

**A randomized, controlled, double blind study to evaluate the efficacy
of intralesional triamcinolone in the treatment of hidradenitis
suppurativa**

STUDY PROTOCOL

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Study Protocol

Title: A randomized, controlled, double blind study to evaluate the efficacy of intralesional triamcinolone in the treatment of hidradenitis suppurativa.

Purpose: To evaluate the effectiveness of intralesional triamcinolone for the treatment of hidradenitis suppurativa

Participants: Patients diagnosed with Hidradenitis Suppurativa that have active inflammatory HS lesions. Up to 60 lesions will be treated. Between 20 and 60 patients will be enrolled dependent on the number of lesions they have treated. (up to 3 per patient)

Procedures (methods): Injection of triamcinolone or placebo into active lesions of hidradenitis suppurativa.

Hidradenitis Suppurativa: Symptoms & Diagnosis

Three criteria must be present for the diagnosis of HS. Firstly, characteristic lesions must be present, often beginning as “blind boils” that transition to abscesses, bridged scars, draining sinus, and post-inflammatory “tombstone double-ended pseudocomedones.”¹ These lesions must be present in the typical areas: the groin, axillae, buttocks, perineal region, and infra- and intermammary folds.¹ The final criterion is that there must be a history of recurrence. The disease is typically chronic with relentless progression that frequently results in significant disability and quality of life impairment.

The acute, painful lesions have been reported to have an average duration of 6.9 days, but permanent painful boils are present in 62% of patients.² Patients develop a median of two lesions per month and average age of onset is 21.9 years.² Rupture of lesions can lead to worsening pain, suppurative discharge, and malodor.³ The current prevalence of HS has been reported to range from 0.05% to 4%, with the number of patients diagnosed substantially increasing in recent years.⁴ The rise in diagnoses is due to either increased knowledge of HS, increased ability to identify the clinical signs, or a true increase based on lifestyle modifications. ⁴

A dermatologist or healthcare professional with HS experience should make the diagnosis and determine the clinical stage. Hurley staging is a quick way to characterize staging of the condition and identify appropriate therapy and likely success of treatment. We will identify the Hurley staging for the involved sites during the study, as this may be helpful in characterizing our population.

Pathogenesis of Hidradenitis Suppurativa

The exact pathogenesis of HS remains unclear, but the hair follicle is most likely the location where the lesion originates. Recent investigations demonstrated that the interleukin-12/interleukin-23/Th17 pathway and tumor necrosis factor α are involved in HS, indicating that the pathogenesis is immune and inflammatory related.^{5, 6} Intralesional steroid injections are commonly used for localized inflammatory skin diseases, such as cutaneous lupus erythematosus, cystic acne, and sarcoidosis, so it seems appropriate that intralesional

triamcinolone will be beneficial for HS.⁷ HS may also be associated with comorbid diseases such as obesity, arthritis, anemia, lymphedema, and metabolic syndrome.⁸ These conditions should be addressed and appropriately managed by health care providers.

Treatment of Hidradenitis Suppurativa

HS is primarily treated with antibiotics, biologics, and surgery in severe cases. First line therapies are clindamycin lotion 1%, Tetracycline, Clindamycin/Rifampicin, and Adalimumab.⁹ Intralesional triamcinolone, the focus of our research study, is a common and routine treatment for acutely flaring HS lesions.

Hidradenitis Suppurativa Negatively Impacts Quality of Life

HS has a greater negative impact on quality of life than other more commonly known dermatologic conditions such as psoriasis, atopic dermatitis, acne vulgaris, and chronic urticaria.¹⁰ This is primarily due to the severe pain, discomfort, pruritus, and malodor associated with HS. Patients also often have an impaired sexual health, suffer from depression, and have a difficulty performing work responsibilities.¹¹ Out of employed HS patients, 58.1% report work absence due to the condition with a mean absence from work duration of 33.6 ± 26.1 days annually.¹⁰ Improving clinical outcomes, such as shortened outbreaks and diminished pain, could have a profound effect on patients' professional endeavors and quality of life.

Present Study

Despite HS being a relatively common disease that is chronic, painful, and debilitating, it has still not received much research or societal attention. To date, limited clinical trial data exists supporting treatment of HS and the management of acute exacerbations. Clinical experience suggests that intralesional triamcinolone may be useful, but its effectiveness has not been extensively assessed. Intralesional triamcinolone injections are commonly used for localized inflammatory skin diseases, so it will likely benefit HS patients as well.⁷

Our proposed study seeks to answer two of the top 10 uncertainties set by The Hidradenitis Suppurativa Priority Setting Partnership: “What is the best management of an acute flare?” and “What is the best management of pain associated with HS?”⁵ Analyzing the efficacy of intralesional triamcinolone at resolving lesions and decreasing pain could help guide dermatologists' treatment of HS and provide better outcomes for patients. Patients with HS at UNC's Dermatology and Skin Cancer Centers will receive varying concentrations of intralesional triamcinolone or a normal saline placebo and their self-reported outcomes will be analyzed.

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Study Aims:

Aim 1. Characterize and compare the 3 regimens in terms of days to resolution of treated lesion. Hypotheses for Aim 1: Days to resolution of treated lesions will be fewer in the treatment groups compared to normal saline placebo, and will be fewer with triamcinolone 40mg/ml compared to triamcinolone 10mg/ml.

Aim 2. Characterize and compare the 3 regimens in terms of pain level on day 5. Hypotheses for Aim 2: Rating of pain will be less in the treatment groups compared to normal saline placebo, and will be less with triamcinolone 40mg/ml compared to triamcinolone 10mg/ml at day 5.

Aim 3. Characterize and compare the 3 regimens in terms of patient rating of the “benefit of the Treatment Hypotheses for Aim 1: Patient rating will be more favorable the treatment groups compared to normal saline placebo, and will be more favorable with triamcinolone 40mg/ml compared to triamcinolone 10mg/ml.

Inclusion/Exclusion Criteria:

Inclusion Criteria:

1. Male and females > or = 16 years of age
2. Diagnosis or history of clinical features consistent with hidradenitis suppurativa for >1 year
3. Patient must have an inflammatory lesion at the time of treatment. This can be an inflammatory nodule defined by a tender, palpable subcutaneous nodule, or an abscess defined as a fluctuant, painful, subcutaneous nodule. Lesions greater than 2 centimeters in size will not be excluded. Inflammatory nodules or abscesses can be treated if they are associated with a sinus tract, which is a

chronic HS lesion defined by tunneled lesion with multiple openings to the surface of the skin. Sinus tracts without associated nodules or abscesses will not be treatment targets.

4. Patient must be off of antibiotics or on a stable course of oral antibiotics for >4 weeks prior to the baseline visit. Allowable antibiotics during treatment course are topical clindamycin, topical chlorhexidine gluconate, oral doxycycline, oral minocycline, or oral clindamycin +/- rifampin.
5. Must be able to provide adequate informed consent for themselves

Exclusion Criteria:

1. Any patient with signs of active infection at the time of screening that is not related to their hidradenitis suppurativa.
2. Patients who have been on non-permitted antibiotics in the 4 weeks prior to baseline. Allowable antibiotics during treatment course are topical clindamycin, topical chlorhexidine gluconate, oral doxycycline, oral minocycline, or oral clindamycin +/- rifampin.
3. Patients who have had surgical intervention of the treated body region (i.e., right axilla) beyond incision and drainage procedures in the last 8 weeks or with open surgical wounds in the treatment region.
4. Patients who have been started on immunomodulatory or biologic treatment (i.e., adalimumab, infliximab) in the past 4 weeks
5. Patients on non-stable doses of opiate analgesics for the last 14 days prior to screening
6. Patients with history of hypersensitivity reactions to triamcinolone
7. Ongoing health or physical exam concerns which the investigator feels may put the patient at significant risk

Study Design

This will be a randomized, double-blind, placebo-controlled trial of two concentrations of intralesional triamcinolone, triamcinolone 40mg/ml and triamcinolone 10mg/ml, with normal saline as a placebo control. Target enrollment is up to 60 lesions with 1-3 lesions treated in each patient enrolled. Screening will be performed during regularly scheduled clinic visits with the principal investigator (C.S.). Informed consent will be signed by the subject. Physical exam will be performed to assure that inflammatory lesions suitable for treatment are present. Once subjects are deemed appropriate for the study, between one and three treatment sites will be marked with sequential lettering with a skin marker and documented by body location. Pain level of each lesion will be recorded. At that time the triamcinolone and/or placebo will be prepared by the co-investigator the drug will be concealed with opaque tape on the syringe. The principal investigator and subject will thus be blinded as the principal investigator administers the treatment.

Following treatment, subjects will be given a paper questionnaire that will ask them to rate their level of pain on a 1-10 scale, the effectiveness of the treatment, and whether they believe the target lesions has resolved. They will record these scores on days 1, 2, 3, 5, 7, 10, and 14. These will be patient-reported outcomes only without any physician assessment as this is felt to be a more clinically relevant outcome. The principal investigator or co-investigator will contact subjects by phone to ensure that logs recording pain and days to resolution are completed in a timely and correct manner, but no data will be collected during the 14-day period in which questionnaires are completed to avoid influencing subject responses at the time of contact. After the final questionnaire is completed (more than 14 days after the intervention is performed), the

co-investigator or principal investigator will contact the subject by phone to remind the subject to mail in their questionnaires and may allow the option to collect the data that the subject has already recorded. At this time, the principal or co-investigator may also ascertain if any previously unreported adverse events occurred during the study period. The days to resolution reported and pain data will be used to compare the effects of varying concentrations of intralesional triamcinolone with normal saline.

Protocol summary:

Day 0: Subject recruited and pre-screened,

- Adult subjects will sign adult consent form and HIPAA authorization
- Subjects aged 16-17 will sign the age 15-17 assent form and parents will sign the parental consent form. HIPAA authorization will be signed.
- History of disease and medications will be taken
- Physical exam will be performed to see if appropriate target lesions are present
- Each lesion will be randomized to a treatment group
- Treatment will be administered via intralesional injection by the principal investigator
- Follow-up paper and pencil questionnaire will be dispensed along with a stamped and addressed return envelope.

Day 1, 2, 3, 5, 7, and 10:

- subject will complete corresponding section of the paper and pencil questionnaire on each of these days to report pain level of each lesion treated and whether each lesion has resolved.
- between day 2-7 the subject will be contacted by phone and reminded to complete their questionnaires. No data will be gathered at this time.

Day 14: subject will complete corresponding section of the paper and pencil questionnaire on each of these days to report pain level of each lesion treated and whether each lesion has resolved. He/she will also answer a question regarding how they view the efficacy of the treatment for each location

Day 14-21:

- investigator or co-investigator will contact the subject by phone to remind the subject to mail the completed questionnaire or allow the option collect the data on pain, lesion resolution, and efficacy that was previously recorded during the study period over the phone. At that time, the primary or co-investigator may ascertain if any adverse effects have occurred that have not already been reported.