

Comparison of the two most commonly used treatments for pyoderma gangrenosum: results of the STOP GAP randomized control trial, Ormerod, et. al. *BMJ*, June 12, 2015

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Level of Evidence: 1

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Pyoderma gangrenosum is a rare inflammatory disorder that causes progressive necrotizing ulceration. It is also considered a diagnosis of exclusion and is often misdiagnosed. There are several variants: classic, cribriform, peristomal and bullous. Clinical findings of pyoderma gangrenosum are a predominantly cutaneous, well demarcated ulcer with purplish edges with tender erythematous nodules or pustules. Pyoderma gangrenosum is associated with underlying autoimmune systemic diseases such as inflammatory bowel disease, rheumatoid arthritis and hematological malignancies. Approximately 25% of cases manifest from iatrogenic trauma, a phenomenon known as pathergy; further soft tissue trauma or debridements can lead to an increase in ulcer size and induce ulcer bed necrosis. The purpose of this study was to test the hypothesis that cyclosporin is superior to prednisolone in the treatment of pyoderma gangrenosum.

A multicentered, parallel group, observer blind randomized controlled trial was conducted for 121 patients that were diagnosed with pyoderma gangrenosum from 39 UK hospitals from June 2009 to November 2012. Clinical diagnosis was then revised in 9 participants leaving 112 participants total for analysis (59 cyclosporin and 53 prednisolone). Oral prednisolone 0.75mg/kg/day was compared with cyclosporin 4mg/kg/day, given to the respective participant groups. Clinic visits took place at baseline, week two, week six and when the ulcer had healed. The primary outcome was speed at which the target leg ulcer was healing. Statistical analysis was performed using various regression models.

For 64 participants the pyoderma gangrenosum improved (decrease in size), with a median decrease of 1.96 cm² in cyclosporine group and 3.04 cm² in the prednisolone group. By six months, the ulcers had healed in 28/59 (47%) participants in the cyclosporine group and 25/53 (47%) participants in the prednisolone group. 40 participants in the cyclosporine group and 35 participants in the Prednisolone group experienced at least one adverse reaction. The notable differences included new onset of diabetes and hyperglycemia in the prednisolone group and headaches, gastrointestinal disturbance and renal dysfunction in the cyclosporin group. Serious adverse reactions included ruptured abdominal aortic aneurysm and acute kidney injury in the cyclosporin group and bowel perforation and infection in the prednisolone group. In the cyclosporine group it took an average of 134 days to heal the ulcer and in the prednisolone group it took 112 days to heal.

In this randomized controlled trial, there was no significant difference between the two most commonly used treatments for pyoderma gangrenosum. Approximately 2/3 of the participants reported adverse reactions. An expert review by Miller et al considered safety, efficacy, and cost which placed prednisolone as preferred treatment. However, previous studies have reported large portions of patients with pyoderma gangrenosum achieving complete response with cyclosporin. Healing responses at six weeks in this study were similar to those observed for randomized control trial of infliximab compared with placebo. In this trial 15% of participants in the cyclosporin and 21% in the Prednisolone group had healed at six weeks. Further studies are required to understand the effectiveness in treating pyoderma gangrenosum with these and other modalities.



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