Topical benzoyl peroxide application on the shoulder reduces Propionibacterium acnes: a randomized study

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Topical benzoyl peroxide application on the shoulder reduces *Propionibacterium acnes;* a randomized study

Running head

***P.acnes* reduction with skin preparation**

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Preoperative topical benzoyl peroxide of the shoulder reduces *P.acnes* and prevents recolonization, compared to chlorhexidine soap.

Abstract

Background: *Propionibacterium acnes (P.acnes)* is a common cause of infection following shoulder surgery. Studies have shown that standard surgical preparation does not eradicate *P.acnes.* The purpose of this study was to examine if topical application with benzoyl peroxide gel (BPO) could decrease the presence of *P.acnes*, compared to the today's standard treatment with chlorhexidine soap (CHS). We also investigated and compared the recolonization of the skin after surgical preparation and draping, between the BPO- and CHS-treated groups.

Methods: A single blinded non-surgical study with forty volunteers – twenty-four men and sixteen women were randomized to preoperative topical treatment at home with either 5 % BPO or 4 % CHS in the area of a deltopectoral approach of their left shoulder. Four skin swabs from the area were taken in a standardized manner at different times: Before and after topical treatment, after surgical skin preparation and sterile draping and 120 minutes after draping.

Results: Topical treatment with BPO significantly reduced the presence of *P.acnes* as CFU on the skin after surgical preparation. *P.acnes* was found in 1/20 subjects of the BPO group, and 7/20 in the CHS-group ($p<0.044$). The results remained after two hours ($p<0.048$).

Conclusion: Topical preparation with BPO before shoulder surgery may be effective in reducing *P.acnes* on the skin and prevent recolonization.

Keywords: Propionibacterium acnes; Preoperative shower; Shoulder; Infection; Benzoyl peroxide; Chlorhexidine

***P.acnes* reduction with skin preparation**

Level of evidence: Level II

Introduction

Propionibacterium acnes (*P.acnes*) is a gram-positive facultative anaerobic rod, a human commensal bacteria who resides in the pilosebaceous ducts of the skin [1, 6]. The reported numbers of shoulder infections after surgery caused by *P. acnes* is increasing and so is the incidence of resistance to antibiotics [1, 3, 11, 16, 21, 26]. The ability of *P.acnes* to create biofilm causes severe infections that may involve reoperation and long-term antibiotic treatment. To decrease the bacterial burden on the skin before operation one strategy is topical preparation at home with chlorhexidine soap (CHS). Despite strict preoperative preparation with chlorhexidine solution in 70 % ethanol earlier studies has shown that chlorhexidine is not able to eradicate *P.acnes* from the skin. From 7% up to 50 % of *P.acnes* may still be present on the skin [10, 15, 23, 25]. Benzoyl peroxide (BPO) is widely used as topical therapy for acne vulgaris, and has so been for more than five decades. The bactericidal effect of BPO on *P.acnes* is well documented, and has not been associated with the development of *P.acnes* resistance. [4, 8, 12, 17]. The purpose of this study was to examine if topical application with BPO could decrease the presence of *P.acnes* on the treated skin, compared to the today's standard treatment with CHS. We also investigated and compared the recolonization of the skin after surgical preparation and draping, between the BPO- and CHS-treated groups.

Material and Methods

A single-blinded non-surgical randomized study, with forty healthy volunteers in aged from 20 to 66, twenty-four men and sixteen women gave informed consent to participate. Exclusion criteria were antibiotic treatment 10 days prior to trial day, presence of diabetes mellitus, local skin lesions and local or systemic corticoid steroid treatment. Participants were randomized in blocks of four to CHS or BPO-pretreatment. The investigator was blinded to allocated treatment. One week prior to the trial day the participants received verbal and written instructions. Thereafter the first skin swab was collected on the left shoulder (Sample A).

The groups prepared as follows:

1. BPO group

   The treatment set up in the BPO-group was designed in collaboration with a dermatologist, who advised on drug concentration and application frequency to minimize local side effects, e.g. erythema, peeling and dryness. Hence the BPO group started the procedure 48 hours before the trial day. After showering and drying they applied a 5 cm strip of 5 % BPO on the left shoulder. They repeated the application the following morning and evening. The fifth and last time was the morning on trial day.

2. CHS group

   According to the local routine protocol the CHS group prepared with 4% chlorhexidine soap on their left shoulder, starting the day before the trial day with two

showers, with a minimum of two hours in between, using two sponges each, and on trial day one shower in the morning with two more sponges.

A treatment diary was administered to each participant for affirmation of each gel application or shower, showing 100 % compliance. On each trial day occasion four volunteers were placed on separate beds in the same operating room with laminar airflow (LAF) with their upper body inside the LAF-circle. Before surgical preparation the next skin swab was collected from the left treated side (Sample B). At the same time a control swab was taken from the contralateral shoulder. A skin swab was collected after the treated left side was prepared for 2 minutes with 0.5% chlorhexidine solution in 70% ethanol, and sterile drape was applied (Sample C). 120 minutes after surgical preparation and sterile draping the last skin swab was collected (Sample D) (Table 1). All skin swabs were taken by rub 15 times over a 10 cm deltopectoral interval, and immediately put into the medium. Within thirty minutes the skin swabs were transported to the laboratory, vortexed for 10 sec before cultured on anaerobic blood agar medium without antibiotics and placed in an anaerobic incubator. After five days in the incubator the number of colony forming units (CFU) were counted and divided into five groups according to the numbers of CFUs (Table 2).The bacterial colonies were classified on agar plates by surface characteristics. *P.acnes* was identified with matrix-assisted laser desorption/ionization time-of-flight (MALDI-ToF) mass spectrometry. Analyzes were blinded and performed by the main author. Code was broken after analyzes were done.

96 **Statistical Analysis**

97

98 For dichotomous variables we used Fischer´s exact test and otherwise Chi-squared test. P-

99 values <0.05 was considered being statistically significant.

100

Results

Before any treatment (sample A), *P.acnes* was detected in 38/40 subjects, and there was no significant difference in CFU between the groups. In the BPO- group, presence of *P.acnes* diminished with treatment (Figure 1a) but not in the CHS-group (Figure 1b). After skin preparation (Sample C) we could detect CFU of P. acnes in only 1/20 in the BPO-group compared to 7/20 in the CHS-group (p=0.044, Figure 2). Two hours later, the BPO-group showed a significantly lower *P.acnes* presence than the CHS-group (p=0.048, Figure 2). There was no significant difference in presence of *P.acnes* before surgical field preparation (Sample B) and after two hours (Sample D) in the CHS-group (Figure 1b), in contrast to the BPO-group (Figure 1a).

The total number of CFU (which might comprise of more bacterial strains than *P.acnes*) also diminished after topical BPO-treatment (p-value 0.035) but not in the CHS-treated group (p=0.284).

Discussion

To the authors knowledge this is the first randomized study which compares topical BPO-treatment to topical CHS-treatment as preoperative preparations. We show that BPO-treatment significantly decreases the presence of *P.acnes* after preoperative preparation and the result remains after 120 minutes. To our knowledge only one other study have investigated the effect of BPO-treatment on shoulders undergoing surgery and presented a reduction of *P.acnes* compared to the untreated contralateral shoulder [24]. It is well-known that chlorhexidine does not eradicate *P.acnes* on the skin after surgical preparation [5, 10, 25], which is in concordance with present study.

We detected a very high proportion of detected *P.acnes* both at the investigated shoulder (38/40) as well as in the control shoulder (37/40). In other studies on shoulders this detection varies between 42-76% [7, 18, 23]. The fact that we used healthy volunteers is hardly a sufficient explanation. Neither gender nor age appear to differ compared to earlier studies. A more likely explanation is the method used. Factors that might effect the results are the swabbed area, the pressure applied on the swab, duration and frequency, which may make comparisons difficult. Skin – treated or even untreated - can be difficult to culture *P.acnes* from, because of its preference to grow deep into the skin. Therefore, prior to this study, we performed a small pilot study where we compared different methods. The pilot study resulted in the choice of procedure with skin- swab that we used in the present study.

It is sometimes stated that *P.acnes* is more prevalent in men [5, 13, 19] something that was not confirmed in our study. This statement may reside on the indirect observation that deep

postoperative infection with *P.acnes* is more often found in the male population [26, 29], whereas other studies using swabs show no gender difference [18, 23]

Dermatological studies indicate that the rapid effect of BPO [4, 14] makes a two day preparation sufficient in reducing *P.acnes* also minimizing side effect such as redness, dry and scaly skin. These side effects appear in the beginning [14, 27] of treatment and may be a drawback in general treatment with BPO in conjunction with shoulder surgery.

Interestingly there was no difference in the prevalence of *P.acnes* in the CHS- group before skin preparation until the swab taken after two hours (Figure 1b), while there was a significant reduction in the BPO-group (Figure 1a). Since a risk factor for surgical site infection is duration of surgery [2, 22, 28], it appears troublesome that the surgical field has the same amount of *P.acnes* as an unprepared shoulder.

To decrease confounding by external bacterial seeding, it must be emphasized that the sampling was performed under as surgery like conditions as possible in an operation room with state-of-the-art laminar air flow and sterile draping. Also subject compliance to assigned treatment was 100%.

There are limitations to our study. Using healthy volunteers may not reflect the anticipated response to BPO in patients – presumably older and with co-morbidities - undergoing shoulder surgery. These may have a different bacterial flora and response to BPO. Furthermore one may anticipate that there is a correlation between *P. acnes* on the skin from swabs and in the deeper layers but that has not to our knowledge been shown; reduction of the latter probably being clinically important. A larger study population could have shown

differences in the CHS-group, but our findings on this subject are consistent with those of other studies [9, 15, 20, 23, 25]. Quantification of colonizing bacteria on the skin pre-operatively has often been used as a marker for risk of post-operative infection, but how well it really corresponds to risk for infections for different bacterial species is not so well studied.

Conclusion

In summary, this non-surgical case study, shows that there is a significant difference between the BPO and CHS group immediately after surgical preparation and that the results remained after 120 minutes. The skin swabs give micro biotic data of the skin, if that has any correlation to SSI we do not know. The most likely explanation is that BPO affects the re-emergence of *P.acnes* from deeper layers and thereby decreases recolonization of the skin. Given this evidence for the effect of BPO on the skin after surgical preparation and over time, topical preparation with BPO before shoulder surgery may be effective in reducing *P.acnes* on the skin and prevent recolonization.

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Figure legends

Figure 1. Skin swabs were analyzed from the treated left shoulder and presence of *P.acnes* (yes or no) was detected. **1a:** BPO-group (n=20). **1b:** CHS-group (n=20). Time of sampling, see Table 1.

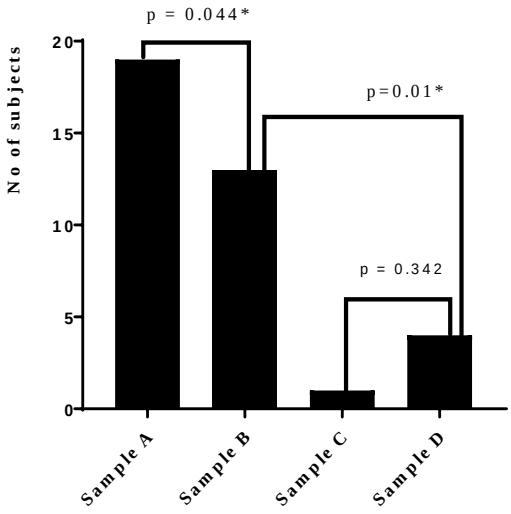
*statistically significant.

Figure 2 Skin swabs were analyzed from left shoulder and presence of *P.acnes* (yes or no) was detected in BPO –treated group n = 20, compared with CHS-treated group, n = 20. Time of sampling, see Table 1.

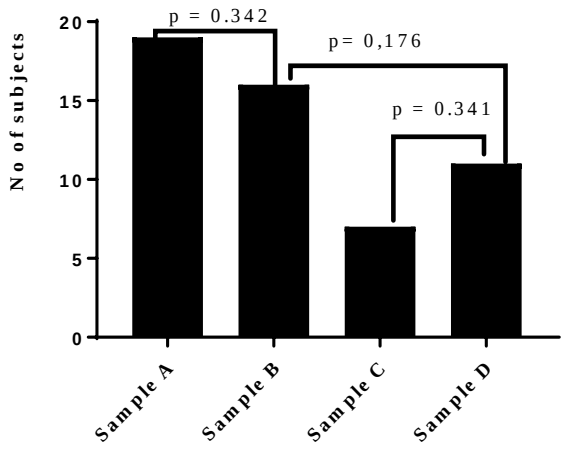
*statistically significant.

P.acnes reduction with skin preparation

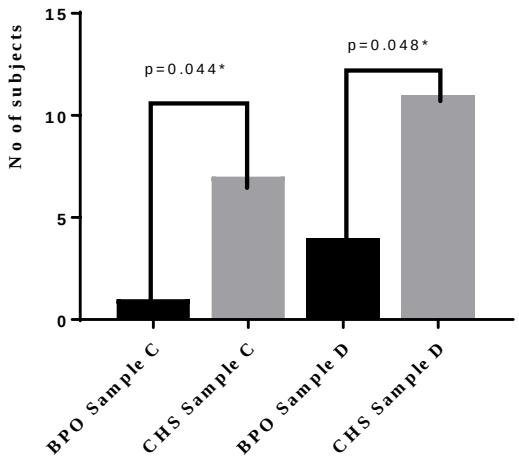
1a. BPO group



1b. CHS group



2. Presence of *P.acnes* between groups



***P.acnes* reduction with skin preparation**

Table 1. Flow chart of skin swab

Sample	Time
A	Before treatment, one week before trial day
B	Trial day, after topical treatment at home
C	After surgical preparation and sterile draping
D	120 min after surgical preparation and sterile drape
Control	Trial day, right shoulder, not treated

Table 2. Grouping of colony forming units (CFU).

Group	0	1	2	3	4
CFU	0	1-15	16-100	>100<1000	>1000