of the epithelial thickness in the STSG wounds revealed a significantly higher epithelium in the control group than in the HAM group on postoperative day 60, that is, a tendency for increased cicatrization. The reduction of cicatrization in the HAM group might be attributable to its anti-inflammatory capacities and its previously described accelerating effect on reepithelialization **[4,6,8,11]** and to an inhibition of fibrosis **[12]**. With respect to the esthetic results in our investigation, HAM-treated defects in this study showed skin-colored epithelium in more cases (87.5%) than in the control group 50%).

During the early wound-healing process, the activation of keratinocytes plays a fundamental role in epithelial remodeling **[13]**, with prolonged proliferation probably being associated with hypertrophic scarring **[14]**. HAM synthesizes numerous growth factors such as epithelial growth factor (EGF), keratinocyte growth factor (KGF), human growth factor (HGF), basic fibroblast growth factor (bFGF), and transforming growth factors (TGF-α, TGF-ß-1, TGF-ß-2, and TGF-ß-3) and is assumed to accelerate reepithelialization and wound-healing by the activation of keratinocytes **[11,15,16]**.

Significantly reduced wound exudation, less pruritus, and fewer dressing changes (with the highest subjective comfort) were observed in HAM-treated wounds.

We need to clarify whether HAM can be standardized for clinical use. The material can indeed be standardized by applying protocols provided by certified tissue banks. However, various culture or cryopreservation techniques are still under investigation **[5,17,18]**.

Conclusions:

In view of the above-mentioned findings obtained in the study and the clinical trial, treatment with HAM as a wound dressing for split-thickness wounds seems to result in improved esthetic results and in less hypertrophic scarring when compared with treatment with conventional methods during the first 75 days of wound-healing. Although no significant difference in the overall speed of reepithelialization is evident in this investigation, the accelerated reformation of the basement membrane might result in improved defensive capacities of the wound against microbial infections, since the basement membrane forms a line of resistance, even if the overlying epithelial layer is not complete. This should be investigated in further studies. The results of this clinical trial reveal that HAM is a well-performing wound dressing for STSG-donor sites with statistically significant but clinically only minor (or even not relevant).

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