Novel Liquid Bandage as a Topical Treatment for Post-Surgical Wound Care

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Abstract

Purpose: A small clinical study was performed to assess the use of a novel poly (urea-urethane) liquid bandage (Nuvaderm, Chesson Labs, Durham, NC) as a post-surgical wound care treatment in patients that underwent skin cancer excision surgery. Nuvaderm is a topical medical device that has been cleared by the United States Food and Drug Administration (FDA). Nuvaderm was evaluated for wound healing, moisture vapor permeability, microbial barrier effectiveness, and ease of use.

Methods: A prospective, single-arm clinical evaluation was performed with adult subjects with skin cancer on the head or body. Excision surgery was performed to remove the cancer and the lesion was subsequently closed with sutures. Nuvaderm was applied to the surgical site and a pressure dressing was applied on top to control any bleeding. After 24 h, patients removed the pressure dressing and self-treated with Nuvaderm liquid bandage daily for approximately 7-14 days. Clinical assessments were performed at roughly 7 or 14 days after surgery for head and body wounds, respectively. The primary effectiveness endpoints were to assess wound healing and infection rate after daily treatment with Nuvaderm. The primary safety endpoint was free from product-related adverse events for the duration of treatment term. In vitro testing was performed for antimicrobial and microbial barrier properties and moisture vapor permeability. These tests were carried out using ASTM E2315 (Standard Guide for Assessment of Antimicrobial Activity Using a Time-Kill Procedure), ASTM F1608 (Standard Test Method for Microbial Ranking of Porous Packaging Materials), and ASTM E96 (Standard Test Methods for Water Vapor Transmission of Materials), respectively.

Results: Initial in vitro studies demonstrated that Nuvaderm is a biocompatible, durable liquid bandage that functions as a microbial barrier with antimicrobial properties and water vapor permeability. 43 patients (61% males), aged 44 to 85 yrs, with skin cancer on the head or body underwent excision surgery to remove the growth or lesion. All patients applied Nuvaderm daily with no infection or serious adverse events. 17 (39%) patients reported a mild stinging sensation at least once when Nuvaderm was applied to the wound site. Of the 42 respondents, 95% were satisfied with how Nuvaderm aftercare treatment relieved symptoms of their surgery. One patient reported erythema around the wound and two reported the wound felt dry and itchy.

Conclusion: This study describes a topical medical device with antimicrobial properties that protects wounds from infection and complements wound healing in patients after skin cancer excision surgery. Nuvaderm liquid bandage compares favorably with current standards of care for post-surgical wound treatments and provides an easy to use wound care system for patients.

Keywords: Wound care; Nuvaderm; Liquid bandage

Introduction

Each year in the United States over 5.4 million cases of non-melanoma skin cancer are treated in more than 3.3 million people [1]. Basal cell carcinoma (BCC) is the most common form of skin cancer with more than 4 million cases diagnosed each year [2]. There are several treatments that can be used to remove skin cancers. The most common surgical methods of treating skin cancer are curettage, excision with margin examination, and Mohs micrographic surgery. Radiotherapy is another common skin cancer treatment, and cryotherapy is sometimes used [3]. The goal of surgical treatment of skin cancer is to remove or destroy the tumor so that no malignant tissue is allowed to proliferate further. The options depend on factors such as tumor size, cancer subtype, and location, as well as a patient’s age and ability to tolerate surgery. Skin cancer like BCC very rarely spreads to other parts of the body and therefore excision surgery is often used and is effective in removing the growth or lesion. Surgical excision usually produces excellent cosmetic results and cure rates are as high as 95%. Healing time is also generally shorter with surgical excision and sutured closures.

A wound from skin cancer excision surgery may involve the epidermis alone or both the epidermis and the dermis. Surgical wounds are a point of vulnerability for patients recovering from surgery, as infectious material can enter the wound and cause complications. Management of surgical wounds is an important part of post-surgical care for patients in the hospital and clinic and during recovery at home. Post-surgical wound care, including healing, can be
troublesome and time consuming. Proper aftercare is necessary to prevent infection and to promote healing of the skin. Additional goals during aftercare are to manage the pain associated with the surgical wound site and to have an appealing cosmetic result. The purpose, therefore, of medical aftercare for surgical wounds is to prevent complications and preserve function, while also managing pain and considering positive cosmetic results.

Current standards of care for post-surgical wounds are dressings with the most common being gauze [4]. Some common problems with solid dressings are that they can stick to wounds or they can become stiff and bulky. Changing solid dressings over the course of recovery can cause further wound damage thereby lengthening healing time and increasing the susceptibility to infection. The primary function of a dressing is to protect and help heal wounds. Liquid bandages may provide an alternative wound care system to eliminate some of the common problems of gauze or other multi-layered systems. A liquid bandage is a semi-transparent adherent material that can be sprayed or painted directly on wounds. Liquid bandages reduce pain by covering nerve endings and they help wounds heal by maintaining a proper moisture balance and keeping bacteria and debris out [5]. Liquid bandages protect the wound by forming a thin film of polymer over the wound and surrounding skin. An adequate liquid bandage should provide a film covering and interaction with the wound to complement the healing process and improve comfort for the patient.

The goals of these studies were to assess a novel poly (urea-urethane) liquid bandage (Nuvaderm, Chesnon Labs, Durham, NC) for wound healing, moisture vapor permeability, microbial barrier effectiveness, and ease of use in patients that underwent skin cancer excision surgery. Nuvaderm is a topical medical device that has been cleared by the United States Food and Drug Administration (FDA).

Methods

Clinical study

This was a prospective, single-arm study at one center to evaluate the safety and effectiveness of a poly (urea-urethane) liquid bandage for post-surgical wound care after skin cancer excision. This study was performed at Parks Dermatology Center (Ormond Beach, FL). Each subject provided informed consent before enrollment in the study. Patients were assessed at roughly 7 or 14 days after surgery for head and body wounds, respectively.

The primary effectiveness endpoints were to assess post-surgical wound healing and infection rate after daily treatment with Nuvaderm. The primary safety endpoint was freedom from unanticipated or major device-related adverse events (AE) for the duration of the treatment phase. Anticipated minor AE is a mild stinging sensation upon application due to the organic solvents in the product. Safety of the product in this non-comparative study was determined by evaluating the incidence of AE.

Subject population

Adults, over 18 yrs of age, with diagnosed skin cancer were considered, regardless of gender, race or ethnicity. All subjects had to be physically able to apply product or have accessible help, to discontinue use of cosmetic or other wound care products on or around the wound area for duration of the study, and to return for follow-up. Potential subjects were included or excluded upon the discretion of the investigator.

Device description

Nuvaderm is classified as a topical medical device by the FDA. It is a biocompatible, poly (urea-urethane) polymeric suspension that forms a uniform film when applied to the wound and skin. The polymer product is dispersed in organic solvents that vaporize rapidly upon application, allowing the suspended polymer to adhere to the contours of the skin to form a flexible, long-lasting, waterproof barrier over the wound and surrounding skin. The film is colorless, transparent, and possesses good moisture vapor permeability. The product has been shown biocompatible per ISO 10993 in cytotoxicity, sensitization, irritation, acute system toxicity, and implantation assays.

Application procedure

Detailed, written instructions for use were provided to each subject. The multi-use packaging system (glass bottles, swab applicators, and atomizer pump sprayer) is designed for convenient storage and application of the product. Product is stored at normal room temperature and humidity. Nuvaderm was applied to the surgical site (over sutured area) and surrounding skin directly after the procedure. A pressure dressing was then applied over the wound site and was left on for 24 h. After 24 h post-surgery, the pressure dressing was removed and the wound was gently washed with antibacterial soap. The wound area was dried thoroughly and Nuvaderm was applied as a smooth uniform coating daily.

Clinical assessments

Each patient was given a patient report diary that included a daily pain/sensitivity scale, an application calendar, and an overall satisfaction questionnaire. Seven days after facial surgery or 14 days after body surgery, the patients had the sutures removed and wound assessed for healing and infection. Photographs of patients' wounds were captured directly after surgery and at the suture removal visit. The patients returned the completed report diary at the suture removal visit. Patients were also asked to return 30 days after surgery for a final wound assessment and photograph.

In vitro testing

The ability of the dried product film to act as a microbial barrier was tested by a modification of ASTM F1608 (Standard Test Method for Microbial Ranking of Porous Packaging Materials) with five species of bacteria (methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant Enterococcus faecalis (VRE), Pseudomonas aeruginosa, Escherichia coli, and Streptococcus pyogenes). This test method is used to determine the passage of bacteria through porous materials intended for use in medical devices. The polymer film was placed into a chamber and exposed to the bacteria (methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant Enterococcus faecalis (VRE), Pseudomonas aeruginosa, Escherichia coli, and Streptococcus pyogenes). The test method is used to determine the passage of bacteria through porous materials intended for use in medical devices. The polymer film was placed into a chamber and exposed to the specific organisms. The filters were then blended and plated on soybean casein digest agar plates and titer values were determined.

Water vapor transmission testing was conducted in accordance with the water method of ASTM E96 (Standard Test Methods for Water Vapor Transmission of Materials). Aluminum cups were filled with water to within 19 ± 6 mm of the top, and the sample films were sealed across the cup mouth. Triplicate samples of the specimen were run. The samples were placed in a sealed chamber with a saturated solution of magnesium nitrate to maintain a controlled humidity. The temperature and humidity were recorded with a solid state sensor, and the cups were weighed periodically until a steady rate for mass loss was
observed. The average temperature over the testing was approximately 23°C, and the average humidity in the chamber was 59%.

*In vitro* testing for antimicrobial properties was carried out using ASTM E2315 (Standard Guide for Assessment of Antimicrobial Activity Using a Time-Kill Procedure). The procedure was used to assess the *in vitro* reduction of a microbial population of test organisms, per USP <51> (methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa*, *Escherichia coli*, *Candida albicans*, *Aspergillus brasiliensis*), after exposure to test material. Solvent neutralization validation was performed using USP <1227>. Because of the immiscibility of the product with water (which is required only to show potential recovery of the test organism in the controls), the product film was reconstituted in the organic solvents based on the percent solid ratio of 15%. Sampling times to determine percent reduction were at 30 s and 30 min.

**Results**

**Baseline characteristics**

43 patients diagnosed with skin cancer were enrolled at a single clinical site over a one-month period (Table 1). This report includes the available data from all enrolled patients (intend to treat population) and treated with the product for the prescribed amount of time (approximately 7 or 14 days after surgery for head and body wounds, respectively). There was no randomization in the single-arm protocol. Since there was no randomization, intent to treat analysis was not applicable; safety and efficacy analyses were done on all subjects that completed the treatment period.

<table>
<thead>
<tr>
<th>Age</th>
<th>44 to 85 yrs (average 68 yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male: 26 (61%) Female 17 (39%)</td>
</tr>
<tr>
<td>Carcinoma Location</td>
<td>Head/Face: 25 Body: 18</td>
</tr>
<tr>
<td>Treatment Period</td>
<td>≤ 8 Days: 25 ≥ 11 Days: 18</td>
</tr>
</tbody>
</table>

Table 1: Subject Baseline Characteristic Summary.

**Safety analysis**

There were a total of 20 Treatment-Emergent Adverse Events (TEAE) reported at the follow-up visits (Table 2). 17 (39%) patients reported a mild stinging sensation when Nuvaderm was applied to the wound site. These AEs were categorized by the investigator as definitely product related and most likely due to the organic solvents in what the polymer product is suspended.

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Number of Patients</th>
<th>Device Related*</th>
<th>SAE / AE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild stinging sensation when product applied</td>
<td>17 (39%)</td>
<td>1</td>
<td>AE</td>
</tr>
<tr>
<td>Erythema around wound site</td>
<td>1 (2.3%)</td>
<td>4</td>
<td>AE</td>
</tr>
<tr>
<td>Wound felt dry and itchy</td>
<td>2 (4.5%)</td>
<td>4</td>
<td>AE</td>
</tr>
</tbody>
</table>

*1=definitely product related, 2=probably product related, 3=possibly product related; 4=probably not product related; 5=definitely not product related.*

One patient reported erythema around the wound and two reported that their wounds felt dry and itchy. These AEs were categorized as probably not product related and most likely was due to normal wound healing effects. There were no unanticipated device-related AE and no product malfunctions were reported. There were no SAE.

**Effectiveness: clinical assessment and infection rate**

43 patients (61% males), aged 44 to 85, with skin cancer on the head or body underwent excision surgery to remove the growth or lesion. All patients applied Nuvaderm daily with no infection or serious adverse events. Figures 1 and 2 show time lapse photos of representative patients. Figure 1 shows a 78-year-old male patient that underwent basal cell carcinoma and squamous cell carcinoma excision on the left forehead. The length of the sutured closure was 42 mm (Figure 1a). The patient applied Nuvaderm daily for seven days and then had the sutures removed (Figure 1b). The patient reported no complications, pain, or stinging sensation upon Nuvaderm application. There were also no signs of infection at or around the wound site. The patient did not apply any other products to the wound, nor did he take oral antibiotics at any time during the course of treatment. 30 days post-suture removal (37 days post-surgery), the wound site was completely healed with no complications and virtually no scarring (Figure 1c). Similarly, Figure 2 shows a 76-year-old male patient that underwent basal cell carcinoma and squamous cell carcinoma excision on the right forehead. The length of the sutured closure was 36 mm (Figure 2a). The patient applied Nuvaderm daily for seven days and then had the sutures removed (Figure 2b). They patient reported no complications, pain, or stinging sensation upon Nuvaderm application. There were also no signs of infection at or around the wound site. The patient did not apply any other products to the wound, nor did he take oral antibiotics at any time during the course of treatment. 30 days post-suture removal (37 days post-surgery), the wound site was completely healed with no complications and virtually no scarring (Figure 2c).

A satisfaction survey was given to all of the patients and it asked of the overall satisfaction of the way the aftercare treatment relieved symptoms as well as if the patient would recommend Nuvaderm over other methods of patient aftercare. 42 patients (of 43) responded to the survey and 95% reported that they were overall satisfied with how the Nuvaderm aftercare treatment relieved symptoms, aided in wound healing, and that they would recommend over other methods of aftercare. One patient did not respond to the questionnaire for unknown reasons.

**In vitro testing**

Nuvaderm is a solution that dries rapidly, with the resulting polymeric film adhering to the contours of the wound and surrounding skin. The ability of the product film to act as a microbial barrier was tested by a modification of ASTM F1608 (WuXi AppTec, Marietta, GA). The five species tested are commonly found in wound site infections [6]. *Staphylococcus aureus* and *Enterococcus faecalis* strains used were methicillin and vancomycin-resistant, respectively. The inoculum concentrations were all greater than $4.5 \times 10^9$ colony forming units per 0.01 mL (Table 3). The five species of bacteria that were tested were unable to pass through the film after 24 h of incubation and a 24 h re-incubation (Table 4). The results, therefore, showed no presence of the challenge organisms beneath the polymer test sample. The positive control sample showed growth of each challenge organism.
Figure 1: Time lapse photos of a 78-year-old male patient after excision of basal cell carcinoma and squamous cell carcinoma on the left forehead. (a) Day 0: 42 mm sutured closure. (b) Day 7 post-surgery: using Nuvaderm daily; sutures removed. (c) Day 37 post-surgery: no application of Nuvaderm after Day 7.

Figure 2: Time lapse photos of a 76-year-old male patient after excision of basal cell carcinoma and squamous cell carcinoma on the right forehead. (a) Day 0: 36 mm sutured closure. (b) Day 7 post-surgery: using Nuvaderm daily; sutures removed. (c) Day 37 post-surgery: no application of Nuvaderm after Day 7.

Table 3: Organisms and Inoculum Concentrations.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Test Sample</th>
<th>Positive Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>24 h Incubation</td>
<td>24 h Re-Incubation</td>
</tr>
<tr>
<td></td>
<td>Rep 1</td>
<td>Rep 2</td>
</tr>
<tr>
<td>Staphylococcus aureus (MRSA)</td>
<td>No Growth</td>
<td>No Growth</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>No Growth</td>
<td>No Growth</td>
</tr>
<tr>
<td>Enterococcus faecalis (VRE)</td>
<td>No Growth</td>
<td>No Growth</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>No Growth</td>
<td>No Growth</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>No Growth</td>
<td>No Growth</td>
</tr>
</tbody>
</table>

Table 4: Microbial Barrier Test Results.

The Nuvaderm polymer is well suited for use in producing films having unique combinations of properties, especially water vapor transmission. Adequate water vapor transmission of a wound dressing is required to prevent excessive dehydration as well as build-up of exudates.
The process of permeation through a polymeric barrier generally involves four steps: absorption of the water vapor into the polymer wall; solubility in the polymer matrix; diffusion through the wall; and desorption from the outer wall. Three samples 65 mm in diameter and approximately 0.3 mm in thickness resulted in an average water vapor transmission rate (WVTR) of 34.4 g/m²·24 h and had an average permeance of 5.0 Perms (Intertek Plastics Technology Laboratories, Pittsfield, MA).

Antimicrobial properties were assessed using a time-kill procedure (WuXi AppTec, Marietta, GA). Solvent neutralization resulted in greater than 70% recovery and the population count was greater than $10^7$ for each organism tested. Methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa*, *Escherichia coli*, *Candida albicans* and *Aspergillus brasiliensis* all had a greater than 99.99% reduction after 30 s of contact with the liquid solution and up to 30 min (longest period that was tested; Table 5). The control solution showed no reduction for any of the organisms.

### Table 5: Antimicrobial Effectiveness of Nuvaderm Against Standard Test Organisms.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Common</th>
<th>Neutralization</th>
<th>Population Count</th>
<th>30 S</th>
<th>30 Min</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus aureus</em> (MRSA)</td>
<td>Bacteria</td>
<td>&gt;70%</td>
<td>$&gt;10^8$</td>
<td>&gt;99.99%</td>
<td>&gt;99.99%</td>
<td>No Reduction</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>Bacteria</td>
<td>&gt;70%</td>
<td>$&gt;10^8$</td>
<td>&gt;99.99%</td>
<td>&gt;99.99%</td>
<td>No Reduction</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>Bacteria</td>
<td>&gt;70%</td>
<td>$&gt;10^8$</td>
<td>&gt;99.99%</td>
<td>&gt;99.99%</td>
<td>No Reduction</td>
</tr>
<tr>
<td><em>Candida albicans</em></td>
<td>Yeast</td>
<td>&gt;70%</td>
<td>$&gt;10^8$</td>
<td>&gt;99.99%</td>
<td>&gt;99.99%</td>
<td>No Reduction</td>
</tr>
<tr>
<td><em>Aspergillus brasiliensis</em></td>
<td>Mold</td>
<td>&gt;70%</td>
<td>$&gt;10^7$</td>
<td>&gt;99.99%</td>
<td>&gt;99.99%</td>
<td>No Reduction</td>
</tr>
</tbody>
</table>

**Discussion**

The *in vitro* and clinical studies have proven that Nuvaderm liquid bandage is an effective topical dressing by means of protecting wounds from infection, providing an optimum environment for healing, and having antimicrobial properties. Nuvaderm is a poly (urea-urethane) copolymer with a large number of monomers. The wide range of reactivity of each monomer results in a highly complex mixture of products with a broad molecular weight distribution. Meticulous combinations of diol, diamine, and diisocyanate monomers were employed to result in a tailored polymer with particular chemical and physical properties for the development of a liquid bandage for use in wound care.

Wound healing is a complicated process that requires an advantageous microenvironment, while keeping the wound clean and protecting from microbial attacks. The most common wound dressings have been gauze, but they can stick to wounds causing damage, increasing the probability of infection, as well as lengthening healing times. Antibiotic gels, ointments, and even the adhesive on tape that are commonly used with gauze dressings can also cause contact dermatitis or be irritating to the skin and wound. The principal functions of wound dressings are to provide a moist environment and to protect from infections.

Liquid bandages are proving to provide an alternative wound care system to combat some of the common problems with gauze or other multilayered systems. The cost-benefit ratio of liquid bandages may also prove to be advantageous for patients. Liquid bandages are superior in covering and protecting hair-bearing areas of the skin as well as the hard to reach areas and joints. For instance, Nuvaderm is easy to use and was proven a satisfactory aftercare treatment for nearly all of the patients in this study. The Nuvaderm film demonstrated the ability to control water loss in vitro and to keep the wound surface moisture regulated for enhanced healing. Nuvaderm also has antimicrobial properties confirmed by inhibiting microbial growth and providing a protective barrier. A major burden for clinic and hospital staff is call backs from patients that have irritations due to the post-surgical wound care treatment. There were no infections reported in the clinical study, but just as important, there were no signs of irritation or contact dermatitis that was attributed to Nuvaderm use. The clinical site had no patient call-backs during the course of the study.

There were no unanticipated AE in the study. The only reported AEs likely related to the device were mild stinging sensations upon application of Nuvaderm to the wound site. This AE was reported in 17 patients. The sensation lasted for only a “few seconds” and was mainly present upon the first application. The carrier solvents for the polymer product are propanone and butanone. Although these solvents are very volatile and vaporize quickly, there are many nerve fibers that get exposed during the excision procedure and react to the solvents. Typically after the first application of the product, the once exposed nerve fibers are covered with the product film and do not respond to the solvents’ effects. Pain management and the mechanism of how the Nuvaderm polymer covers the exposed nerve fibers and eliminates or reduces the pain will be investigated in further studies.

**Conclusion**

In conclusion, we have demonstrated that Nuvaderm liquid bandage can be used as a post-surgical wound care treatment by helping create an optimum environment for wound healing. The organic polymer has no pharmaceutical agents and is permeable to oxygen and water vapor. The clinical study showed that Nuvaderm was well-tolerated by patients and the aftercare was easy and saved time and expense for patients and the clinical staff. Independent laboratory testing demonstrated that the product has antimicrobial properties and serves as a barrier to protect the wound from invading organisms.
Limitations

The results of this study should be interpreted in the context of several limitations. First, the sample size was too small to allow statistically valid assessment of potentially confounding covariates (e.g., baseline wound severity or size, location of excision, or subject age) on study outcomes. Because of the nature of the product, the study could not be blinded. Despite these limitations, the findings constitute important observations that support safety and effectiveness of the product for this use.

Disclosures

This study was funded by Chesson Laboratory Associates, Inc. Dr. Swick is an employee of Chesson Laboratory Associates, Inc. and received compensation for services. Ms. Mencke is an employee of Parks Dermatology Center and received compensation for services. Dr. Suah was the principal investigator and is a member of Chesson Laboratory Associates, Inc. Scientific Advisory Board and is a stockholder. Dr. Suah received compensation for services.

References