Prospective Case Series on a Combination Methylene Blue, Gentian Violet, and Ovine Forestomach-derived Extracellular Matrix Dressing for Hidradenitis Suppurativa

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Study Title: Prospective case series on the use of methylene blue, gentian violet, and ovine forestomach-derived extracellular matrix wound dressings for Hidradenitis Suppurativa

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Sponsor or funding source: Departmental (dressings provided by Appulse Medical)

Background, Rationale and Context

Hidradenitis suppurativa (HS) is a chronic and debilitating inflammatory disease most frequently affecting the axilla, groin, and inframammary regions.[1] Symptoms include nodules, abscesses, sinus tract formation, malodorous drainage, and scarring. These symptoms interfere with everyday activities, which can lead to social embarrassment and isolation.[2] Patients with HS suffer psychological effects, such as increased levels of anxiety, depression, and loneliness, which impair quality of life.[3,4]

Patients suffer with the burden of at home wound care for recurrent, draining nodules. Persistent lesions affect patients' lives by limiting their daily activities. Currently, patients are instructed to use gauze and tape to cover draining wounds, but this can be insufficient and difficult due to the nature and location of lesions associated with HS. Patients suffer with caring for their wounds, which can lead to frustration. Providing patients with a standard wound care regimen to take home can improve patients' quality of life and control of their disease. General recommendations for wound care in HS patients are limited. Improvements in the standard of care for wound management in HS are needed to aid patients.[5]

Objective

The objective of this case series is to monitor time and outcome of healing of wounds associated with HS using Endoform [ovine forestomach], Hydrofera Blue [methylene blue and gentian violet], and Hypafix tape.

Methods and Measures

Design

This will be a single-center, case series evaluating the length of time wound healing occurs using methylene blue, gentian violet, and ovine forestomach wound dressings to HS lesions. Patients of Wake Forest Dermatology clinic with a diagnosis of HS with draining nodules and open wounds will be recruited in clinic. Participants will be provided with methylene blue, gentian violet, and ovine forestomach products at screening/baseline visit. Lesions will be measured and recorded. Participants will complete a Numerical Rating Scale of Patient Reported Pain (NRS/Appendix I). Upon enrollment, participants will be provided with a standard cleansing protocol to be followed at home including using antibacterial soap prior to applying wound dressings. Dressings are to be changed every 3 days. In addition, they will be instructed to avoid bleach baths or acidic products for the duration of their involvement in the study. After visit 1, participants will return for follow-up at week 1, week 2, week 4, and week 8. At each visit, wounds will be measured and photographed, NRS will be completed, and participants will be provided with wound dressing products as needed.

Setting

Wake Forest Baptist Health Department of Dermatology Clinic during scheduled follow-up appointments. All study procedures will occur in-person.

Subjects selection criteria

- **Inclusion Criteria**

- Individuals with hidradenitis suppurativa with non-healing wounds or draining abscesses/nodules
- Individuals over 18 years of age

- **Exclusion Criteria**
  - Individuals younger than 18 years of age
  - Individuals without a diagnosis of HS
- **Sample Size**
  - 10 participants will be provided with wound care dressings from Appulse Medical.

Interventions and Interactions

Methylene blue, gentian violet, and ovine forestomach wound dressings will be provided by Appulse Medical. These wound care products are used for local management of wounds. This study is monitoring the impact these wound care products have on wounds associated with HS. Additionally, NRS assessments will be administered to evaluate the impact wound healing has on patient reported pain.

Endoform (ovine forestomach) is a natural dermal template used in all phases of wound healing. This product helps to stabilize, build, and organize tissue in acute and chronic wounds.

Hydrofera Blue is an antibacterial foam dressing that contains methylene blue and gentian violet to manage wounds. This is a safe, non-cytotoxic product that can be worn for 7 days while not inhibiting growth factors. This products wicks bacteria into the foam and away from the wound surface using natural negative pressure through capillary flow.

Hypafix tape aids in stabilization of wound dressings. This product is easy to apply, skin friendly, and comfortable to use.

Screening Visit/Visit 1

- Informed consent will be obtained
- Photographs of wounds at baseline will be taken
- Wounds will be measured, and appropriate amount of wound dressings will be administered and application instructions will be provided
  - Clean the wound with antibacterial soap.
  - Apply Endoform dermal template first, trimming it to fit the lesion, followed by Hydrofera Blue and fixed using Hypafix tape.
- Basic demographics, BMI, and smoking history will be recorded
- Participants will receive a standardized cleansing regimen to follow at home (Appendix II)
- Completion of NRS
- Completion of Dermatology Life Quality Index (DLQI/Appendix III)
- Completion of Sartorius Hidradenitis Suppurativa Score (Appendix IV)

Visits 2, 3, 4, 5

- Photographs of wounds at baseline will be taken
- Previous and new wounds will be measured, and appropriate amount of wound dressings will be administered
- Completion of NRS
- Completion of DLQI
- Completion of Sartorius Hidradenitis Suppurativa Score

Outcome Measure(s)

1. Assess the time for wound healing to occur using Endoform and Hydrofera Blue products.
2. Asses the percent healing that occurs over 8 weeks of follow-up using Endoform and Hydrofera Blue products.
3. Assess changes in patient reported pain via NRS
4. Assess changes in Sartorius scale

Analytical Plan

Wound area will be calculated by measuring length multiplied by width of the lesions. Wounds will be measured at each visit, and percent (%) change in area of lesion will be recorded.

Time versus % area healed will be analyzed. Post hoc analyses will be conducted to explore the relationship between participants' self-report on psychosocial measures and wound healing time.

Results will be analyzed initially using descriptive statistics. Comparison between groups will be done using chi square tests for proportions, and t-tests or ANOVA procedures for continuous variables. Regression analysis will be performed to identify independent outcome predictors. Other inferential statistical analysis will be conducted as appropriate.

Human Subjects Protection

All information provided will be kept confidential. Subjects will remain deidentified.

Subject Recruitment Methods

Subjects who meet the inclusion and exclusion criteria will be eligible for participation in this study. Participants will be recruited from the Wake Forest Department of Dermatology clinic by either the PI or members of the study team.

Informed Consent

Written informed consent will be obtained by members of the study team. The risk of harm or discomfort that may occur as a result of taking part in this research study is not expected to be more than in daily life or from routine physical or psychological examinations or tests. The rights and welfare of study will be protected through the use of measures to maintain the confidentiality of study information. Study results will be presented or published in lieu of providing individual subjects additional information regarding the study.

Confidentiality and Privacy

Confidentiality will be protected by collecting only information needed to assess study outcomes, minimizing to the fullest extent possible the collection of any information that could directly identify subjects, and maintaining all study information in a secure manner. To help ensure subject privacy and confidentiality, only a unique study identifier will appear on the data collection form. Any collected patient identifying information corresponding to the unique study identifier will be maintained on a linkage file, store separately from the data. The linkage file will be kept secure, with access limited to designated study personnel. Following data collection subject identifying information will be destroyed 3 years, consistent with data validation and study design, producing an anonymous analytical data set. Data access will be limited to study staff. Data and records will be kept locked and secured, with any computer

data password protected. No reference to any individual participant will appear in reports, presentations, or publications that may arise from the study.

Data and Safety Monitoring

The principal investigator will be responsible for the overall monitoring of the data and safety of study participants. The principal investigator will be assisted by other members of the study staff.

Reporting of Unanticipated Problems, Adverse Events or Deviations

Any unanticipated problems, serious and unexpected adverse events, deviations or protocol changes will be promptly reported by the principal investigator or designated member of the research team to the IRB and sponsor or appropriate government agency if appropriate.

References

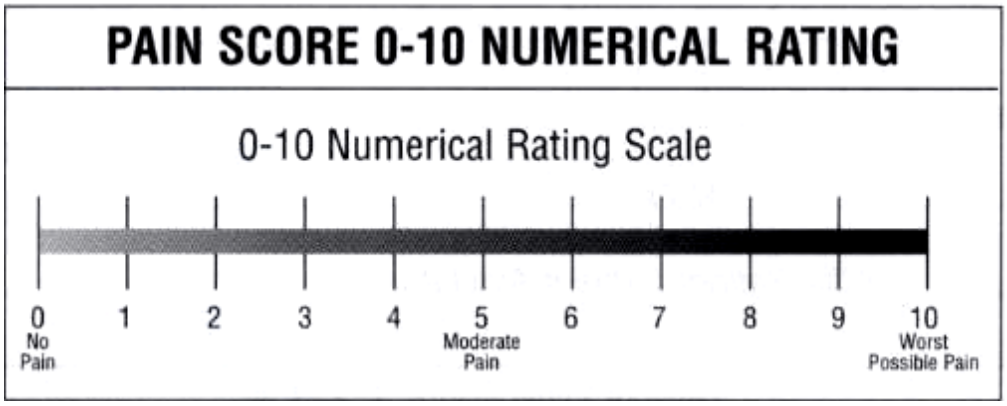
1. Alikhan A. Hidradenitis Suppurativa. *JAMA dermatology.* 2016;152(6):736.
2. Alavi A, Anooshirvani N, Kim WB, Coutts P, Sibbald RG. Quality-of-life impairment in patients with hidradenitis suppurativa: a Canadian study. *American journal of clinical dermatology.* 2015;16(1):61-65.
3. Patel ZS, Hoffman LK, Buse DC, et al. Pain, Psychological Comorbidities, Disability, and Impaired Quality of Life in Hidradenitis Suppurativa [corrected]. *Current pain and headache reports.* 2017;21(12):49.
4. Kouris A, Platsidaki E, Christodoulou C, et al. Quality of Life and Psychosocial Implications in Patients with Hidradenitis Suppurativa. *Dermatology.* 2016;232(6):687-691.
5. Dini, V., Oranges, T., Rotella, L., & Romanelli, M. (2015). Hidradenitis Suppurativa and Wound Management. *The International Journal of Lower Extremity Wounds*, 14(3), 236–244.

Appendix I- Numerical Rating Scale of Pain (NRS)

Numerical Rating Scale of Pain

Subject Visit: ☐**V1-Baseline** ☐**V2- Week 1** ☐**V3- Week 2** ☐**V4-Week 4** ☐**V5- Week 8**

Please mark on the scale below your level of pain:



Appendix II- Cleansing regimen

When to change your dressing:

- Your dressing must be changed **at least every 3 days**.
- Change your dressing if the Hydrofera Blue foam has turned white or is visibly soiled.

To change your dressing:

1. Cleanse gently with antibacterial soap. We recommend Dial soap.
2. Dry well after showering.
3. After cleansing, apply Endoform dermal template first, trimming it to fit the wound.
4. Apply Hydrofera Blue on top of Endoform dermal template.
5. Fix the dressing in place with Hypafix tape if not using Hydrofera Blue products containing adhesive.

Please avoid using bleach baths and acidic products for the duration of the study.

Appendix III

DERMATOLOGY LIFE QUALITY INDEX **DLQI**

Name: Date: Score:

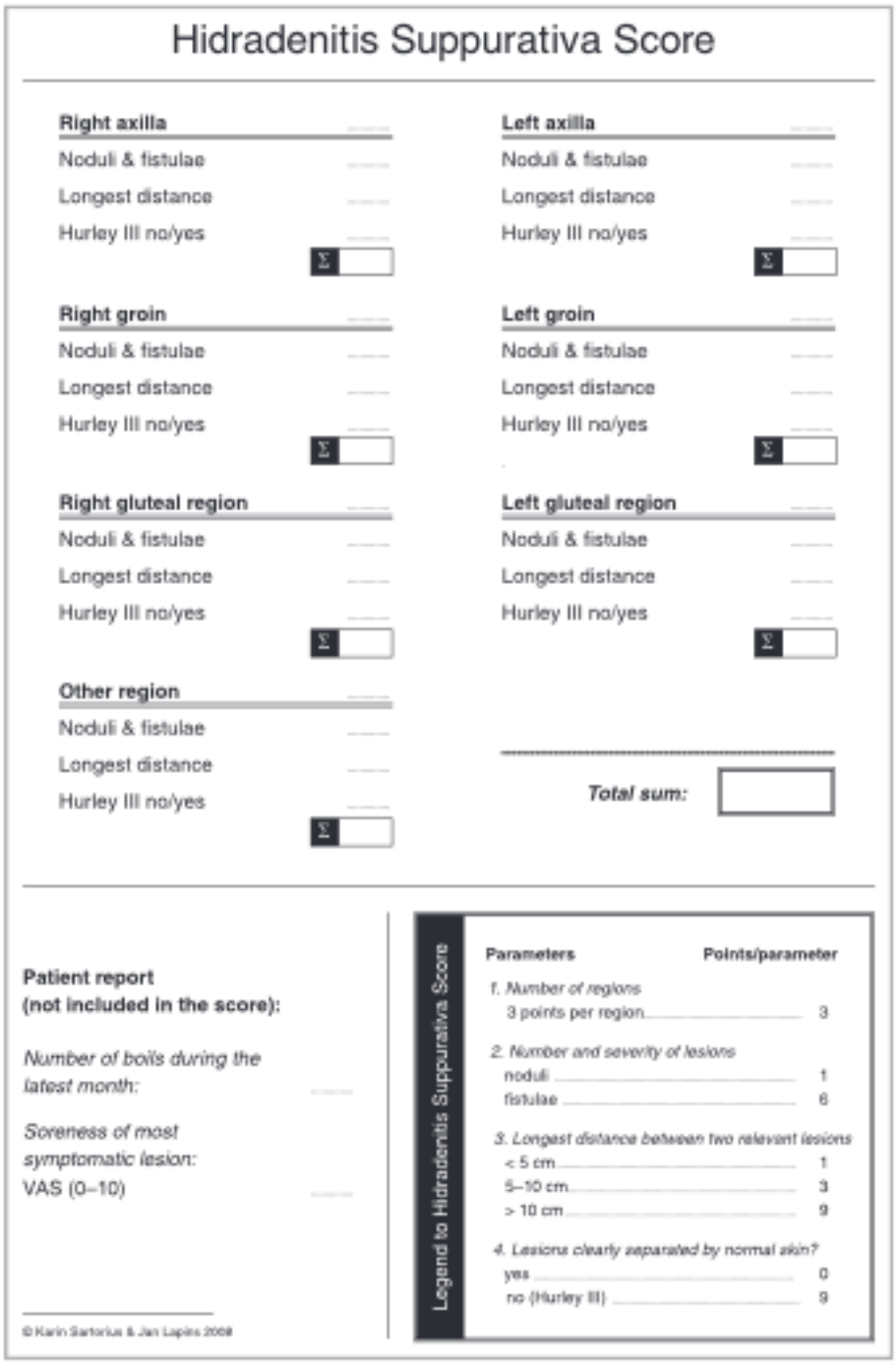
The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please check one box for each question.

1.	Over the last week, how **itchy**, **sore**, **painful** or **stinging** has your skin been?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	
2.	Over the last week, how **embarrassed** or **self conscious** have you been because of your skin?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	
3.	Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **yard?**	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
4.	Over the last week, how much has your skin influenced the **clothes** you wear?	Very much	☐ ☐	

		A lot A little Not at all	☐ ☐	Not relevant ☐
5.	Over the last week, how much has your skin affected any **social** or **leisure** activities?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
6.	Over the last week, how much has your skin made it difficult for you to do any **sport**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
7.	Over the last week, has your skin prevented you from **working** or **studying**?	yes no	☐ ☐	Not relevant ☐
	If "No", over the last week how much has your skin been a problem at **work** or **studying**?	A lot A little Not at all	☐ ☐ ☐	
8.	Over the last week, how much has your skin created problems with your **partner** or any of your **close friends** or **relatives**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
9.	Over the last week, how much has your skin caused any **sexual difficulties**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
10	Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐

Please check you have answered EVERY question. Thank you.

Appendix IV – Sartorius scale



Hidradenitis Suppurativa Score

Right axilla
Noduli & fistulae
Longest distance
Hurley III no/yes
Σ

Left axilla
Noduli & fistulae
Longest distance
Hurley III no/yes
Σ

Right groin
Noduli & fistulae
Longest distance
Hurley III no/yes
Σ

Left groin
Noduli & fistulae
Longest distance
Hurley III no/yes
Σ

Right gluteal region
Noduli & fistulae
Longest distance
Hurley III no/yes
Σ

Left gluteal region
Noduli & fistulae
Longest distance
Hurley III no/yes
Σ

Other region
Noduli & fistulae
Longest distance
Hurley III no/yes
Σ

Total sum:

Patient report
(not included in the score):

Number of boils during the latest month:

Soreness of most symptomatic lesion:
VAS (0–10)

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Legend to Hidradenitis Suppurativa Score

Parameters	Points/parameter
1. Number of regions	
3 points per region	3
2. Number and severity of lesions	
noduli	1
fistulae	6
3. Longest distance between two relevant lesions	
< 5 cm	1
5–10 cm	3
> 10 cm	9
4. Lesions clearly separated by normal skin?	
yes	0
no (Hurley III)	9