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Keratin-based products for effective wound care management in superficial and partial thickness burns injuries

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ARTICLE INFO

Article history:
Accepted 23 October 2015

Keywords:
Partial thickness burns
Keratin dressings

ABSTRACT

This $n = 40$ cohort study on superficial and partial thickness burns compares novel keratin-based products with the standard products used at our facility. The keratin products are found to facilitate healing with minimal scarring, be well tolerated with minimal pain and itch, be easy to use for the health professional and be cost effective for the health care provider. For these reasons they are being adopted into use at our facility.

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1. Introduction

Superficial and partial thickness burns account for the majority of burn presentations in the hospital setting and patient management with topical dressings and outpatient followup is often appropriate. An ideal product meets the needs of the wound, the patient, the health practitioner and the healthcare provider. The wound requires protection from external infection and trauma, and something to promote rapid epithelialisation and scar minimisation. The patient seeks comfort and a rapid return to activities of daily living (ADLs); the practitioner seeks ease of use and the provider, minimal cost and use of limited health resources.

We report a cohort study comparing a range of keratin-based products (a thick keratin gel (keragel®), a thin keratin gel (keragelT®), and a keratin matrix (keramatrix®), from the Replicine® range (Keraplast Technologies LLC, www.keraplast.com)) with standard care. The aim of the study was to determine the effectiveness of these keratin-based products in the management of superficial (where only the epidermis is damaged) and partial thickness (where the epidermis and part, but not all, of the dermis is damaged) burns by comparing their ability to meet the above requirements against current standard care.

Potential fitness-for-purpose of the keratin-based products was supported by pre-clinical animal studies [1] and a clinical randomised control trial (RCT) on partial thickness donor site wound healing [2] and scar management [3]. The keratin in this range of products has been shown to stimulate keratinocyte activity [4] increasing migration and proliferation rates, and up-regulating the expression of key basal membrane proteins (types IV and VII collagens). This mechanism is consistent with results observed in the clinical trials described above and is well aligned to the needs for the classes of burns being studied. The ease of product use was confirmed in a clinical case study series on venous leg ulcers [5] and in clinical studies of patients with Epidermolysis Bullosa [6,7]. This is the first systematic clinical trial of keratin-based products for burns patients.

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http://dx.doi.org/10.1016/j.burns.2015.10.024
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2. Methods

The study was approved by the institutional review board (Upper South B Regional Ethics Committee, New Zealand). The inclusion criteria for the patient cohort was: burns presenting at Christchurch Hospital Emergency Department (ED) within 24 h of injury and involving less than 10% total body surface area (TBSA). The exclusion criteria were: infected burns (burn where the bioburden was likely to impede healing, as assessed by the duty plastic surgery team based on a combination of pain, swelling, pus and erythema), full thickness burns (as assessed by the duty plastic surgery team) and any burns not expected to heal by conservative approaches within approximately 14 days and likely to require skin grafting.

Patients in the treatment group ($n = 40$) presented at the ED and were consented to enroll in the study. For burns with low exudate, if they were judged not to need a secondary dressing for protection (e.g. on the face), the thin keratin gel alone was used as this would dry quickly. For burns with low exudate, if they were judged to need a secondary dressing for protection, the thick keratin gel was used and then covered with a non-adherent dressing such as Mepitel®, Silflex® or similar and then a Tegaderm™ film dressing was applied to secure, waterproof and for ease of performing ADL's. For burns with moderate exudate the thick keratin gel was again used and covered with a non-adherent dressing, cotton gauze and then a Tegaderm™ film dressing. For burns with high levels of exudate (typically on the trunk/legs), the keratin matrix dressing was used and covered with a non-adherent dressing, an absorbent pad dressing such as Melolin® or Mesorb® or similar and then a Tegaderm™ film dressing. In some cases hydration of the keratin matrix dressing with saline prior to application ensured increased compliance of the matrix and assisted with body contour moulding. Finally, for burns where exudate level for the subsequent 2 days was unpredictable, the thick keratin gel was applied and covered with a keratin matrix and Tegaderm™. The choice of keratin dressing to use was made by the duty plastic surgery team. Subsequent treatment was provided in the community by the same independent community nurse. Again the choice between thin gel, thick gel or matrix was based on exudate management and secondary dressing needs. Intact blisters were typically left for 2 days (unless these were over joints and would restrict movement) then debrided and all non-viable tissue was debrided. Overall, a moist wound healing approach was taken avoiding excess free liquid but not allowing the wound to dry. Oral analgesics were available to patients for dressing changes.

Digital photographs were taken at presentation and at each dressing change every 2–4 days. During dressing changes, patients' levels of itch and pain and their ability to resume ADLs were recorded in the clinical notes. Patients were clinically discharged once epithelialisation was complete and any not discharged were assessed in a hospital outpatient clinic by the same Plastic Surgeon 12–14 days after injury. At time of wound epithelialisation, patients were provided with the thin keratin gel to apply daily for 1 month to assist with scar management. Patients' scars were inspected by the same community nurse at 6 and 12 months after injury, and a Patient Observer Scar Assessment Scale (POSAS) measurement was recorded and digital photographs were taken at these time points.

A control group ($n = 40$) of patients was retrospectively identified. They had burns that met the inclusion criteria and presented during the same time period that patients were being enrolled into the treatment group. These patients were treated with protocols representing Standard Care for the Plastics Department. This includes Acticoat™, Biobrane® and an assortment of non-adherent dressings and topical liquids. All cohort patients had burn data recorded at presentation including cause of burn, TBSA and depth of burn. Healing times and oral antibiotic use were attained from patient clinical notes.

For each patient in both the treatment and control groups, resource utilisation data and associated costs were collected from hospital patient management records. The costs were categorised as: Emergency Department, Operating Theatre, Inpatient, Outpatient, Medical Staff, Support Staff and Other. In our facility's cost accounting system, nursing costs are included in either inpatient, outpatient or emergency department costs (as appropriate). The cost of consumables is excluded and no corrections were made for inflation. To statistically compare measurements from treatment and control groups, ANOVA or χ^2 test, as appropriate, was used to determine if differences are statistically significant with $P < 0.05$.

3. Results

Forty patients with 61 distinct burn wounds were enrolled to treatment, including 32 Caucasian, 7 Maori or Pacific Island and 1 Asian patient ethnicity, with an age range of 7 months to 69 years. The majority of the burn wounds healed rapidly with only 2 (4%) taking more than 10 days. Fig. 1 provides a Consort Diagram; 36 patients with 49 burn wounds were analysed.

Localised infection was noted in two burn wounds on the first three patients enrolled. Following outpatient treatment with oral antibiotics and a silver-based dressing, they healed with no further complications. Subsequently, the treatment method was revised to that described in the methods section and intact blisters were retained for 2 days, and then debrided to decrease the infection risk. The choice of secondary dressings was also revised to provide more absorption and avoid 'pooling' and the subsequent 37 patients showed no signs of clinical infection. The three patients enrolled prior to the method change have been excluded from the analysis as described in the CONSORT diagram, Fig. 1.

One patient presented with a scald burn, it was predicted that she would start to epithelise within 14 days and she was enrolled into the treatment group. After 14 days she had not started to epithelise and so she followed our facility's protocol and received debridement and split skin grafting at that time. Hence, she has been treated as 'discontinued intervention' and excluded from the analysis.

POSAS assessments of mature scars were conducted on 29 of the 36 patients in the treatment group, inclusive of 41

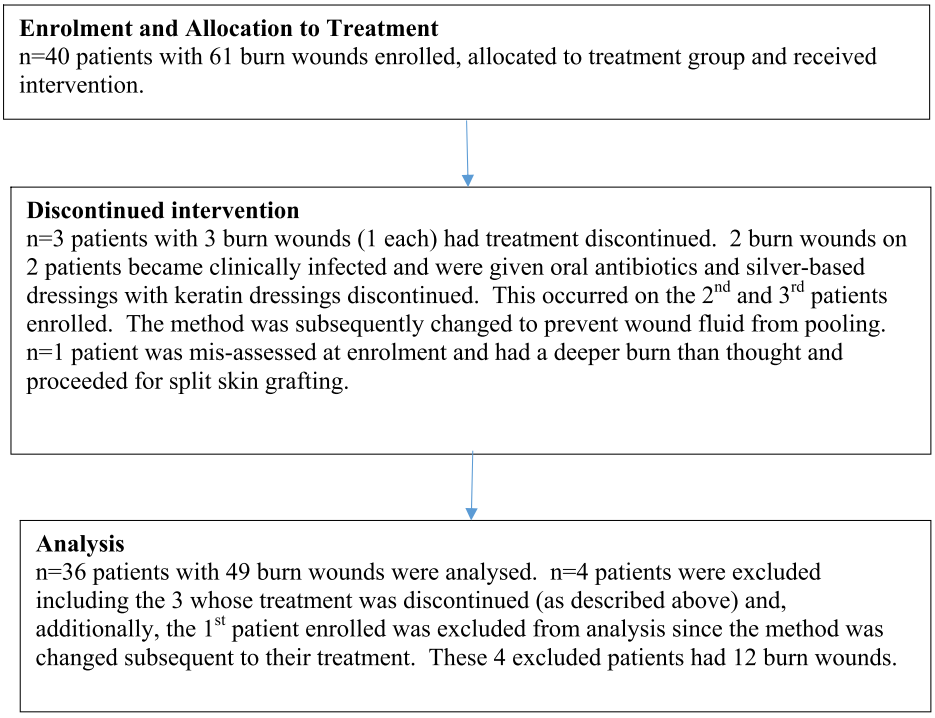

Fig. 1 – Consort diagram.

of 49 burn wounds. For many of the patients, no scarring was visible at ~6 months and a repeat assessment at 12 months was not needed. The results presented in Table 1 are for the last assessment made for each patient which best represents the long term scar prognosis. Overall, good concordance between the observer and patient scores was noted with most wounds receiving the lowest score (1) for all components (the maximum score being 10), except the observer 'pigmentation' trait and the patient 'colour' trait. Permanent skin change effects noted by the observer post treatment were generally very good, with 30 of 41 burn wounds (73%) scoring '1' i.e. normal skin appearance, eight burn areas (20%) scoring 2 or 3 for pigmentation changes i.e. a very minor change and three cases (7%) scoring >3 i.e. a moderate skin change.

Patients reported low itch and pain levels and found dressing changes very comfortable, many stating it decreased any burning pain on application. In many cases, the patients opted not to take the oral analgesics that were made available. Infants responded well to dressing changes in their own home and were generally not anxious about subsequent dressings. Protection of the injured areas was good without being obtrusive and patients were generally able to resume normal ADLs with dressings in place.

The 40 patients in the control group had similar causes of burn and no significant difference was noted in the average area or depth of the burns, refer Table 2. Healing outcomes are compared in Table 3 and resource utilisation is translated to monetary costs in Table 4. The healing outcomes are non-inferior and the cost per patient for the control group was $5016, compared to $2635 for the treatment group.

4. Discussion

Moist wound healing that was convenient for both the patient and the practitioner was achieved with the keratin dressings. The keratin gel was replenished at each dressing change (every 2–3 days). As healing progressed, the thick keratin gel was substituted for the thin keratin gel, which dries at a faster rate (~5 min after application), providing increased ease of use. The thick keratin gel was used on burns with minimal exudate and difficult to dress contours such as the face, neck and hands. The keratin matrix was used on exuding burns on the trunk or legs. The matrix gelled when interacting with the wound exudate and resorbed, often remaining on the wound for 8 days prior to being washed off at time of wound epithelialisation. Initially, if exudate levels were not high but the burn was expected to exude, the keratin matrix was used in combination with the keratin gel. The keratin gel was also useful to treat dry margins of the burns around the keratin matrix. The keratin gel was sometimes used without a covering dressing (e.g. face), it formed a robust barrier providing protection against trauma and bacterial colonisation, and maintained a moist healing environment encouraging keratinocyte proliferation and migration.

Prior to the method change after patient 3, wound management had allowed free liquid pooling to occur and this is believed to be the likely cause of the bacterial colonisation. The keratin-based products are very porous and were not the cause of such 'pooling'. The change in method resulted in moist wound healing without complications for the subsequent patients. This suggests that our

Table 1 – POSAS assessments.

Burn	Patient	POSAS – observer scores (1 = normal skin – 10 = worst scar imaginable)						POSAS – patient scores (1 = no effect – 10 = maximum effect)						
		Vascularisation	Pigmentation	Thickness	Relief	Pliability	Total	Pain	Itch	Colour	Stiffness	Thickness	Irregularity	Total
1	1	Patient excluded from analysis												
2	2													
3	2	Patient excluded from analysis												
4	2													
5	3													
6	3													
7	3													
8	3	Patient excluded from analysis												
9	3													
10	3													
11	3													
12	4	No POSAS data for this patient												
13	5	1.5	1	1	1	1	5.5	1	1	2	1	1	1	7
14	6	1	1	1	1	1	5	1	1	1	1	1	1	6
15	7	1	1	1	1	1	5	1	1	2	1	1	1	7
16	8	1	1	1	1	1	5	1	1	1	1	1	1	6
17	9	1	4	1	1	1	8	1	1	3	1	1	3	10
18	10	No POSAS data for this patient												
19	11	1	2	2	1	1	7	7	1	1	1	1	1	12
20	12	1	3	3	1	1	9	1	1	3	1	1	3	10
21	13	1	1	1	1	1	5	1	1	1	1	1	1	6
22	14	No POSAS data for this patient												
23	14													
24	15	1	1	1	1	1	5	1	1	1	1	1	1	6
25	16	1	1	1	1	1	5	1	1	1	1	1	1	6
26	17	1	1	1	1	1	5	1	1	1	1	1	1	6
27	17	1	5	1	1	1	5	1	1	3	1	1	3	10
28	18	No POSAS data for this patient												
29	19	No POSAS data for this patient												
30	20	Patient excluded from analysis												
31	21	1	3	1	1	1	7	1	1	3	1	1	1	8
32	22	1	1	1	1	1	5	1	1	1	1	1	1	6
33	23	1	1	1	1	1	5	1	1	1	1	1	1	6
34	23	1	1	1	1	1	5	1	1	1	1	1	1	6
35	23	1	1	1	1	1	5	1	1	1	1	1	1	6
36	23	1	1	1	1	1	5	1	1	1	1	1	1	6
37	23	1	1	1	1	1	5	1	1	1	1	1	1	6
38	24	1	1	1	1	1	5	2	1	2	1	1	1	8
39	24	1	1	1	1	1	5	2	1	2	1	1	1	8
40	24	1	1	1	1	1	5	2	1	2	1	1	1	8
41	25	1	1	1	1	1	5	1	1	2	1	1	1	7
42	26	1	1	1	1	1	5	1	1	2	1	1	1	7
43	27	1	1	1	1	1	5	1.5	1	3	2	2	2	11.5
44	27	1	1	1	1	1	5	1.5	1	1	1	1	1	6.5

45	28	1	1	1	1	1	5	1	1	1	1	1	1	6
46	28	1	2	1	1	1	6	1	1	2	1	1	1	7
47	29	1	6	1	1	1	10	1	1	10	1	1	1	15
48	30					No POSAS data for this patient								
49	31	1	3	1	1	1	7	1	1	6	1	1	6	16
50	32					No POSAS data for this patient								
51	33	1	1	1	1	1	5	1	1	1	1	1	1	6
52	34	1	1	1	1	1	5	1	1	1	1	1	1	6
53	35	1	1	1	1	1	5	1	3	2	1	1	1	9
54	36	1	1	1	1	1	5	1	2	1	1	1	1	7
55	37	1	1	1	1	1	5	1	1	1	1	1	1	6
56	38	1	1	1	1	1	5	1	1	1	1	1	1	6
57	39	1	1	1	1	1	5	1	1	1	1	1	1	6
58	39	1	1	1	1	1	5	1	1	1	1	1	1	6
59	40	1	3	1	1	1	7	1	1	2	1	3	2	10
60	40	1	3	1	1	1	7	1	1	2	1	3	2	10
61	40	1	2	1	1	1	6	1	1	2	1	3	2	10

treatment regime (which does not include topical or systemic antibiotics) is suitable for this cohort of wounds less than 24 h old and not heavily colonised at presentation.

The keratin products were well tolerated by patients with minimal pain or itch, and a relatively quick return to regular ADLs. The vast majority of treatment was provided in the patient's home by the same independent nurse. Many patients did not need to attend their hospital outpatient clinic follow-up appointment as the burn wounds had healed uneventfully. These keratin products facilitated community based management of this cohort of patients in contrast to the control group, where a significant number of operating theatre visits and hospital admissions were required, along with a significantly greater number of outpatient dressing changes.

In comparison to the treatment group, the control group had a slightly (but not statistically significantly) larger proportion of paediatric patients under the age of 4 years and a statistically significantly smaller proportion of patients older than 15 years. Children may heal faster than adults but this is not believed to be of great significance in the results of this study. The majority of patients in the control group were treated with an anti-microbial dressing (typically Acticoat™) and a high number of children with Biobrane® under general anaesthetic. The treatment group had a statistically significantly greater ration of partial thickness to superficial burns but this is not believed to be significant and there was no statistically significant difference in TBSA.

The method of allocation of patients to treatment or control groups is not suited to making precise outcome comparisons; however the results suggest that the outcomes for the treatment group patients using the keratin-based products were not unfavourable with straightforward healing. A high proportion of cases had minimal or no noted permanent changes to the injured skin. Epithelialisation and hence healing rates were observed to be as fast as, or faster, than the control group. This is consistent with previous clinical experience with the keratin-based products on other wound types. It is recognised that there are inaccuracies associated with the way healing time was measured in this study, healing time was measured to be 'the time until the burn was seen to be fully epithelialised by a health professional'. During the latter stages of healing there were intervals of 5 or more days between assessments for some patients (from both treatment and control groups) and hence some inaccuracy in the measurement of healing time. More frequent wound reviews in the treatment group would result in apparently faster healing times. The standardised regime of the treatment group may in itself have provided better outcomes than the non-standardised regime of the control group.

Permanent skin changes and scarring correlate with delayed epithelialisation and the treatment group consistently avoided this. The few cases with permanent skin changes may have been a result of the initial burn being deeper than first thought. Prophylactic use of many antimicrobial dressings (including nanocrystalline silver) has been associated with delayed wound healing [8] and these treatment group outcomes demonstrate that clinical infection can be minimised

Table 2 – Comparison of burns in the control and treatment groups.

Patient and burn details	Control group	Treatment group
Age		
<4 years	20	13
4–15 years	6	3
>15 years	14*	24*
Cause		
Hot drink	22	19
Flame	5	8
Oil (>100 °C)	4	4
Contact hot surface	4	5
Chemical	3	2
Electrical	1	1
Unknown	1	1
Depth		
Partial thickness	21*	30*
Superficial	19*	7*
Not stated	0	3
TBSA		
Mean	3.33%	2.71%
Minimum	1%	1%
Maximum	8%	9%
Treatment		
Acticoat – used on trunk & limbs	21	Keratin gel and/or keratin matrix
Biobrane – used on trunk and limbs, especially on children	11	
Topical liquid – used on head and neck where no secondary dressing is needed	6	
Mepitel/Jelonet	1	

* Denotes a statistically significant difference between treatment and control groups ($P < 0.05$).

Table 4 – Comparison of overall costs for control and treatment groups.

Item	Control group cost (NZ$) per pt.	Treatment group cost (NZ$) per pt.
Emergency department	931	562
Operating theatre	1111	179
Inpatient	1064	497
Outpatient	353	166
Medical staff	1292	753
Support staff	210	362
Other	55	116
Total	5016*	2635*

* Denotes a statistically significant difference between treatment and control groups ($P < 0.05$).

with good practice in the absence of topical antimicrobial dressings.

Healing outcomes are compared in Table 3, the most notable feature was the extent to which the control group used hospital resources: paediatric patients required hospital admission for dressing changes under sedation (inpatient time) and often had surgical management under general anaesthetic (often the inpatient time was waiting for theatre). The number of hospital outpatient clinic appointments was much greater for the control group, whereas the treatment group were seen more frequently in the community. A significant number of patients in the control group were prescribed a course of oral antibiotics, this resource utilisation is translated to monetary costs in Table 4; the cost per patient for the control group was $5016, compared to $2635 for the treatment group. The main resource costs included operating theatre expenses, inpatient costs and outpatient medical staffing costs. The cost of consumables is excluded in both groups, their cost is a small proportion of the overall cost of care.

Table 3 – Comparison of clinical outcomes and resource utilisation for control and treatment groups.

Clinical outcomes and resource utilisation		Control group	Treatment group
Complications		1 × infection (Biobrane)	
Healing time (days)	Mean	14.4*	8.7*
	Median	14	7
	Minimum	7	4
	Maximum	25	33
	Missing data	4 patients	N/A
Use of operating theatre		Yes × 19 patients*	Not required*
		No × 21 patients	
Hospital inpatient time (days)	Mean	2.6*	Not required*
	Median	1	
	Minimum	0	
	Maximum	12	
Outpatient appointments (number per patient)	Mean	3.3*	1.2*
	Median	3	1
	Minimum	0	0
	Maximum	9	3
Oral antibiotics		Yes × 15 patients*	
		(Min 2 days, max 7 days)	None*
		(Mean 4.9 days, median 5 days)	
		No × 25 patients	

* Denotes a statistically significant difference between treatment and control groups ($P < 0.05$).

5. Conclusions

Superficial and partial thickness burns account for a large number of burn presentations in the hospital and community setting and can heal effectively and efficiently with conservative treatment. There is an unmet need for products that assist the healing process and meet the needs of the wound (rapid epithelialisation and scar minimisation), the patient (comfort, convenience and allow timely return to ADLs), the healthcare practitioner (providing ease of use in the community or outpatient clinic setting) and the healthcare provider (cost effective resource utilisation). The range of keratin-based products trialled in this study fulfils those needs and has been adopted by the treating facility.

Conflict of interest

Clive Marsh is an employee of Keraplast Research, whose product was studied in the present work. Sharon Cassidy is a consultant for Keraplast Research. Fiona Loan and Jeremy Simcock declare no conflict of interest.

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