Comparative Efficacy and Safety Results of Topical Hemostatic Powder and Sterile Compressed Foam Sponge in Second Intention Healing Following Mohs Micrographic Surgery

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Abstract

Post-procedural care for punch biopsies, excisions and Mohs micrographic surgery (MMS) typically require the placement of sutures and continued self-care by patients. However, second intention healing (SIH) is also an acceptable wound care following such procedures. This study compared two hemostatic agents for SIH in 24 subjects who had undergone MMS for the removal of non-melanoma skin cancers of the face with a final defect size of 0.5mm to 2.0cm. At least 50% of the subjects were receiving ongoing anti-coagulation with warfarin and/or aspirin.

This poster presents results of a single-center, open-label, randomized, parallel-designed pilot study to compare the safety and efficacy of a non-prescription topical hemostatic powder containing a hydrophilic polymer and a potassium-based salt (Group I) to a sterile, compressed surgical sponge (Group II) for SIH post-MMS with a focus on hemostasis and rate of healing. Assessments at baseline and at weeks 3, 6, and 12 included wound size, global assessments of efficacy, application site assessment such as erythema, erosion, ulceration, inflammation, swelling, infection, crusting, necrosis, peeling, contact dermatitis, hyper/hypo pigmentation, and scarring. Also, subjects graded site irritation, pruritus, burning, tenderness, and pain at each visit. Time to hemostasis was also measured at each application of the hemostatic agent at the time of surgery. Group I subjects achieved hemostasis at a mean of 52.5 seconds after the first stage of MMS vs 60 seconds in Group II. Hemostasis times following stage 2 MMS were 32.5 seconds and 120 seconds, respectively. By week 12, wound size was reduced by a median of 182mm^2 in Group I and 161.5mm^2 in Group II at week 12. At week 3, mean global assessment of wound healing was "very effective" in 58.3% of Group I subjects and 25% of Group II subjects at week 3. At week 12, this assessment was 100% and 67%, respectively. No differences were reported in ulceration, inflammation, necrosis, peeling, contact dermatitis and other cutaneous parameters. Both scarring and erythema were reduced in Group I. Overall, both treatments were safe and effective in wound healing post-MMS. In addition, investigator's efficacy assessment of subjects treated with the hemostatic powder following 4mm punch biopsies will also be discussed.

Introduction

- Post-procedural care for punch biopsies, excisions and Mohs micrographic surgery (MMS) typically require the placement of sutures and continued self-care by patients. However, second intention healing (SIH), the process of healing a wound without surgical closure, is also acceptable wound care following such procedures.
- SIH optimizes healing in a moist, hypoxic environment with a topical antibiotic or white petrolatum under a dressing. It has been suggested that SIH is actually the preferred method of healing for 25%-33% of wounds following MMS.[1]
- SIH is particularly well-suited to concave areas of the face. Partial-thickness or small full-thickness wounds of the lower eyelid[2], alar crease or medial canthus often heal especially well by this method, with cosmetic results that may be superior to those obtained with local flaps or skin grafts.
- Convex sites, including the tip of the nose, may heal with a shiny appearance and sometimes hypertrophy while flat regions typically have results that are in between. Scenarios in which SIH is indicated are listed in Table 1.

Table 1. Possible Scenarios for SIH after MMS[1]

Recommended	*May be Advisable*
Recurrence after MMS	High-risk areas
Recurrence after multiple treatments	Concave areas
Tumors with special biological behavior	Posterior aspect of auricle
- aggressive basal cell carcinoma	Temples
Basal or squamous cell carcinoma with:	Lip if vermillion border is not involved
- bone or perineural involvement	Forehead
- large size	Antihelix
- increased risk of metastasis	Defects symmetrically located in the interface of 2 anatomical subunits
- immunosuppressed host	>3 MMS stages
	Coagulation disorders
	Advanced age

- SIH may result in slight hypopigmentation. However, patients are typically more concerned with the return of a normal contour than by moderate pigmentary alterations.[2]
- SIH can result in cost savings of as much as 50% with an acceptable level of patient satisfaction, particularly in elderly patients who may have contraindications to reconstructive surgery.[3]
- It has been suggested that SIH is an under-utilized option not only post-MMS but also following punch biopsies and excisions.[3] The clinical use of SIH decreased after the development of more complex wound repair methods such as grafts and flaps and primary suture.[3]

Study Objective

- This poster describes the results of a study comparing two hemostatic agents, a non-prescription hemostatic powder and a sterile surgical sponge, for SIH as well as the investigator's efficacy assessment of subjects treated with the hemostatic powder following 4mm punch biopsies.

Materials and Methods

- This single-center, open-label, randomized, parallel-designed pilot study enrolled 24 patients scheduled to receive MMS. Subjects were randomized to receive either a topical hemostatic powder (THP) (Group I) or a sterile compressed sponge (CS) (Group II). THP is a non-prescription device.
- THP stops bleeding by binding to the wound area and forming an artificial seal that blocks the flow of blood. Its protective seal remains in place until wound healing is complete at which time it falls off naturally. Because it functions independently of the endogenous blood clotting cascade, concomitant medications, including anticoagulants, need not be discontinued.
- Its ingredients are a non-toxic mixture of a hydrophilic polymer and a potassium-based salt. It is neither a vasoconstrictor nor a cauterizing agent. Its components are not metabolized, and none is biologically-derived. THP has passed all Food and Drug Administration biocompatibility tests, eliminating the risk of transmitting human or animal pathogens and minimizing the potential for allergic or sensitization reactions.
- CS is a commonly-used sterile, pliable, hemostatic surgical sponge prepared from treated, purified pork-gelatin solution. It is capable of absorbing and holding many times its weight in whole blood.
- The 24 patients were ≥18 years of age who were scheduled to have non-melanoma skin cancers of the head and neck removed by MMS, with final defect sizes of 0.5mm to 2.0cm.
- At least 50% of those enrolled were to be undergoing anticoagulation with either aspirin and/or warfarin. Exclusion criteria were females of child-bearing age who were pregnant, nursing or not practicing a reliable method of birth control, as well as those with allergies or sensitivity to any component of either test device. Also excluded were individuals with recent coagulation disorders or other medical conditions that might contraindicate participation, as well as evidence of recent substance abuse or a history of poor compliance. Patient disposition and baseline demographics and characteristics are summarized in Table 2.

Table 2. Patient Baseline Demographics and Characteristics

BASELINE CHARACTERISTICS	Group I (THP)	Group II (CS)
Disposition		
Number of Patients Enrolled	12	12
Subjects Completed Study (%)	100%	100%
On Anticoagulant Therapy	41.7%	41.7%
Baseline Demographics		
Mean Age (years)	74.2±10.2	72.5±10.3
Gender		
Male	75.0%	91.7%
Female	25.0%	8.3%
Ethnicity		
Caucasian	100%	91.7%
Biracial	0.0%	8.3%

- Wound length and width in millimeters, were obtained and study devices were applied at baseline immediately following MMS. Efficacy assessments were made at weeks 3, 6 and 12.
- The primary endpoint was physician global assessments of healing on a scale of 0-3 (0=not effective at all; 1=slightly effective; 2=moderately effective; 3=very effective).
- Investigator application site assessments, including erythema, erosion, ulceration, inflammation, swelling, infection, crusting, necrosis, peeling, contact dermatitis, hyper/hypopigmentation and scarring were graded on a scale of 0-3 where 0=none, 1=mild, 2=moderate and 3=severe.
- The subjects used the same 0-3 scale to assess irritation, itching, burning, pain, and tenderness. Time to hemostasis was measured in seconds after each stage of Mohs surgery starting from the time of first application of the hemostatic agent to the wound.
- Adverse event monitoring included any pathological or unintended change in the structure, function, or chemistry of the body that occurred during the study—regardless of presumed causality.
- Standardized wound care by patients consisted of gentle cleansing and pat-drying, followed 5 minutes later by an application of antibiotic ointment to the entire wound in a .75 inch thick layer. After moistening the gauze portion of an adhesive bandage, it was applied to the wound and kept in place throughout the day and until the next morning.

RESULTS

Time to Hemostasis

- For Group I (THP), the median time to hemostasis was 52.5 seconds after the first stage of MMS and 32.5 seconds after stage 2. For Group II (CS), median times to hemostasis were 60.0 seconds and 120 seconds, respectively. When both stages were averaged, the median times to hemostasis were 42.5 and 60.0 seconds, respectively.
- For patients with previous anticoagulant therapy the median time to hemostasis was 60.0 seconds and 81.0 seconds for stage 1 MMS and 105.5 seconds and 120.0 seconds for stage II MMS in Groups I and II, respectively.
- For those with no previous anticoagulant therapy, median times to hemostasis were 30.0 seconds and 60.0 seconds, respectively for stage 1 and 20.0 and 147.0 seconds for stage 2 in Groups I and II, respectively (Table 3).

Table 3. Median Time to Hemostasis (In Seconds)

Median Time to Hemostasis (Overall)	Group I (THP)	Group II (CS)
Stage 1	52.5	60.0
Stage 2	32.5	120.0
Median Time to Hemostasis (with Previous Anticoagulant Therapy)	**Group I (THP)**	**Group II (CS)**
Stage 1	60.0	81.0
Stage 2	105.5	120.0
Median Time to Hemostasis (with No Previous Anticoagulant Therapy)	**Group I (THP)**	**Group II (CS)**
Stage 1	30.0	60.0
Stage 2	20.0	147.0

Wound Size

- Wound size decreased more rapidly and to a greater degree, although not statistically significantly so, in Group I (THP) even though the mean wound size at baseline was 213.2±140.1mm^2 in Group I versus 156.0±74.1mm^2 in Group II (CS). By week 3, the mean wound size was 10.8±13.8mm^2 in Group 1 and 24.7±36.0mm^2 in Group II. This represents a mean decrease of 94.3%± 8.1 and 80.0%± 26.1, respectively. By week 6, the mean wound sizes were 0.0mm^2 and 1.3±4.6mm^2, respectively. This represents a mean decrease of 100.0% and 98.4%±5.7. At week 12, wounds had healed in both groups with a mean change from baseline of 100% in both groups. Figure 1 summarizes the changes in wound size over the study period.

Investigator Global Assessments

- Improvements in mean global assessments of healing were significantly greater at each time point in GroupI compared to Group II (Figure 2). At week 3, the mean global assessment score for wound healing was 2.58±0.51 (moderately to very effective) in Group I and 1.83±0.83 (slightly to moderately effective) in Group II (P=0.0256). At week 6, the scores were 3.00±0.00 (very effective) in Group I and 2.50±0.52 (moderately to very effective) in Group II (P=0.0063). At week 12, the mean scores of moderate to very effective healing were 3.00 and 2.67±0.49 (P=0.0357).

Investigator Assessments of Application-Site Reactions

- No ulceration, infection, necrosis or peeling was noted in either treatment group at any time point. The mean erythema score at week 3 was 0.58±0.79 (mild to none) in Group I and 1.17±0.72 (mild to moderate) in Group II. At week 6, they were 0.33±0.78 and 0.58±0.67, and at week 12, they were identical in both groups, 0.08±0.29.
- Erosion scores were identical in both groups at weeks 3 and 12, 0.42±0.51, and 0.0, respectively. While the mean inflammation scores were 0.08±0.29 in Group I and 0.17±0.39 in Group II at week 3, by weeks 6 and 12, 100% of both groups had no inflammation.
- Group I had no swelling at any time point, but 8.3% of Group II had moderate swelling at week 3. In weeks 6 and 12, no subject in either group had inflammation.
- At week 3, 100% of Group I had no scarring while 8.3% of Group II had mild and 8.3% had moderate scarring. At week 6, 91.7% of Group I had no scarring and 8.3% had mild scarring. At week 6, in Group II, 41.7% had no scarring, 25% had mild and- 33.3% had moderate scarring. At week 12, 91,7% of Group I had no scarring, and 8.3% had mild scarring versus 41.7% of Group II subjects who had no scarring, 41.7% who had mild scarring, and 16.7% who had moderate scarring (P=0.011). Figure 3 summarizes the mean scores for scarring from baseline to week 12.
- Crusting was not significantly different between the groups at any time point. Mean crusting scores were 0.33±0.49 and 0.25±0.45 at week 3, 0.00 in both groups at week 6, and 0.00±0.00 in Group I and 0.08±0.29 in Group II at week 12.
- Contact dermatitis was identical in both groups with 91.7% of both groups having no contact dermatitis and 8.3% having mild contact dermatitis at week 3. At both time points thereafter, 100% of each group had no contact dermatitis. Pigmentary changes were seen only in Group I of which 8.3% of subjects had mild pigmentary changes at week 6. At weeks 3 and 12, 100% of both groups had no pigmentary alterations.

Subject Self-Assessments

- At week 3, the mean irritation scores were identical in both groups, but at week 6, the mean irritation scores were 0.08±0.29 and 0.17±0.39, with 18.2% of Group I and 16.7% of Group II having at least a 1-point increase from baseline. Irritation scores were identical between groups at week 12, with 9.1% of Group I and 8.3% of Group II having had increases of at least 1 point.
- At baseline, 90.9% of Group I had no itching and 9.1% had mild itching while 100% of Group II reported no itching. However, from baseline to week 3, the mean itching score was 0.18±0.40 in Group I and 0.83±0.72 in Group II (P=0.0194). At week 6, 27.3% of Group I and 41.7% of group II reported increase of at least 1 point in itching, and none of Group I but 25% of Group II had at least a 2-point increase in itching. By week 12, 18.2% of Group I and 58.3% of Group II reported increases of at least 1 point (P=0.0894) (Figure 4).
- Neither group reported burning at baseline, but at week 3, 8.3% of Group II subjects reported moderate burning versus 100% of Group I who reported no burning. These scores remained identical through week 6. But at week 12, 100% of Group I had no burning while 8.3% of Group II continued to report mild burning. There was at least a 1-point increase in burning score at week 12 in 8.3% of Group II and none of Group I.
- At baseline, reports of pain were slightly higher in Group I, with 9.1% reporting mild pain versus 0% of Group II. At week 6, 91.7% of both groups reported no pain, 8.3% of Group I reported severe pain, and 8.3% of Group II reported mild pain. At week 12, 100% of Group II had no pain while 91.7% of Group I reported no pain, and 8.3% reported mild pain.

Adverse Events

- No treatment-related adverse events were reported during the course of the study, and 100% of both groups completed the full 12 weeks.

Use of THP Following 4mm Punch Biopsies

- In a series of 10 patients with suspicious cutaneous lesions, 4mm punch biopsies were performed. After biopsies were completed and THP was applied appropriately, there were no difficulties postoperatively.
- Patients were instructed not to apply any creams or ointments to the biopsy site, but were encouraged to protect the sites with a dressing each day and to avoid trauma to the area. They were instructed to leave the dressing in place while showering and to replace it afterwards.
- There were no complications postoperatively in any of the 10 cases. No infections or bleeding episodes occurred in any patients, including those using anticoagulants.
- Healing time was slower than with sutured punch biopsy wounds. This is not unexpected, since punch biopsy wounds involve full thickness of skin (extending into subcutaneous fat) so healing times of 3-4 weeks (or longer depending on patient and/or anatomic site) is expected.

Discussion

Comparative global assessments of THP showed greater efficacy and more rapid onset of action in second intention wound healing compared with CS following MMS (at week 12). THP tended to reduce erythema and it produced less scarring. There was also a trend towards a more rapid reduction in wound size with the THP. No peeling, ulceration, infection, or necrosis were noted in either group. By week 12, neither group had pigmentary changes. Subject-reported itching and burning trended slightly higher in Group II while pain was greater in Group I, although not significantly so. Overall, both hemostatic agents were found to be safe and effective in second intention healing following MMS. It will be important to substantiate the results of this pilot study with larger numbers of subjects for greater statistical power.

Figure 1. Mean Percentage Changes in Wound Size (mm^2)

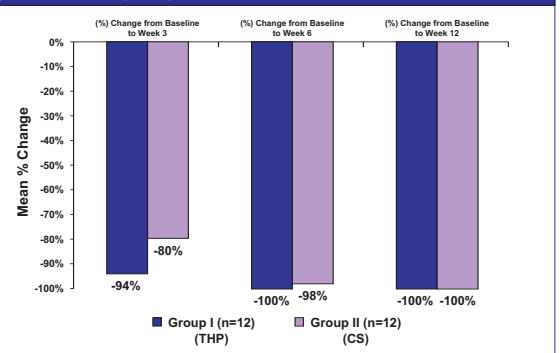


Figure 2. Mean Scores of Moderate to Very Effective Healing

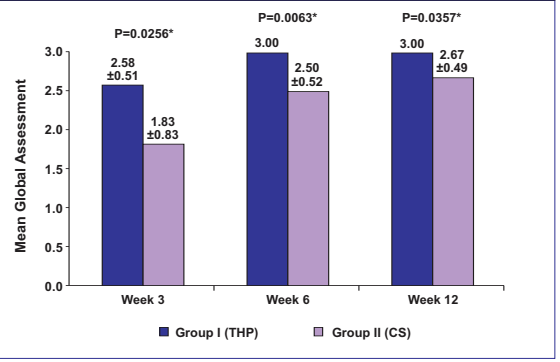
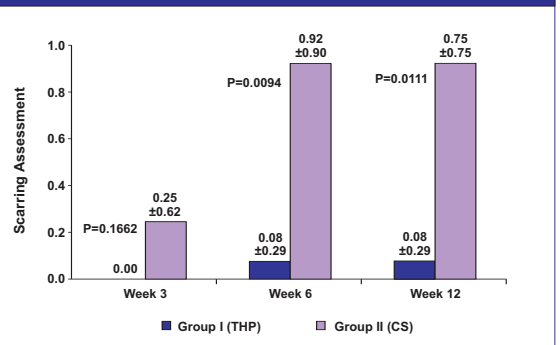


Figure 3. Investigator Assessments of Scarring



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Acknowledgement
The production of this poster was supported by Biolife.