Original Article

The Isolated and Investigated Results of In Vitro Resistance to Antibiotic of *Propionibacterium acnes* in Acne Patients Using Topical Corticosteroids

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Background: Acne is an inflammation of the hair follicle and sebaceous gland. In fact, when having acnes, patients often treat themselves by various methods. In particular, abuse of topical corticosteroids is a very common problem today. This results in clinical cases, especially the increase in bacterial, superficial infection and bacterial resistance, which should be taken into account.

Objective: To identify the infection proportion of *Propionibacterium acnes* (*P. acnes*) distributed according to the characteristics of acne patients using topical corticosteroids and the antibiotic resistance rate of *P. acnes* in these patients in Can Tho Dermatology Hospital.

Materials and Methods: An analytical, cross-sectional descriptive study of 90 acne patients using topical corticosteroids who came to Can Tho Dermatology Hospital from April 2015 to October 2016.

Results: The overall rate of *P. acnes* that was isolated from acne patients using topical corticosteroids: 38.9%. In which, comedones (25.7%), cystic nodules (11.4%) and pustules (48.6%). Acne levels mainly were moderate (45.7%) and severe (35.3%). This was mostly concentrated in patients with sensitive skin (60%). The antibiotic resistance rate of *P. acnes*: Tetracycline (100%), Levofloxacin (65.7%), Erythromycin (91.4%), Trimethoprim/Sulfamethoxazole (94.3%), Cefuroxime (54.3%) in which, the resistance to more than 3 antibiotics was 54.3%.

Conclusion: The *P. acnes* rate isolated from acne patients using topical corticosteroids was 38.9%. The most common type of acne was pustules and this occurred mainly in patients with sensitive skin. Tetracycline, Erythromycin and Trimethoprim/Sulfamethoxazole (94.3%) were antibiotics with the highest resistance rate.

Keywords: Acne, Topical corticosteroid, *Propionibacterium acnes*, Antibiotic resistance

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Acne is an inflammation of the hair follicle and sebaceous gland. Acne treatment affects the stages of pathophysiology and depends on the degree of disease, skin properties, occupations, habits. In fact, when having acne, patients often treat themselves by various methods of which, self-treatment by inappropriate methods and the abuse of topical corticosteroids are common problems today especially in some developing Asian countries. In Vietnam, people in rural areas do not have adequate knowledge for using drugs to cure diseases in general and treat acne in particular. The overuse of antibiotics, which may be responsible for the development of drug-resistant bacteria, or the abuse of topical corticosteroids in self-treatment, is a very common reality currently. The problem can affect the clinical situation and become more complex and cause drawbacks to acne treatment[1,2].

In 2008, the authors had made a survey about self-using topical corticosteroid for treating acne. The results were remarkable with nearly 90% of patients using many kinds of topical corticosteroid before going to the clinicians. Betamethasone dipropionate was the most common with 51%. Moreover, in rural areas of the north of Vietnam, many people even combined lots of substances in one cream without the prescription of the doctors, including dexamethasone and acid acetylsalicylic.

Can Tho Dermatology Hospital is a specialized hospital in the Mekong Delta. The number of patients with acne has been increasing and the treatment is often difficult, especially with those suffering from topical corticosteroids overusing. Therefore, the implementation of the topic is really necessary. The topic aims at two objectives: (1) Identify the infection rate of *P. acnes* distributed according to the characteristics of acne patients using topical corticosteroids in Can Tho Dermatology Hospital; (2) Identify the antibiotic

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resistance rate of *P. acnes* in acne patients using topical corticosteroids in Can Tho Dermatology Hospital.

Materials and Methods

Subjects

Ninety acne patients using topical corticosteroids came to Can Tho Dermatology Hospital from April 2015 to October 2016. Acne lesions are divided into inflammatory and non-inflammatory lesions. (1) The inflammatory lesions consisted of red papules, pustules, nodules and cysts. (2) The non-inflammatory lesions consist of open comedones (blackheads) and closed comedones (whiteheads). These kinds of lesions usually distribute at face, chest and back[3].

The authors divided these patients into 4 acne levels base on the studies of Hayashi in 2008 and Tutakne in 2003. With the Hayashi study, severe acne levels were categorized into 4 levels by the number of inflammatory lesions: 0 to 5 lesions (mild); 6 to 20 lesions (average); 21 to 50 lesions (severe); over 50 lesions (very severe)[4]. With the Tutakne study, severe acne levels were categorized into 4 levels by the type of lesions: papules or comedones with whiteheads and blackheads (mild); the mild lesions and pustules (average); the mild lesions, pustules and abscesses (severe); the mild lesions, pustules, abscesses and cysts (very severe)[5].

Methods

The present study was designed cross-sectional descriptive and analytic. The authors collected the sample conveniently at Can Tho Dermatology Hospital from April 2015 to October 2016 following three steps:

(1) Interviews: Direct interviews with patients according to the prepared data collection form which included age, gender, occupation, location, chief complaint, medical history, used cosmetic, and some factors related to acne patients who used and unused corticosteroid (e.g. habits, knowledge,…).

(2) Clinical examination: to define clinical characteristics included types of lesions, distributed area, severe levels.

(3) Testing technique for *P. acnes*: The fluid from the lesions of acne was extract in the process of examination. Then, it was immediately transmitted to the laboratory of Can Tho Dermatology Hospital within 2 hours to do the isolation and in vitro investigation to determine the resistance of *P. acnes* to some antibiotics consisted of Tetracycline, Levofloxacin, Erythromycin, Trimethoprim/Sulfamethoxazole, Cefuroxime.

The data collected were analyzed by using SPSS for windows version 18.0 software.

Results

The P. acnes rate isolated from acne patients using topical corticosteroids

In 90 cases of acne patients, *P. acnes* was isolated from 38.9% cases as shown in Table 1. In fact, they used lots of kinds of acne treating cream for a few months, but they did not completely cure the acne. After that, they changed to the cream which contained corticosteroid. By using this drug, their acne situation got better in a very short time (only few weeks). However, after one or two months using it, the inflammatory acne erupted and became even worse than before. According to the study of Momin in 2010, using topical steroid increased the concentration level of free fatty acids. Then, the number of bacteria would raise in the hair follicle[6].

The P. acnes rate distributed according to diagnosis

Through the isolation, pustules were the most common kind of acne and have the highest rate of *P. acnes* with 48.6%. Meanwhile, cystic nodules have the lowest rate as shown in Table 2.

The P. acnes rate distributed according to acne level

Nearly a half of patients were at the moderate level of acne and the distributed rate of P. acnes also accounted for the highest at this level with 45.7% as shown in Table 3. The second position belong to the severe level (35.3%). This result also correlated with the *P.acnes* rate isolated from the type of acne lesions above.

The P. acnes rate distributed according to skin sensitivity

As shown in Table 4, the majority of *P. acnes* rate was isolated from patients with sensitive skin (60%). Based

Table 1. The general rate *P. acnes* isolated

The general rate of *P. acnes*	n (%)
Yes	35 (38.9)
No	55 (61.1)
Total	90 (100)

Table 2. The *P. acnes* rate distributed according to diagnosis (n = 35)

Distribution according to diagnosis	n (%)
Comedones	9 (25.7)
Pustules	17 (48.6)
Cystic nodules	4 (11.4)
Other	5 (14.3)
Total	35 (100)

Table 3. The *P. acnes* rate distributed according to acne level

Distribution according to acne level	n (%)
Mild	6 (17.1)
Moderate	16 (45.7)
Severe	12 (35.3)
Very severe	1 (2.9)
Total	35 (100)

on the explanation of Baumann Leslie, many studies proved that on the surface of our skin had two significant substances (LL-37 and α-defensin) that could help maintain a healthy state of the skin, but also supported the ability of bacteria inactivation. However, topical corticosteroids could inhibit the production of these substances and made our skin become sensitive[7].

The antibiotic resistance rate of P. acnes on acne patients with topical corticosteroids

The antibiotic resistance rate of P. acnes

In the past, Tetracycline and Erythromycin used to be the main antibiotics for acne treatment. In present study, it was showed that 100% and 91.4% cases resisted to Tetracycline and Erythromycin, respectively. The antibiotic that had been the most effective for *P. acnes* with the lowest rate of resistance was Cefuroxime (54.3%) as shown in Table 5.

The resistance rate of P. acnes with several antibiotics

The resistance rate of *P. acnes* to 2 antibiotics was 45.7%, the majority of resistance rate was to ≥3 antibiotics with 54.3% as shown in Table 6.

Discussion

The P. acnes rate isolated from acne patients with topical corticosteroids

Results showed that in 90 cases of acne patients, 35 (38.9%) cases contained *P. acnes*. This result was comparable to that of Hassanzadehet et al, (2008), who investigated the bacterial infection rate in 100 acne patients aged 18 to 24, which indicated 41% of *S. aureus* infections, 53% *S. epidermidis* and 33% *P. acnes* infection[8]. Similarly, Zandi et al isolated from 92 acne patients 41 cases of *P. acnes*, 32 cases of *S. epidermidis* infection and 5 cases of *S. aureus* infection[9].

Dhillon and Varshney isolated superinfection bacteria from 50 acne patients with clinical signs of cystic nodules or pustules and showed 45% *S. aureus* infection, 49% *S. epiderrmidis* infection, 41% *P. acnes* infection[10]. About the distribution of *P. acnes* rate according to diagnosis, the *P. acnes* rate isolated comedones (25.7%), cystic nodules (11.4%) and pustules (48.6%). The results also showed that the *P. acnes* rate distributed on acne patients was concentrated at moderate (45.7%) and severe levels (35.3%). Similar to some previous studies, Keisuke Nakase et al, in a study of antibiotic resistance of *P. acnes* from comedone lesions from a University Hospital in Japan from 2009 to 2010. The study investigated the relationship between bacterial antibiotic resistance and acne severity. Results showed that in 69 cases, the rate isolated was 18.8%. The resistance rate to Tetracycline was 4.3% (3/69)[11].

The antibiotic resistance rate of P. acnes on acne patients with topical corticosteroids

The antibiotic resistance rate of *P. acnes* to Tetracycline (100%), Levofloxacin (65.7%), Erythromycin (91.4%), Trimethoprim/Sulfamethoxazole (94.3%), Cefuroxime (54.3%). Compared with some previous studies, the resistance rate of *P. acnes* with antibiotics tended to increase (from 20% in 1978, to 62% in 1996). Another study showed that the rate of bacteria resistant to erythromycin gel 2% was 87%. Leyden J., the resistance of *P. acnes* to erythromycin 51%, clindamycin 42%[12].

Dhillon and Varshney (2013) isolated superinfection bacteria from 50 acne patients with clinical signs of cystic nodules or pustules and showed 45% *S. aureus* infection, 49% *S. epiderrmidis* infection, 41% *P. acnes* infection. When antibiotic resistance was detected, 83% of bacteria resistant to Neomycin, 61% resistant to Kanamycin, 52% resistant to Erythromycin, 50% resistant to Cephalothin, Gentamicin and Clindamycin[10].

The research of Schafer F and Fich F in 2013 revealed that in 83 cases of acne, the *P. acnes* rate isolated was 80 (96%) and 27 cases were resistant to antibiotics (33.7%) of which, 26.3% Trimethoprim/Sulfamethoxazole, 12.5% Erythromycin, and 7.5% Clindamycin. Resistance to Erythromycin and Clindamycin were due to the effect of topical antibiotic use[13].

To explain why topical corticosteroid can cause resistance, the study about adverse effects of topical

Table 4. The *P. acnes* rate distributed according to skin sensitivity

Distribution according to skin sensitivity	n (%)
Yes	21 (60)
No	14 (40)
Total	35 (100)

Table 5. The antibiotic resistance rate of *P. acnes*

Antibiotic	Sensitive (S) n (%)	Resistant (R) n (%)	Intermediate (I) n (%)
Tetracycline	0 (0)	35 (100)	0 (0)
Levofloxacin	9 (25.7)	3 (65.7)	3 (8.6)
Erythromycin	1 (2.9)	32 (91.4)	2 (5.7)
Trimethoprim/Sulfamethoxazole	2 (5.7)	33 (94.3)	0 (0)
Cefuroxime	11 (31.4)	19 (54.3)	5 (14.3)

Table 6. The resistance rate of *P. acnes* with several antibiotics

Antibiotics	n (%)
1 antibiotic	0 (0)
2 antibiotics	16 (45.7)
≥3 antibiotics	19 (54.3)
Total	35 (100)

corticosteroids showed the potential to inhibit the replication of genes coding as good peptides, which could work against normal skin infections[14].

Conclusion

The results of research on 90 acne patients with topical corticosteroid using in Can Tho Dermatology Hospital from April 2015 to October 2016 showed that the *P. acnes* isolation rate for acne patients with topical corticosteroids was 38.9%. of which, comedones (25.7%), cystic nodules (11.4%), pustules (48.6%), moderate (45.7%), severe, (35.3%), sensitive skin (60%). In addition, the antibiotic resistance rate of *P. acnes* to Tetracycline (100%), Levofloxacin (65.7%), Erythromycin (91.4%), Trimethoprim/Sulfamethoxazole (94.3%), Cefuroxime (54.3%). The *P. acnes* rate resistant to ≥3 antibiotics accounted for the majority 54.3%, mostly in female patients, ≥25 years old, severe and very severe acne, patients treated with antibiotics previously.

The present study results could help the clinical dermatologist in choosing antibiotics for acne treatment especially in some developing Asian countries. In addition, not only the dermatologist but also other clinical physician should give adequate advice on antibiotics used to prevent the increasing trend of antibiotics resistance.

What is already known on this topic?

Generally, *Propionibacterium acnes* was one of the main factors of acne occurring. In most of the acne treatment guidelines, oral antibiotics still played an important role and had been used for a long time. Limiting the use of antibiotics and monitoring the resistance to antibiotics were always of the most concern in clinical treatment. In dermatology, many researches about the situation of antibiotics resistance of *P. acnes* have been initiated almost every year.

What this study adds?

With the use of nourishing creams which contain corticosteroid by Asians in general and Vietnamese in particular, treating acne eruption in these people would be extremely challenging. The present study revealed that acne occurred in these patients usually at the moderate to severe levels. Moreover, the skin would become more sensitive, so the clinicians must consider carefully in choosing the appropriate topical cream supporting the acne treatment. Finally, the antibiotics resistance of patients using topical corticosteroid before were at a high rate, even 100% with the Tetracycline group while they had been using it in treating acne because of its antibacterial and anti-inflammation effectiveness. The other popular antibiotic groups also had a high resistance rate.

Potential conflicts of interest

The authors declare no conflicts of interest.

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