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ORIGINAL ARTICLE

Neer Award 2018: Benzoyl peroxide effectively decreases preoperative *Cutibacterium acnes* shoulder burden: a prospective randomized controlled trial

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Background: Benzoyl peroxide (BPO) solutions effectively reduce *Cutibacterium acnes* (formerly *Propionibacterium acnes*) on the face, neck, and back in nonoperative settings. This study compared preoperative application of BPO vs. chlorhexidine gluconate (CHG) in decreasing shoulder *C acnes* skin burden in surgical patients.

Methods: Eighty patients undergoing shoulder surgery were prospectively enrolled in a randomized double-blind trial at 1 institution from August 2015 to April 2017. Participants were randomized to 5% BPO or 4% CHG for 3 consecutive days. The nonoperative shoulder had no intervention and served as the negative control. Skin cultures of both shoulders were obtained via a detergent scrub technique the day of surgery at anterior, lateral, and posterior sites and the axilla.

Results: Fewer positive cultures were obtained from the BPO-treated side compared with the contralateral side ($P = .0003$), and no change was shown for the CHG group ($P = .80$). Shoulders treated with BPO showed a statistically significant reduction in *C acnes* counts compared with CHG at anterior ($P = .03$) and posterior ($P = .005$) portal sites. No significant difference was found at the axilla ($P = .99$) or lateral portal site ($P = .08$). No postoperative infections or wound complications occurred in either group.

Conclusions: BPO is more effective than CHG at reducing *C acnes* on the shoulder. Decreasing the skin burden of *C acnes* may reduce intraoperative wound contamination and postoperative infection. BPO should be considered as an adjunctive preoperative skin preparation considering its potential benefit, low risk, and low cost.

Level of evidence: Level I; Randomized Controlled Trial; Treatment Study

Keywords: *Cutibacterium acnes*; *Propionibacterium acnes*; surgical site infection; shoulder; benzoyl peroxide; chlorhexidine gluconate; preoperative skin preparation

This work was presented as Poster P0802 at the 2018 Annual Meeting of the American Academy of Orthopaedic Surgeons, New Orleans, LA, USA, March 6-10, 2018.

The University of Maryland, Baltimore Institutional Review Board approved this study (study number HP-00064296).

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Cutibacterium acnes (formerly *Propionibacterium acnes*) is a gram-positive anaerobic bacillus that resides on the skin and in the sebaceous glands associated with hair follicles. *C acnes* is the cause of facial and truncal inflammatory acne vulgaris and can also be pathogenic after shoulder surgery, resulting in septic arthritis, indolent shoulder pain, or arthroplasty failure.[15] *C acnes* forms a biofilm on implant surfaces, and cultures taken at the time of surgical revision of failed shoulder arthroplasties are commonly positive for the bacteria.[11]

The deep sebaceous glands of hair follicles harbor as many as 10^5 *C acnes* organisms per follicle.[10] *C acnes* in the sebaceous glands are not completely eliminated by chlorhexidine gluconate (CHG) or Betadine (Purdue Pharma LP, Stamford, CT, USA), most likely because topical surgical preparations cannot reach bacteria in the sebaceous glands.[10,11] Surgical incisions transect the sebaceous glands, allowing *C acnes* to enter surgical wounds.[10] Preoperative intravenously administered antimicrobial prophylaxis with traditional skin preparation has not been shown to successfully eliminate *C acnes* from the surgical field.[11] Thus, although there is evidence to explain the pathogenesis of *C acnes* infections in this patient population, no current strategies have been proven to decrease the risk of postoperative *C acnes* infection.

Acne vulgaris caused by *C acnes* can be successfully treated clinically using benzoyl peroxide (BPO) solutions, which enhance follicular penetration of the sebaceous glands.[3,4,12] Consequently, BPO is a potentially promising presurgical skin treatment to decrease the *C acnes* burden and possibly decrease the risk of wound contamination and infection. However, the effect of BPO on *C acnes* in patients undergoing shoulder surgery compared with the effect of CHG is unknown. The effect of BPO on wound healing after shoulder surgery is also unknown.

This study evaluated the effect of BPO compared with CHG on the *C acnes* skin burden in patients undergoing shoulder surgery as a double-blind randomized controlled trial. We hypothesized that BPO would more effectively decrease the *C acnes* burden at multiple shoulder sampling sites compared with CHG.

Materials and methods

Eighty patients were prospectively enrolled in a double-blind randomized controlled trial from 2015 through 2017 (NCT02510144 at clinicaltrials.gov.). Inclusion criterion was indication for primary or revision shoulder surgery. Arthroscopic surgery and arthroplasty were both included. Patients were excluded if they were younger than 18 years or had a history of shoulder infection or allergy to BPO or CHG.

All patients provided informed consent to participate in this study. Patients were randomized to 118 mL of 5% BPO gel or 4% CHG skin cleanser by a random number generator after patients elected to have surgery. Treatment solutions were allocated in opaque bottles with detailed application instructions. Patients, surgeons, and outcome analyzers were blinded to treatment group.

Participants were instructed to use the solution over the operative shoulder and axilla for 3 mornings before surgery (preoperative day −2, preoperative day −1, and the morning of surgery). Patients were instructed to apply the solution to the rinsed shoulder for 3 minutes before washing it away. Compliance was facilitated with reminder phone calls 2 days before surgery and was measured with a survey on the day of surgery.

On the day of surgery, samples were obtained from the operative (experimental) and nonoperative (control) shoulders at 4 sites: anterior, lateral, and posterior arthroscopic portal sites and the axilla. Samples were obtained before surgical draping and application of operative skin preparation to isolate the independent effect of the preoperative wash. Demographic data and medical comorbidities were also collected.

A detergent scrub technique presented by Williamson and Kligman[17] was used to identify pathogens. This is a standardized dermatologic technique for *C acnes* quantification for the deep sebaceous glands that obviates the need for full-thickness dermal biopsy specimens and is genotypic standardized.[9] Each site was cleansed of surface bacteria by thoroughly wiping the area for 30 seconds with sterile gauze soaked with 0.1% Triton X-100. The sample area was delineated by a 3.8-cm^2-diameter round hole in a business card–sized plastic template held firmly to the skin. The resulting sample area was scrubbed twice with moderate pressure for 30 seconds using a sterile cotton swab that was dipped in Bacto Letheen broth (Becton Dickinson, Franklin Lakes, NJ, USA) before each scrub. The tip of the swab was then placed in the 2-mL tube of Bacto Letheen broth.

All samples were placed into individual transport bags and delivered on ice to an independent on-campus *C acnes* laboratory. The hospital microbiology laboratory was not used because of a known high false-positive rate. All samples in Letheen broth were serially diluted into 0.05% Tween-80 in four 10-fold dilutions. Then, 50 μL of each dilution was placed on a designated section of a custom agar plate containing *Brucella* agar supplemented with yeast extract, dextrose, and cysteine. Plates were allowed to dry, placed in an anaerobic jar with BBL GasPak Plus (Becton Dickinson) anaerobic system envelope, and incubated anaerobically at 35°C to 37°C for 7 days. Colony-forming units (CFU) of *C acnes* were counted at the lowest dilution that could be read (Fig. 1). A 14-day incubation caused complete desiccation of the agar plates. Delayed incubation in a thioglycollate broth is an option for any extended time period beyond 1 week, but that technique was not used in this study.

A priori power analysis was performed based on previous BPO literature for the upper back.[9] We assumed a 10-fold increased relative reduction in the *C acnes* burden with BPO compared with CHG. Power was set at 0.8, α was set at 0.05, and 74 participants were necessary (Stata/SE software; StataCorp, College Station, TX, USA).

Positive cultures were compared on the treated side vs. the nontreated site as a pooled χ^2 statistic. Each portal site was individually compared using analysis of variance with the Tukey post hoc analysis. A logarithmic reduction in CFU was calculated and compared with the nonoperative side for each of the 4 sites. BPO was compared with CHG via a Student *t* test (Stata/SE).

Results

The study enrolled 80 patients. Four eligible patients declined to participate (95% participation), and 4 patients admitted to incomplete preoperative skin application (5% noncompliance). All 80 patients were included in an intention-to-treat analysis (Fig. 2).