

Staphylococcus aureus in Acne Pathogenesis: A Case-Control Study

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Abstract

Background: There is considerable evidence which suggests a possible pathogenetic role for *Staphylococcus aureus* (*S. aureus*) in acne vulgaris. **Aim:** The study was to determine *S. aureus* colonization and antibiotic susceptibility patterns in patients with acne and of healthy people. **Materials and Methods:** In the case-control study, a total of 324 people were screened for nasal carriage of *S. aureus*: 166 acne patients and 158 healthy persons. One control subject was individually matched to one case. Nasal swabs from anterior nares of individuals were cultured and identified as *S. aureus*. Antibiotic sensitivity was performed with recognized laboratory techniques. **Results:** *S. aureus* was detected in 21.7% of the subjects in acne, and in 26.6% of control groups. There was no statistical difference in colonization rates between two groups ($P=0.3$). In patient group, most of *S. aureus* isolates were resistant to doxycycline and tetracycline ($P=0.001$), and were more sensitive to rifampicin compared to other drugs. In control samples, the isolated demonstrated higher resistance to cotrimoxazole compared to patient samples ($P=0.0001$). There was no difference between groups regarding resistance to rifampicin, vancomycin, methicillin, and oxacillin. **Conclusion:** It is still unclear whether *S. aureus* is actually a causal agent in the pathogenesis of acne. Based on microbiological data of both healthy and acne-affected persons, we propose that contribution of *S. aureus* in acne pathogenesis is controversial.

Keywords: Acne, Antibiotic resistance, *S. aureus*

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Introduction

Acne vulgaris is the most common disorder of human skin that affects up to 80% of adolescents and young adults in their lives.^[1] Several studies suggest that the emotional impact of acne is comparable with disabling diseases, such as diabetes and epilepsy.^[2] The social and psychological impacts of acne are sometimes so complicated that they cause serious problems in patients' self-esteem and socialization.^[3] In conjunction with the considerable personal burden, it also accounts

for substantial health care burden.^[2] The development of acne is a multifactorial process involving both endogenous and exogenous factors,^[4] including excessive sebum secretion, ductal hypercornification, and changes in the microbial flora especially colonization with *Propionibacterium acnes* (*P. acnes*).^[5] Antibiotic therapy has been integral to the management of acne for many years. The widespread use of antibiotics has unfortunately led to the emergence of resistant bacteria.^[6] In addition, changing patterns of antibiotic sensitivity and the emergence of more virulent pathogens, such as community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA), have led to marked changes in how clinicians use antibiotics in clinical practice.^[7]

There is significant *in vitro* evidence suggesting a possible pathogenetic role for *S. aureus* in acne vulgaris. This is in contrast to some studies which implicated both *S. epidermidis* and *P. acnes* as bacteria-causing acne

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vulgaris.^[5] *S. aureus* is the most common nosocomial pathogen,^[8] with mortality rates ranging from 6% to 40%.^[9] It is a pathogen of more concern because of its ability to cause a various array of life-threatening infections and its capacity to adapt fast to the different environmental conditions.^[10] The organism is normally present in the nasal vestibule of about 35% of apparently healthy individuals.^[11] One cross-sectional study of patients who were undergoing evaluation for acne, showed that 43% participants were colonized with *S. aureus*.^[12]

Considering to development of a resistance in microorganisms causing acne to antibiotics and the differences in species and strains of the microorganisms in different areas, this study was undertaken to delineate the frequency of *S. aureus* colonization among patients with acne and to clarify the antibiotic susceptibility patterns in patients suffering from acne and healthy individuals.

Materials and Methods

This case-control study was conducted during 6 months from March to August 2009, in university hospitals in Isfahan, Iran. Ethical approval was taken from the ethical committee of Isfahan University of Medical Sciences. Written informed consent was obtained from the participants. Subjects in the case group were 166 acne patients referred to clinic of dermatology, between 18 and 30 years. The control subjects were 158 people with no acne, coming for a dermatologic consultation except for acne and none of them were not on any treatment for acne in last medical history. The study samples were consecutively selected from the case and control groups. Control participants were matching in sex, age, and ward location with the acne patients. The participants in both cohorts were not on any antibiotic for at least 6 weeks, and none of them had nasal abnormalities and chronic diseases. Patients were examined for the presence of acne by a dermatologist according to Global Acne Grading System (GAGS). Score of 1-18 was considered as mild acne, 19-30 as moderate, 31-38 as severe, and above 39 as very severe.^[13] Exclusion criteria for the patient group were as follows: other skin diseases associated with acne, treatment with immunosuppressive agents, and diagnosed psychiatric disease.

At the end, a total of 324 volunteers were enrolled in a cohort, and screened for nasal carriage of *S. aureus*. The nasal specimens from anterior nares of the individuals were collected using labeled sterile cotton wool swabs. All swabs were obtained by one of the two investigators with use of a standard method and were taken to the laboratory within 2 hours of collection. Each of all the

swab samples was inoculated directly onto sterilized blood agar plate and incubated at 37°C for 24 hours. The isolates were identified as *S. aureus* based on colony morphology, Gram stain, catalase test, coagulase test, DNase test, and mannitol salt agar fermentation.

Susceptibility to antibiotics was assessed by the disc diffusion method, as recommended by the Clinical Laboratory Standards Institute (CLSI), formerly National Committee for Clinical Laboratory Standards.^[14] The panel of antibiotic used in sensitivity tests included the following: oxacillin, erythromycin, tetracycline, doxycycline, clindamycin, rifampicin, cotrimoxazole, methicillin, and vancomycin. The susceptibility was performed on Mueller-Hinton agar (MHA). The strain's suspension was matched with 0.5 McFarland standards to give a resultant concentration of 1.5×10^8 CFU/mL (colony-forming unit per milliliter).

Statistics

Data gathered were analyzed using Chi-Square and Mann-Whitney tests and through Statistical Package for the Social Sciences (SPSS) software version 15.0 with considering *P* value of <0.05 as statistically significant.

Results

We carried out a matched case control study. Cases and controls were recruited from university hospitals in Isfahan, Iran. Since the study based on voluntary participation, it was completed with 166 participants in patient group and 158 participants in control group. The mean ages of the subjects were 22 ± 3.8 years and 24 ± 3.2 years in patient and unaffected groups ($P=0.43$). Based on acne severity classification, severe acne had the highest frequency in the patient group.

A total of 76 of the 324 participants (23%) were colonized with *S. aureus*. It was detected in 36 (21.7%) of the subjects in the acne group and in 42 (26.6%) of the control group [Table 1]. There was no statistical difference in *S. aureus* colonization rates between acne patients and healthy controls (OR 0.8; 95% CI, 0.6–1.1; $P = 0.3$).

The sensitivity of *S. aureus* isolates to the tested antibiotics is shown in Table 1. In the patient group, most of *S. aureus* isolates were resistant to doxycycline and tetracycline (72% and 69%) ($P = 0.001$), and were more sensitive to rifampicin compared to other drugs (89%). In control samples, the isolated demonstrated higher resistance to cotrimoxazole compared to patient samples ($P=0.0001$). There was no difference between two groups regarding resistance to rifampicin, vancomycin, methicillin, and oxacillin ($P > 0.05$).

Table 1. Antibiotic susceptibility of *Staphylococcus aureus* isolates from volunteers in the two groups

Antibiotic	Patient group (N = 166)n (%)			Control group (N = 158)n (%)			P value
	S	I	R	S	I	R	
Rifampicin	32 (88.9)	0	4 (11.1)	39 (92.9)	0	3 (7.1)	NS
Vancomycin	31 (86.1)	4 (11.1)	1 (2.8)	42 (100)	0	0	NS
Cotrimoxazole	30 (83.3)	2 (5.5)	4 (11.1)	18 (42.9)	10 (23.8)	14 (33.3)	0.0001
Methicillin	25 (69.4)	4 (11.1)	7 (19.4)	33 (78.6)	4 (9.5)	5 (11.9)	NS
Clindamycin	22 (61.1)	0	14 (38.9)	40 (95.2)	0	2 (4.8)	0.001
Erythromycin	21 (58.3)	1 (2.8)	14 (38.9)	33 (78.6)	0	9 (21.4)	0.04
Oxacillin	16 (44.4)	4 (11.1)	16 (44.4)	20 (47.6)	8 (19.1)	14 (33.3)	NS
Tetracycline	11 (30.6)	0	25 (69.4)	32 (76.2)	0	10 (23.8)	0.001
Doxycycline	10 (27.8)	0	26 (72.2)	36 (85.7)	0	6 (14.3)	0.001

S: Sensitive; I: Intermediate; R: Resistant, NS: Not significant

Discussion

Acne is a multifactorial disease of as yet incompletely elucidated etiology and pathogenesis.^[15] A microbial etiology of acne has been suggested since the beginning of the last century.^[16] Elucidating the ambiguous determinants of this phenomenon is of major public health interest. As a first step towards understanding the microbial etiology of acne, we have assessed *S. aureus* colonization and antibiotic resistance in acne patients.

The results of the present study showed an overall prevalence of 21.7% of *S. aureus* in acne patients and 26.6% in healthy persons. Carrying *S. aureus* in nares was shown in various studies performed in different countries among healthy individuals; 23.4% in Malaysia, 33.3% in Nigeria, 26.5% in Tabriz, and 40% in Jordan.^[17] In this respect, Fanelli *et al.* also determined the frequency of *S. aureus* colonization among patients with acne. They reported that 25% of patients had *S. aureus* solely in their nose; and 19% had *S. aureus* in both their nose and their throat.^[12] In addition, one *in vitro* study performed in acne vulgaris found that in aerobic culture of skin lesions, *S. aureus* was present in 41% of subjects, and in anaerobic bacterial culture, *S. aureus* was present in 39% of subjects.^[5] The comparison of results shows that it is still unclear whether *S. aureus* is actually a causal agent in the pathogenesis of acne. Based on a review of the microbiological data of both healthy and acne-affected persons, we propose that *S. aureus* has no role in acne pathogenesis. Nevertheless, the findings of the present study suggest that *S. aureus* colonizations in patients and healthy populations can be a potential source of infections. It is notable that asymptomatic colonization can persist for months to years,^[18] therefore effective strategies to prevent *S. aureus* infections are urgently needed.^[19]

In the last part of current study, antibiotic susceptibility patterns showed that most of *S. aureus* isolates were resistant to doxycycline and tetracycline in acne group.

Since these antibiotic agents previously used to treat acne, the results indicate that the widespread use of antibiotics can lead to antimicrobial resistance with serious problems not limited to *P. acnes*, but also to other bacterial species.^[20] The choice of antibacterial should take into account the severity of the acne, cost-effectiveness, benefit-risk ratios, and the potential for the development of resistance.^[21] The treatment options in acne are far from ideal,^[22] therefore the improved understanding of acne pathogenesis should lead to a logical therapy to successfully treat this skin disease. Moreover, the results of the study demonstrated that rifampicin was the most sensitive antibiotic for acne vulgaris, which is consistent to reports by some other investigators.^[5] On the basis of these results, we propose that rifampicin can be a suitable antibiotic for acne, but to achieve a better treatment, a combination of rifampicin with other antibiotic drugs may be more efficient. (We mentioned and referred that in some studies rifampicin was the most sensitive antibiotic for acne).

Limitations of the present study were small sample size and very little published evidence. It is noteworthy to mention that present survey may be affected by selection bias because our sampling framework was limited to specific setting with specific aim. Further comprehensive research with larger population should be considered to fully define the potential role of *S. aureus* in acne pathogenesis, until the results can be generalized more accurately.

Conclusions

Based on our results we propose that contribution of *S. aureus* in acne pathogenesis is controversial. In fact, this hypothesis should be investigated by future investigations. We believe that because of changeable drug-sensitivity of bacterial strains, it seems important to perform assessment of bacterial flora and antibiotic susceptibility of isolates in acne cases, especially in clinically severe and resistant to treat. Beside the presence

of resistant strains of *S. aureus* to various antibiotics in this study emphasizes the need to discourage antibiotics' abuse and the implementation strategies for elimination of carriage of *S. aureus*.

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