A Randomized Clinical Study Comparing a Novel Transforming Powder Dressing to a Carboxymethylcellulose-Silver Dressing in Skin Graft Donor Sites

Introduction

Skin graft donor sites are a necessary and painful byproduct of graft procedures used to regenerate large sections of damaged skin. The split thickness skin graft (STSG) is typically harvested from large sections of a patient's own skin using a microtome and has a thickness of 1-3 mm depending on the blade and surgical technique. The resulting donor site is usually painful and irritating to the patient but will typically heal in 10-20 days with moist wound healing techniques. The acute nature of the donor site makes it a good choice of wound for a pilot study to evaluate a dressing and compare pain and discomfort associated with a wound and treatment.

We report on the results of a single center, randomized, prospective clinical study comparing a novel Powder Wound Dressing (PWD)* to a carboxymethylcellulose dressing containing silver (CMC-Ag) when applied to patients having two split thickness skin graft donor sites. Results include an analysis of time to healing, pain, and patient comfort.

Objectives

- To evaluate the time-to-wound healing in skin graft donor sites with a new treatment PWD compared to standard of care treatment CMC-Ag
- To evaluate pain level, incidence of infection, and patient's satisfaction comparing the PWD to CMC-Ag
- To compare tolerance of the two dressings.

Methodology

This study was designed as a single center, prospective, randomized study in which each patient served as his/her own control. Each patient was to have at least two split-thickness donor sites identified prospectively as A or B. One skin donor site was dressed with PWD, the other with CMC-Ag in a randomized fashion. This study was performed in compliance with Good Clinical Practices including the archiving of essential documents. Prior to study initiation, the protocol was reviewed and approved by the Institutional Review Board (IRB) of UTSW Medical Center and the IRB of Parkland Health and Hospital System, Dallas, Texas.

Number of subjects (planned and analyzed)

40 patients were planned to be enrolled at one clinical trial site in the U.S. Enrollment into the study was closed after 20 patients were enrolled and 19 were treated with the study devices.

Major criteria for inclusion

1. Male or female patient between the ages of 3 and 85 (in order to maintain a broad representation of ages, no more than 50% of the patients enrolled in the study were to be between the ages of 3 and 18, inclusive.)
2. Patient in general good health
3. Patient with two independent skin donor sites of approximately the same dimensions

Major Criteria for Exclusion

1. Male or female patient less than 3 years of age or more than 85 years of age
2. Acutely infected wounds
3. Wounds with surrounding cellulitis

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Efficacy Assessments

Efficacy Analyses

Time to Healing

Mean days to healing were estimated using survival analysis methods. Matched pairs t-test was used.

Pain Scores

Pain scores were averaged for each patient and each donor site side as follows: Day 2 to Day 5, Day 6 to Day 10, Day 11 to Day 15. Average pain scores at each of these 3 time points were compared between sides using a mixed model repeated measures ANOVA analysis that accounted for the treatments being observed on the same patient.

Safety Assessments

Adverse Events

Throughout the course of the study, all adverse events were monitored and reported on an Adverse Event Case Report Form. When adverse events occurred, the main concern was the safety of the study subjects.

Procedure:

The NPD is a powder dressing that transforms from a powder into a moist wound dressing. This PWD is designed to provide high moisture vapor transpiration and does not typically require a secondary dressing. The CMC-Ag is a woven material containing 1.2% ionic silver. This dressing was applied to the surface of the wounds and anchored into place using staples.

The investigator first identified the skin donor sites (A and B) for each patient and took baseline digital images and measurements immediately following surgery (Day 1). The investigator then applied the dressings provided by the Sponsor and labeled as A or B by the Sponsor in a random fashion. Typical meticulous wound care and adequate analgesic medical coverage were provided for the duration of the study. Patients were monitored daily as part of standard procedure while they were in the in-patient setting. If and when patients moved to the out-patient setting, they were to be monitored every other day at the study center. At each visit, the investigator determined whether each skin graft donor site had healed per standard care guidelines (i.e. >95% re-epithelialization). Subjects were questioned about pain level, and adverse events were monitored. The last study visit was on Day 24 or on the day when both wounds had been assessed as "healed", whichever came first. If one or both of the graft donor sites were not healed on Day 24, a Follow-Up Visit (25-30 days post-surgery) was to be scheduled at the investigator's discretion. The medical staff recorded all dressing changes during the course of the study.

Results

Efficacy evaluation

Data Sets Analyzed

All 19 Subjects enrolled were included in the efficacy analysis.

Demographic and Other Baseline Characteristics

Demographic Characteristics

Table 01 summarizes Subject demographic information. Age ranged from 8 to 78 years and averaged 38.6. Only 4 subjects were female (21%) and 15 were male (79%).

Table 01 – Summary of Demographic Characteristics

Number of Subjects	19 (100%)
Age (years)	
Mean (SD)	38.6 (19.7)
Median (Min-Max)	38.0 (8, 78)
Gender	
Male	15 (79%)
Female	4 (21%)

Source: Datalist 16.2.1

Donor Site Characteristics

Table 02 summarizes the donor sites characteristics. The mean (SD) size was 294 cm² (281.5) for PWD site and 281 (150.3) for CMC-Ag sites.

Table 02 – Summary of Donor Site Characteristics

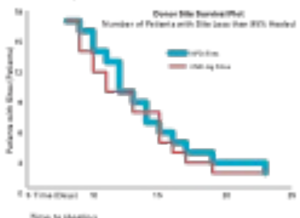
	PWD	CMC-Ag
Number of Subjects	19	19
Size (cm²)		
Mean (SD)	294 (281.5)	281 (150.3)
Median (Min-Max)	198 (36, 1000)	187 (64, 750)

Source: Datalist 16.2.4

Efficacy Results

Twenty Patients (15 male, 4 female) were enrolled into the study and 19 received study devices. Twelve subjects (63%) completed the study as planned, while 7 subjects (37%) prematurely discontinued due to adverse event (1 subject), subject's request (1 subject), protocol violation/non compliance (1 subject), lost to follow-up (3 subjects) and other reason (1 subject who became confused).

Time to Healing



Time to Healing

There was no significant difference in time-to-healing between the two treatment sides.

Table 03 – Mean Time to Healing Based on patients with healing day ≤ 24 days†

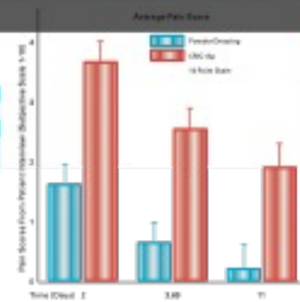
	PWD	CMC-Ag	Difference PWD minus CMC-Ag	p-value
N	11	11	11	
Mean Estimate	14.1	12.6	1.1	0.16
Standard Error	0.85	0.56	0.71	
Minimum	10	9	-1	
Maximum	22	20	3	
95% Confidence Interval	12.3, 15.9	11.3, 14.0	-0.5, 2.6	

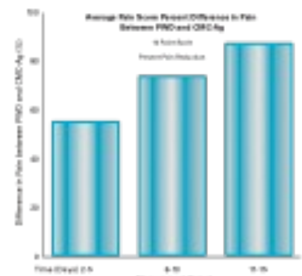
† p-value from matched pair t-test.

Pain Scores

Pain Scores

Pain scores showed significant differences at all time periods between the two dressings, with PWD eliciting lower pain scores than CMC-Ag. Between day 2 and day 5, the average pain score recorded was 2.69 on the CMC-Ag side versus 1.65 on the PWD side (p<0.0001). Similarly on days 6 to 10, the average pain score was 2.57 on the CMC-Ag side compared with 0.67 on the PWD side (p<0.0001).





Subject's Satisfaction Survey

Table 04 summarizes responses to the 3 subject satisfaction survey questions at the final visit. Questions were based on a 10-point scale with 1 being the worst score and 10 being the best score (except for pain).

When asked about comfort of the dressing at the edges, study subjects found PWD to be more comfortable than CMC-Ag (average score of 8.6 versus 5.8, p<0.001). Likewise, study subjects reported experiencing less pain when the dressing came in contact with clothes or bedding at the PWD side compared with the CMC-Ag side (average pain score of 2.1 versus 5.1, p<0.001).

There was no significant difference between the two dressings regarding how well the dressing remains in place after application as both dressings performed well on that measure (average score of 9.5 for PWD versus 8.8 for CMC-Ag).

Table 04 – Summary of Subject Satisfaction Survey Results

FINAL VISIT		PWD	CMC-Ag	p-value a
Number of Subjects with Response:		17	17	
Q1 – On a scale of 0 to 10, with 0 being not at all and 10 being very secure, did the dressing remain in place after application?	Mean (SD)	9.5 (0.94)	8.8 (1.91)	0.09
	Median	10	10	
	(Min-Max)	7 to 10	5 to 10	
Q2 – On a scale of 0 to 10, with 0 being very uncomfortable and 10 being very comfortable, did you find the edges of the dressing to be comfortable?	Mean (SD)	8.6 (2.27)	5.8 (1.87)	<0.001
	Median	10	6	
	(Min-Max)	2 to 10	2 to 9	
Q3 – On a scale of 0 to 10, with 0 being no pain and 10 being the worse pain you have ever experienced, did you notice significant pain when the dressing came in contact with your clothing or bedding?	Mean (SD)	2.1 (2.5)	5.1 (2.8)	<0.001
	Median	1	5	
	(Min-Max)	0 to 10	2 to 9	

a p-value from matched pair t-test

Discussion

Protocol Deviations

Timely Follow-up After Release of Subjects from In-patient Hospital Setting

One main deviation from the protocol was that timely follow-up proved to be difficult after subjects were released from the hospital and asked to return for regular clinical check-up. A number of patients did not have twice-weekly follow-up. This impacted the precision with which the time to healing could be determined in this study. Both donor sites were impacted in the same manner by these protocol deviations.

Randomization Deviation

It was noted that for 2 subjects (Subjects 01 and 08), the A versus B randomization sequence of the 2 donor sites was reversed. For the randomization list, in both cases, PWD should have been applied to donor site B, but was applied to donor site A instead.

The clinical study personnel instituted a "second check" procedure to confirm site A and site B and which packet was to be applied to each. This deviation was not expected to impact either the safety of the subjects, or the validity of the data collected from these 2 subjects.

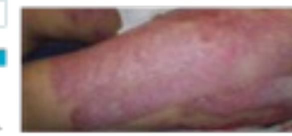
Donor Sites as Wound Healing Model

The use of donor sites as wounds in a healing model provides for a reproducible wound but also makes wound healing endpoint comparisons difficult for comparative treatments since the wound is partial thickness and acute. Thus the result of equivalent healing times was not unexpected.

One major complaint among patients with donor sites is pain and comfort management, therefore, a dressing which reduces pain and increases patient comfort is an important finding for any donor site wound healing study.

An important extension of this study would be to determine if similar pain and comfort findings extend to wounds of a more chronic nature.

Initial Powder Dressing Application



Donor Site at Healing

Conclusions

In this clinical study it was demonstrated that for acute donor sites, a comparison of time to healing provides no statistically significant difference in the rate or percentage of donor sites closed between day 8 and day 23 (p=0.16) when covered by the NPD or the CMC-Ag.

For the mean pain scores of donor sites covered with the two dressings, the NPD showed a statistically significant difference of less pain at three different time periods (p<0.0001 at 2-5 days, p≤0.001 at 6-10 days, and p=0.004 at 11-15 days).

For patient comfort, there was a statistically significant difference in comfort with the NPD having greater comfort (scale of 1-10 with 10 being more comfortable) (p<0.001).

Patients with donor sites can benefit in the areas of pain management and comfort if the NPD is used to treat the graft site over the CMC-Ag dressing.

References

1) Wiechula R, 2001. Post Harvest Management of Split Thickness Skin Graft Donor Sites. A Systematic Review No. 13, The Joanna Briggs Institute, Adelaide.
2) Fitzgerald RH, Bharara M, Mills JL, Armstrong DG. Use of a Nanoflex powder dressing for wound management following debridement for necrotising fasciitis in the diabetic foot. Int Wound J. 2009;6(2):133-139.

Acknowledgements

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*Altrazeal™ Transforming Powder Dressing