Clinical outcomes and response of patients applying topical therapy for pyoderma gangrenosum: A prospective cohort study

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Background: Pyoderma gangrenosum (PG) is an uncommon dermatosis with a limited evidence base for treatment.

Objective: We sought to estimate the effectiveness of topical therapies in the treatment of patients with PG.

Methods: This was a prospective cohort study of UK secondary care patients with a clinical diagnosis of PG that was suitable for topical treatment (recruited between July 2009 and June 2012). Participants received topical therapy after normal clinical practice (primarily topical corticosteroids [classes I-III] and tacrolimus 0.03% or 0.1%). The primary outcome was speed of healing at 6 weeks. Secondary outcomes included the following: proportion healed by 6 months; time to healing; global assessment; inflammation; pain; quality of life; treatment failure; and recurrence.

Results: Sixty-six patients (22-85 years of age) were enrolled. Clobetasol propionate 0.05% was the most commonly prescribed therapy. Overall, 28 of 66 (43.8%) ulcers healed by 6 months. The median time to healing was 145 days (95% confidence interval, 96 days to ∞). Initial ulcer size was a significant predictor of time to healing (hazard ratio, 0.94 [95% confidence interval, 0.88-1.00); $P = .043$). Four patients (15%) had a recurrence.

Limitations: Our study did not include a randomized comparator.

Conclusion: Topical therapy is potentially an effective first-line treatment for PG that avoids the possible side effects associated with systemic therapy. It remains unclear whether more severe disease will respond adequately to topical therapy alone. (J Am Acad Dermatol 2016;75:940-9.)

Key words: cohort; corticosteroid; pyoderma gangrenosum; side effects; tacrolimus; topical therapy.

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Conflicts of interest: None declared.

This study was conducted as part of a randomized controlled trial of systemic treatments for pyoderma gangrenosum (Controlled-Trials.com ISRCTN35898459 [registered April 20, 2009]). Ethics and regulatory approvals were obtained (ethics approval, 09/H0903/5; Medicines and Healthcare Products Regulatory Agency approval, 19162/0213/001).

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Pyoderma gangrenosum (PG) is an uncommon, painful ulcerative inflammatory dermatosis that is associated with considerable morbidity[1,2] and a reported 3-fold increased risk of death.[3]

The most commonly prescribed treatments for patients with PG are systemic therapies (eg, prednisolone, cyclosporine, intravenous immunoglobulin, or biologic therapies). Nevertheless, topical treatments (eg, corticosteroids and calcineurin inhibitors) have also been recommended for localized disease[4,5] and may be a useful first-line therapy for some patients.

We conducted a multicenter prospective cohort study to investigate the efficacy of topical therapy as a first-line treatment for PG. This cohort study was conducted alongside a randomized controlled trial (RCT) of systemic treatments for PG (ie, the *S*tudy of *T*reatments f*O*r *P*yoderma *GA*ngrenosum *P*atients [STOP GAP]), in which oral prednisolone was compared to cyclosporine.[6] Our objective was to provide prospectively collected estimates of treatment response for patients receiving topical therapy for PG.

CAPSULE SUMMARY

- Pyoderma gangrenosum is a painful ulcerating disease. The current evidence base for treatment is limited.
- In a large prospective study of topical treatments, 44% of patients were healed by 6 months. Ulcer size was a predictor of healing, and 15% of patients with pyoderma gangrenosum had a recurrence.
- Clobetasol propionate 0.05% is a potentially useful first-line therapy for patients with pyoderma gangrenosum, particularly for patients with small lesions.

METHODS

Ethics and regulatory approvals were obtained and participants gave written informed consent. The Independent Trial Steering Committee and Independent Data Monitoring Committee provided oversight as part of the STOP GAP group.

Study design

This was a prospective cohort study of patients with a clinical diagnosis of PG for whom topical therapy was indicated. Patients with more severe PG (ie, requiring systemic therapy) were enrolled into a parallel RCT[6] but were eligible for inclusion in the topical therapy cohort study if systemic therapy was contraindicated or if the patient preferred to receive topical treatment. Participants were enrolled for ≤6 months or until the target PG ulcer had healed. Medications were prescribed as per local practice at the recruiting hospital.

Research questions

This study sought to answer the following 4 questions:

1. What is the typical treatment response in patients for whom topical therapy is indicated?
2. What proportion of participants require escalation of treatment to systemic medication?
3. What is the impact of PG on patient-reported quality of life?
4. What factors predict treatment response?

Participants

Recruitment took place in 28 secondary care hospitals throughout the United Kingdom. Participants were identified from dermatology, rheumatology, gastroenterology, and general medicine clinics.

Participants were ≥18 years of age and had a clinical diagnosis of PG that was confirmed by the recruiting dermatologist—with a biopsy specimen obtained to exclude alternative etiologies if clinically indicated—and ≥1 measureable ulcer. The decision whether to treat with topical therapy or not was based on the views of the dermatologist in discussion with patients.

Patients were excluded if they had pustular or granulomatous PG variants, because they may have responded differently to therapy and because measurement of a single ulcer was not possible. Patients were also excluded if they had received oral prednisolone, cyclosporine, or intravenous immunoglobulin for the treatment of PG in the previous month or were participating in another clinical trial.

Ongoing treatment with systemic therapies for the management of underlying comorbidities (eg, rheumatoid arthritis) was permitted.

Interventions

Patients received topically applied interventions for the treatment of PG. The dermatologist was free to prescribe whichever therapy and dosage regimen they preferred according to local practice. In the United Kingdom, it was normal practice to apply topical interventions to the inflammatory edge of the ulcer. Systemic therapies for the treatment of PG were prohibited but were continued if they were taken for other conditions.