Egg Membrane as a New Biological Dressing in Split-Thickness Skin Graft Donor Sites: A Preliminary Clinical Evaluation

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Background: This preliminary investigation attempted to determine the effectiveness of egg membranes as a new biological dressing to promote infection-free healing and provide pain relief over split-thickness skin graft (STSG) donor sites.

Methods: Eighteen patients, with 28 STSG donor sites who were admitted to the LinKou Burn Center from August 1997 to July 1999, were selected for this trial. The bilateral thighs were the main donor sites for STSG. To compare different dressings, Surgilon®, B.G.C.® (β-glucan collagen), and Biobrane® were applied to the same donor sites, and epithelialization, pain relief, fluid accumulation, hematoma formation, and the occurrence of rejection or infection were monitored post-application.

Results: The average wound healing time with egg membrane application was 11.64 ±1.29 (range, 10 to 13) days. Meanwhile, the average wound healing times for B.G.C.® (6 patients) and Biobrane® (6 patients) were 14.5±0.84 and 14.0 ±0.63 days, respectively. Finally, Surgilon® (16 patients) had the longest healing time, at 16±1.41 days. On average, complete pain relief was achieved by 7.3±0.70 days for egg membrane application, while for B.G.C.®, Biobrane®, and Surgilon®, complete pain relief occurred by 7.0± 0.89, 6.0±0.63, and 10.0±0.37 days, respectively. Finally, no infection or rejection developed during healing.

Conclusions: From this preliminary study, egg membrane may be an ideal STSG donor site dressing, as it possesses properties of pain relief, wound protection, promotion of healing, and low cost. However, the limited unit size must be overcome, and its clinical application for burn wounds should be studied.
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Key words: **egg membrane, biological dressing, donor site dressing.**

Many different dressings have been applied to split-thickness skin graft (STSG) donor sites to relieve pain and promote wound healing,[1,2] including sofratulle, mebo,[3] opsite,[4] calcium alginate,[5] and others. Porcine skin has also been preferred as a dressing for partial thickness skin defects. However, porcine skin has higher antigenicity and the tendency to be taken, or incorporated into the wounds,[6,7] Biobrane®, a composite dressing, is not only expensive, but also delays reepithelialization.[8]

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Meanwhile, egg membrane, which protects the chicken embryo wall, is comprised mainly of glycoprotein without cellular components, and thus is not taken up by the wound and theoretically should be a good material for donor side coverage.

The relevant literature contains only 1 preliminary report on egg membrane as a biological dressing.[9] There is an animal study on the antigenicity of egg membrane performed by Chuang and presented at the 54th General Scientific Meeting, Surgical Association, Republic of China, in 1995.[10] The present study discusses our clinical experience of using egg membrane and compares its effectiveness as a dressing for STSG donor sites with those of other commercial dressings.

METHODS

Eighteen patients who entered the LinKou Burn Center from August 1997 to July 1999 were selected for this trial, regardless of age or gender. All patients had isolated donor sites and were free of other clinical conditions that might have affected wound healing. Split thickness skin grafting was used for burn injury, crushing injury, or necrotizing fascitis. The bilateral thighs were the main donor sites for STSG, and an air-driven Zimmer® dermatome was used to take the split thickness skin graft. Table 1 lists the thicknesses of the harvested grafts.

Egg membrane was obtained from hen eggs; sterilization was performed with gamma irradiation (3.0 Mrad); and a bacterial culture was employed to ensure the safety of the material. Egg membrane was prepared and stored under a constant temperature of 4 °C during the week before surgery. The membrane was then applied to the donor site immediately after harvesting the graft and was kept in place using gauze dressing moistened with normal saline. The egg membranes were evaluated daily to assess their adherence, the existence of hematoma or serous discharge, or evidence of infection. Patients were asked for their subjective opinion of pain at the donor site, rating the pain on a scale of 0 to 4 (Table 2). During the post-application time, the conditions of epithelialization, pain relief, and even rejection were evaluated. All observations were recorded on a flow sheet; photographs were taken; and observations were updated daily by the same observer. Patients were followed-up for at least 2 years to monitor the possible development of hypertrophic scars or persistent dyschromia.

To provide a comparison with egg membrane, other dressings were also applied to the same donor sites, including B.G.C.®, Biobrane®, and Surgilon® (Fig. 1), and the results were evaluated using the above protocol. Totally, B.G.C.® and Biobrane® were

Table 1. Demographic Profiles

Patient	Gender	Age (yrs)	Causes	TBSA of skin defect (%)	STSG thickness (inch)	TBSA of donor site (%)
Case 1	F	15	Flame burn	12	0.006	3
Case 2	F	69	Flame burn	8	0.008	2
Case 3	F	19	Contact burn	1	0.010	<1
Case 4	F	58	Crushing injury	10	0.010	2
Case 5	F	<1	Necrotizing fascitis	7	0.006	4
Case 6	M	30	Scald burn	15	0.010	5
Case 7	M	31	Scald burn	6	0.008	2
Case 8	M	36	Scald burn	10	0.008	3
Case 9	F	28	Scald burn	2	0.008	1
Case 10	F	48	Flame burn	35	0.008	3
Case 11	F	16	Flame burn	50	0.008	6
Case 12	F	38	Flame burn	36	0.008	3
Case 13	M	59	Flame burn	33	0.010	3
Case 14	M	40	Flame burn	25	0.008	6
Case 15	M	52	Scald burn	18	0.008	6
Case 16	F	12	Flame burn	5	0.008	5
Case 17	F	26	Flame burn	3	0.008	3
Case 18	M	25	Scald burn	6	0.006	3

Abbreviations: TBSA: total burn surface area; STSG: split-thickness skin graft

Table 2. Pain Scale

Scale	Definition
0	No pain felt
1	Slight pain, no medication required
2	Mild pain, medication is possibly required
3	Moderate pain, oral analgesic is necessary
4	Severe pain, parenteral analgesic is mandatory to prevent insomnia

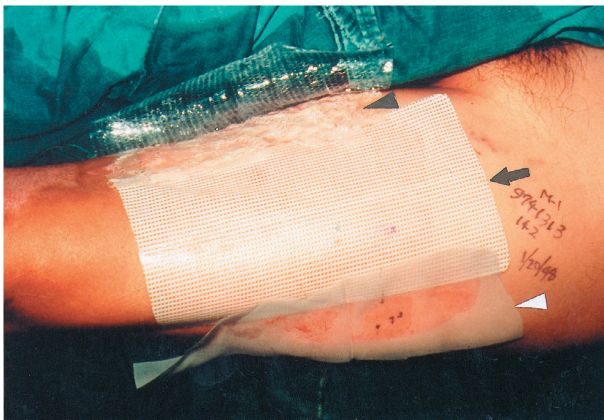

Fig. 1 Case 11. Three different dressings (black arrowhead: egg membrane; arrow: B.G.C.®; white arrowhead: Surgilon®) were applied to the same donor site of the left thigh. The egg membrane is protected by op-site for secure adherence.

used in 6 patients, and Surgilon® in 16 patients. Analysis of variance (ANOVA) was used to calculate the results of comparisons among different dressings.

RESULTS

Table 2 lists the demographic data of the 18 patients. The sample consisted 12 females and 6 males, aged from 3 months to 69 years (averaged 33.5 years). Of the 18 patients, 16 had burn injuries, while 1 each had an extremity crushing injury and necrotizing fascitis, respectively. The thickness of the cuts was kept to around 10/1000 in inches wherever possible, but the thickness for comparison between different dressings was fixed at 8/1000 in inches . The donor site area was between 1% and 6% (averaged 2.92%) of the total body surface area (TBSA).

This investigation defines "healing" as complete epithelialization (no existence of a discharging wound). The average duration for healing took 11.64 $\pm$1.29 (range, 10-13) days for egg membrane, 14.5 $\pm$0.84 days for B.G.C.®, and 14$\pm$0.63 days for Biobrane®. Surgilon® took the longest time to heal (16$\pm$1.41 days) (Table 3, Fig. 2). Next, donor site pain was evaluated in 16 patients. The average time for complete pain relief, i.e., reaching 0 on the pain

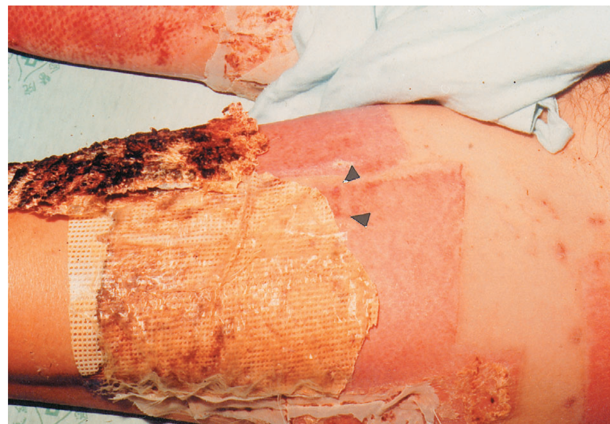

Fig. 2 Case 11. Appearance of the donor site on day 10 post-application. The wound treated with egg membrane epithelialized well, while that treated with B.G.C.® healed with partial erosion (arrows). Compared with egg membrane and B.G.C.®, the wound treated with Surgilon® did not heal within the same time period.

Table 3. Comparisons Between Different Dressings

	Egg membrane (18 patients)	Biobrane® (6 patients)	B.G.C.® (6 patients)	Surgilon ® (16 patients)	*p
Reepithelialization (Days)	$11.6\pm1.29^{A\dagger}$	14 ± 0.63^{B}	14.5 ± 0.84^{B}	16 ± 1.41^{B}	<0.001
Complete pain relief (Days)	7.3 ± 0.70^{A}	6 ± 0.63^{A}	7 ± 0.89^{A}	10 ± 0.37^{B}	<0.001

*: calculated by ANOVA;
†: Bonferroni multiple comparison: Statistical significance was method

scale, was 7.3±0.70 days. Oozing beneath the egg membrane occurred in 11 patients, and the average dry-out time was 6.45±0.70 days. Serious discharge developed in 9 patients and faded away on average after 3.66±1.15 days.

Donor sites dressed using Biobrane® achieved complete pain relief by 6±0.63 days, and egg membrane and B.G.C.® achieved the same results, but by 7±0.89 days (Table 3). However, donor sites dressed with Surgilon® continued to exhibit slight pain even on day 10±0.37 postoperatively. Regarding the timing to complete epithelialization and pain relief, there was a statistically significant difference among different dressings ($p < 0.001$, ANOVA). One patient treated with egg membrane developed a hypertrophic scar during the 2-year follow-up.

DISCUSSION

An ideal wound dressing should provide an environment suitable for rapid infection-free healing, cause minimal pain, and require minimal nursing care. Although some commercial synthetic or composite materials currently meet these requirements, they are expensive and not very user-friendly. Among true biological dressings, human amniotic membranes have proven their usefulness in partial thickness skin wounds as a temporary dressing that can promote reepithelialization. However, Unger and Roberts found delayed healing time and no significant reduction in pain in their investigation that applied lyophilized amniotic membranes to 8 skin graft donor sites.[11] Additionally, amniotic membranes are limited as dressings owing to their potential threat of human disease transmission.[12,13] In clinical applications, amniotic membranes are fragile, difficult to manipulate, easily macerated, and not readily available. Nevertheless, amniotic membranes remain popular, especially in developing countries.[14] Porcine skin is another material that has been widely used as a biological dressing. However, as Salisbury et al.[15] noted, porcine xenografts were incorporated into the wounds of 35% of patients, leading to pronounced inflammatory responses and prolonged healing time. Cadaver skin is very difficult to obtain in Oriental countries because of a lack of donors. Finally, collagen sheets are easily macerated; excessive wound discharge occurs; and the material is only suitable for superficial donor site wounds.[16,17] Egg membrane, the protective covering for chicken embryos, is a complex mixture of proteins and glycoprotein. Egg membrane was first employed in clinical trials in 1981, as described by Maeda and Sasaki.[9] Maeda and Sasaki presented 3 cases with satisfactory epithelialization and concluded that egg membrane is an inexpensive and reliable biological dressing. Egg membrane is a thin (60-70 µm), highly-collagenized fibrous connective tissue comprised of both inner and outer layers. Egg membrane is comprised mainly of protein, making up 88%-96% of its dry weight[18], and its unique structure provides reasonable adhesion and vapor transmission. Egg membrane is a cell membrane sheet that contains no nuclear DNA. Theoretically, egg membrane has low antigenecity. Egg membrane used for wound coverage in an animal model confirmed this property, as described by Chuang in 1995,[10] and clinical observations have also confirmed this fact from our experience. To safely utilize this material, gamma irradiation is used to inactivate the viruses possibly maintained in the egg membrane, and to the best of our knowledge, gamma irradiation effectively achieves this task.[19]

While the size of 1 egg membrane is approximately 40-50 cm^2, after remodeling, only 20 cm^2 is available for clinical use (Fig. 3). This investigation found that the average healing time, at 11.64±1.29 days, was satisfactory. Compared with Biobrane®, egg membrane was found to perform equally well with regards to hemostasis and adherence, and performed even better in permeability and minimizing fluid accumulation. In the present results, wounds dressed with egg membrane healed faster than those dressed with Biobrane®, on average at 11.64 vs. 14.0 days, although the difference was not statistically significant because of the limited sample size. Meanwhile, Hansbrough et al. reported an average of 9.8 days for wound healing in their clinical experience with applying Biobrane® to partial-thickness burns of various depths.[20] The flexibility and durability of egg membrane was inferior to that of Biobrane®. Biobrane's® flexibility and durability enable it to be applied to numerous diverse donor sites, while its near-transparency facilitates wound monitoring. Concerning pain at donor sites, egg membrane effectively reduced pain sensations, similar to results for Biobrane® and B.G.C.®. Meanwhile,

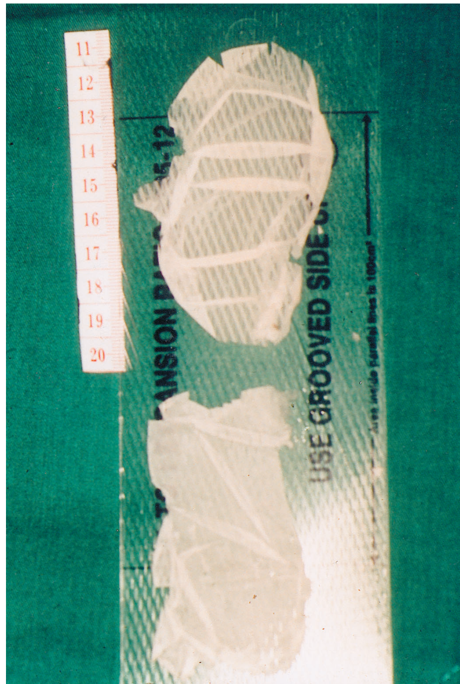

Fig. 3 The size of 1 egg membrane is approximately 40-50 cm^2.

Surgilon® was the least effective in pain relief. However, it should be emphasized that the observations regarding pain relief made in this study were all extremely subjective.

Egg membrane is inexpensive and readily obtainable almost anywhere. Compared to Biobrane® and porcine skin, egg membrane costs only 1/8 and 1/10 as much, respectively. Consequently, egg membrane is an extremely cost-effective biological dressing.

Disadvantages of egg membrane are its relatively low transparency, flexibility, and durability. The lack of transparency interferes with wound monitoring. However, egg membrane, although less transparent than Biobrane®, still permits better wound evaluation than do non-transparent dressings such as B.G.C.®. Furthermore, the lack of flexibility and durability of egg membrane limits its application to various donor sites, such as to the back or to wounds located over joints. In addition, the limited size per unit of egg membrane is another drawback that needs to be overcome, since it hinders the applicability of egg membrane to extensive donor sites or partial thickness wounds. Determining ways to produce larger pieces of egg membrane is the subject of an ongoing study.

Wound depth is one of the major factors influencing healing time. This investigation thus compared different dressings on STSG donor sites with equivalent wound depths. The comparative results show that egg membrane is effective as a biological dressing on STSG donor sites; its application to some partial thickness burn wounds and skin graft donor sites is encouraged.

Conclusions

Egg membrane effectively promotes quick epithelialization of STSG donor sites and reduces subjective pain sensations. Furthermore, egg membrane is cost-effective for STSG donor sites. However, further application of egg membrane to extensive wounds requires that the problem of its limited unit size be overcome.

REFERENCES

1. Tavis MJ, Thornton J, Danet R, Bartlett RH. Current status of skin substitutes. Surg Clinics North Am 1978;58:1233-48.
2. Pruna SK, Babu M. Collagen based dressings - a review. Burns 2000;26:54-62.
3. Atiyeh BS, Ghanimeh G, Kaddoura IL, Ioannovich J, Al-Amm CA. Split-thickness skin graft donor site dressing: preliminary results of a controlled, clinical comparative study of MEBO and Sofra-Tulle. Ann Plast Surg 2001;46: 87-8.
4. James JH, Watson AC. The use of Opsite, a vapour permeable dressing, on skin graft donor sites. Brit J Plast Surg 1975;28:107-10.
5. Ho WS, Ying SY, Choi PC, Wong TW. A prospective controlled clinical study of skin donor sites treated with a 1-4,2-acetamide-deoxy-B-D-glucan polymer: a preliminary report. Burns 2001;27:759-61.
6. Bromberg BE, Song IC, Mohn MP. The use of pigskin as a temporary biological dressing. Plastic Reconstr Surg 1965;36:80-9.
7. Rappaport I, Pepino AT, Dietrich W. Early use of xenograft as a biological dressing in burn trauma. Am J Surg 1970;120:471-7.
8. Yang JY, Tsai YC, Noordhoff MS. Clinical comparison of commercially available Biobrane preparations. Burns 1989;15:197-203.
9. Maeda K, Sasaki Y. An experience of hen-egg membrane as a biological dressing. Burns 1981;8:313-6.
10. Chuang SS, Yang JY. A new biological dressing material,

egg membrane, for the wound coverage-the clinical observation in animal model, presented at the 54th General Scientific Meeting, Surgical Association, Taiwan, ROC, March 24, 1995, Taipei, Veterans General Hospital.
11. Unger MG, Roberts M. Lyophilized amniotic membranes on graft donor sites. Br J Plast Surg 1976;29:99-101.
12. Colocho G. Graham WP III, Greene AE, Matheson DW, Lynch D. Human amniotic membrane as a physiologic wound dressing. Arch Surg 1974;109:370-3.
13. Quinby WC Jr, Hoover HC, Scheflan M, Walters PT, Slavin SA, Bondoc CC. Clinical trials of amniotic membranes in burn wound care. Plast Reconstr Surg 1982; 70:711-7.
14. Ramakrishnan KM, Jayaramam V. Management of partial-thickness burn wounds by amniotic membrane: a cost-effective treatment in developing countries. Burns 1997;23(suppl. 1):S33-6.
15. Salisbury RE, Wilmore DW, Silverstein P, Pruitt BA: Biologic dressings for skin graft donor sites. Arch Surg 1973;106:705-6.
16. Yang JY. Clinical application of collagen sheet, YCWM, as burn wound dressing. Burns 1990;16:457-61.
17. Sawada Y, Yotsuyanagi T, Sone K. A silicone gel sheet dressing containing an antimicrobial agent for split thickness donor site wounds. Brit J Plast Surg 1990;43:88-93.
18. Leach RM. Biochemistry of the organic matrix of the eggshell. Poult Sci 1982;61:2040-7.
19. Reid BD. The Sterways process: a new approach to inactivating viruses using gamma radiation. Biologicals 1998; 26:125-9.
20. Hansbrough JF, Sirvent RZ, Carroll WJ, Dominic WJ, Wang XW, Wakimoto A. Clinical experience with Biobrane biosynthetic dressing in the treatment of partial thickness burns. Burns 1984;10:415-9.

以蛋膜 (Egg Membrane) 使用在薄層皮膚移植 (Split-Thickness Skin Graft) 取皮區為生物性敷料：初步臨床評估

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背 景： 當病人需要薄層皮膚移植時，常必須面臨取皮區傷口劇烈疼痛且癒合過慢之痛苦。而理想之敷料除了能預防感染並且可以解決上述兩個問題。本篇研究的目的即在研究蛋膜在取皮區作為一生物性敷料之角色。

方 法： 從1997年8月至1999年7月共有18個病人，28個薄層取皮區包含在此次研究。兩側大腿為主要之取皮區，為了比較其他不同的敷料，在同一個取皮區我們使用不同敷料，如B.G.C.®，Biobrane®，Surgilon®和蛋膜，來比較其表皮生成速度，痛覺的緩解，分泌物貯積，血腫生成的不同，以及是否有排斥或感染之現象。

結 果： 蛋膜傷口癒合時間為11.64 ±1.29天，分布從10至13天。而B.G.C.® (6 個病人) 和Biobrane® (6個病人)，分別為14.5±0.84和14±0.63天。Surgilon® (16個病人) 癒合最慢，需16 ±1.41 days。病人完全不感覺取皮區會痛，平均在蛋膜需7.3±0.70天。然而B.G.C.®，Biobrane®，以及Surgilon®，分別需要7 ±0.89，6±0.63和10±0.37天。在整個治療過程並沒有發現感染或是排斥的現象。

結 論： 不管是痛覺的緩解，傷口癒合的情形。蛋膜可以是一種理想的生物性敷料。 然而單位面積過小以及未來使用在燙傷傷口，仍需進一步的研究。

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關鍵字： 蛋膜，生物性敷料，取皮區照護。

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