

ORAL ANTIBIOTICS IN ACNE VULGARIS: THERAPEUTIC RESPONSE OVER 5 YEARS

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ABSTRACT

Introduction: Antibiotic resistant *P. acnes* have influenced acne therapy worldwide resulting in increased use of topical and systemic retinoids. Judicious use of oral antibiotic is important for effective therapeutic outcome.

Objectives: To determine the response and side effects of oral antibiotic treatment in acne vulgaris. To determine the type of antibiotic used, therapy duration and the types of concomitant topical therapy.

Methods: Retrospective analysis of the therapeutic response to oral antibiotics therapy in acne vulgaris in the Dermatology Department, Hospital Kuala Lumpur. New cases of acne vulgaris from 2005 to 2009 were randomly selected. The clinical notes of 250 patients treated with oral antibiotics were reviewed.

Results: About 60% of patients achieved good to excellent response to therapy while satisfactory response was seen in 26%. Only 8% patients experienced minor side effects. Doxycycline was the most frequently prescribed antibiotic, followed by tetracycline and erythromycin ethylsuccinate. The prescribing pattern was consistent over the years. The mean duration of treatment is four to five months. Oral antibiotic was augmented with topical therapy in 98.8% of patients.

Conclusion: Good to excellent therapeutic response was achieved in the majority of patients and results observed have remained stable over the last five years.

Keywords: Antibiotics, acne vulgaris.

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INTRODUCTION

Acne has been called the bane of youth. A common condition affecting adolescents, its prevalence varies in different countries. 45 million people in the United States,¹ 52.2% of a community studied in Hong Kong,² and 67.5% of secondary school students in Muar, Malaysia,³ are affected by acne vulgaris. Pathogenesis of acne is the interplay between follicular epithelial hyperproliferation with resultant follicular plugging, excessive sebum production, inflammation, and *Propionibacterium acnes* (*P. acnes*) activity. Microcomedones are the precursor of acne lesions. Implicated in its formation are the androgen hormones, the enzyme 5 α -reductase type 1, alterations in follicular linoleic acid levels and interleukin 1 α .⁴ The growth of *P. acnes* in microcomedones is facilitated by presence of excessive sebum. *P. acnes* exaggerates abnormal follicular desquamation, produces chemokines, activates toll like receptor 2 on inflammatory cells, activates complement C5a production and stimulate macrophages to release IL-8 and TNF- α .⁵ The resultant inflammation manifests clinically as pustules, papules, nodules or cysts.

Acne vulgaris is treated according to clinical severity aiming to prevent physical and psychological scarring. Topical therapies include antibacterial, anti-inflammatory, comedolytics, retinoids and antibiotic formulations. Systemic antibiotics are indicated for moderate to severe acne and treatment resistant inflammatory acne.⁶ However, widespread and prolonged use has led to development of antibiotic resistant *P. acnes*. In Europe, prevalence ranges from 51% to 94%.⁷ Resistance is highest to clindamycin and erythromycin, followed by tetracycline. Similar results were observed by Coates *et al.*⁸ in the United Kingdom. In addition, antibiotic resistant *P. acnes* were demonstrated to be on the rising trend from 34.5% in 1991 to 94% in 1997 and 55.5% in 2000. In Singapore, the overall resistance rate was 14.9%.³ Erythromycin accounted for 69.2%, followed by clindamycin 50%, co-trimoxazole 38.5%, doxycycline 23% and tetracycline 11.5%.³

Since late 1990s, antibiotic resistant *P. acnes* has influenced acne therapy. Analysis of the trends in prescription of acne medications in the United States from 1990 to 2000 by

Thevarajah *et al.*⁹ showed a shift towards non-antibiotic treatment with increased use of topical and systemic retinoids. In the United Kingdom, antibiotic prescription declined by 33% from 1995 to 2000.¹⁰ The rising rates of antibiotic resistance *P. acnes* may be curbed if management guidelines^{6,11} are adhered to. We aimed to analyze the therapeutic response of oral antibiotic treatment in our acne vulgaris patients, and the prescribing practices in the Dermatology Clinic, Hospital Kuala Lumpur.

METHODS

This is a retrospective analysis of the therapeutic response of oral antibiotic treatment in acne vulgaris in the Dermatology Department, Hospital Kuala Lumpur from 2005 to 2009. Primary objectives were to determine the response and side effects to therapy. Secondary objectives were to determine the frequency and duration of each oral antibiotic treatment, and to determine the types of concomitant therapy prescribed. Inclusion criteria were: treatment of acne vulgaris included oral antibiotics and patient's treatment record is available and complete. Patients whose treatment does not include oral antibiotics were excluded.

New cases of acne vulgaris referred to our centre each year from 2005 to 2009 were identified using the Dermatology Department Database. The clinical notes were randomly

selected using computer generated random numbers. The first 50 records for each year that met the inclusion criteria were selected for analysis. Severity of acne was graded as mild, moderate or severe according to the Consensus Conference on Acne Classification.¹² Response to therapy was based on physician's global assessment (PGA): none (<25%), satisfactory (25-50%), good (50-75%) and excellent (75%).

Statistical analysis

Descriptive statistical analyses were conducted using the statistical software SPSS version 16.0. Non-parametric tests used for confirmatory data analysis were Chi-square test for independence and Kruskal-Wallis test.

RESULTS

A total of 32,689 patients with acne vulgaris were seen in our centre from 2005 to 2009. Two hundred and fifty patients with acne vulgaris who received oral antibiotic treatment were included in our analyses. The patients' demographics and characteristics are shown in Table 1. Our patients are mainly young adult females who presented about three years after developing acne. Half of these patients had prior oral antibiotic treatment as the majority had moderately severe disease.

Doxycycline was the most frequently prescribed antibiotic. A small number of patients were treated with tetracycline or

Table 1: Socio-demographic and clinical characteristics of patients

Characteristics	Number (%)
Age at presentation, median years (range)	21 (12-62)
Age of onset, median years (range)	17 (10-41)
Gender: Male	97 (38.8)
Female	153 (61.2)
Ethnic: Malay	166 (66.4)
Chinese	45 (18)
Indian	35 (14)
Others	4 (1.6)
Duration of acne prior to presentation, median months (range)	36 (1-324)
Previous treatments: Oral antibiotics	136 (55)
Over the counter treatments	65 (26)
Traditional/herbal/alternative products	17 (7)
Oral isotretinoin	15 (6)
Beautician/beauty centers	7 (3)
No treatment	7 (3)
Severity of acne on presentation: Mild	23 (9)
Moderate	207 (83)
Severe	20 (8)
Major sites affected: Face only	126 (50.4)
Trunk only	6 (2.4)
Face and trunk	89 (35.6)

erythromycin ethsuccinate (erythromycin ES). The prescribing pattern has been consistent over the last five years (Figure 1).

The dosages of the most commonly prescribed antibiotics were: doxycycline 100 mg twice daily, tetracycline 500 mg twice daily and erythromycin ES 400 mg twice daily.

Oral antibiotics therapy was augmented (in 98.8% of patients) with topical benzoyl peroxide, tretinoin, sulphur in calamine and adapalene (Table 2). Eight (1.2%) patients were not prescribed concomitant topical therapy. The median duration of treatment was four to five months. There was no significant difference in the duration of therapy between the consecutive years, $p=0.533$.

Table 2: Concomitant topical treatment prescribed for acne vulgaris

Type of treatment	Number (%)
Topical benzoyl peroxide	193 (77.2)
Topical tretinoin	176 (68.8)
Sulphur in calamine lotion	69 (27.6)
Adapalene	4(1.6)

Figure 1: Oral antibiotic prescribing pattern for treatment of acne vulgaris

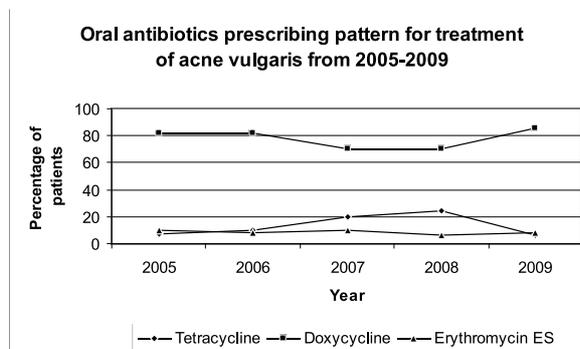
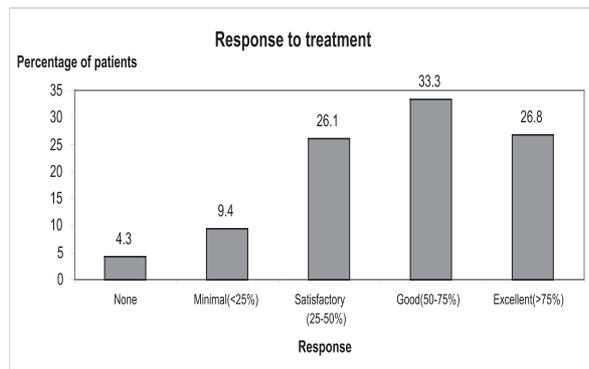


Figure 2: Overall therapeutic response to oral antibiotics



About 60% of patients achieved good to excellent response to therapy. In 26%, the response was satisfactory. A small number of patients responded minimally or none at all, Figure 2.

As the majority of patients were treated with doxycycline, treatment response to doxycycline was analyzed separately. Over the years, therapeutic response to doxycycline has remained stable, Figure 3. Comparison of minimal to satisfactory response with good to excellent response between each consecutive year was non-significant respectively.

8% of patients experienced minor side effects due to therapy. One patient developed exanthematous rash secondary to doxycycline while the others suffered minor gastrointestinal disturbances.

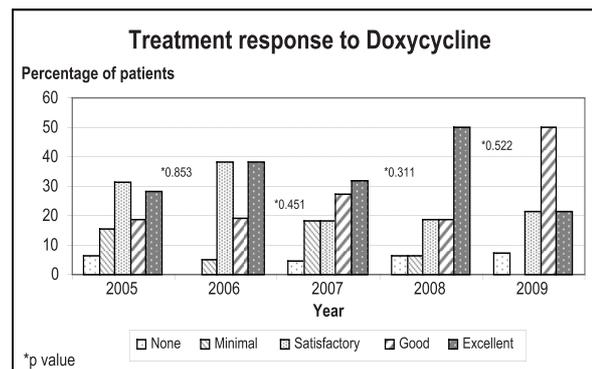
DISCUSSION

Antibiotic resistant *P. acnes* is currently a major issue influencing acne therapy. Selection of antibiotic and duration of therapy are major factors contributing to the emergence of resistance. There is currently no data on *P. acnes* resistance pattern or antibiotic therapeutic response in our country.

Our choice of antibiotic and therapy duration is in accordance with current management guidelines^{6,11} and the prescribing pattern has been consistent over the last five years. Doxycycline is the preferred first line oral antibiotic followed by tetracycline and erythromycin ES. Doxycycline has also been shown to be more effective in reducing *P. acnes* compared to tetracycline.¹³ In addition, doxycycline results in earlier clinical response.¹⁴ The use of erythromycin should be limited due to high resistance rates.^{8,15} In our centre, erythromycin is prescribed to patients contraindicated or intolerant to doxycycline or tetracycline.

The recommended duration of oral antibiotic therapy is a minimum of six to eight weeks and a maximum of 12 to 24 weeks.^{6,11} The mean duration of therapy in our patients ranged

Figure 3: Therapeutic response to oral doxycycline



from 16 to 20 weeks. Therapeutic response is assessed six to eight weeks after treatment is initiated.¹⁶ In patients whom satisfactory improvement is observed, therapy is continued for at least a further six to eight weeks. In cases of poor clinical response despite adequate compliance, oral antibiotic is substituted to a second line agent.^{16,17}

The majority of our patients (98.2%) were concomitantly treated with topical agents. Oral antibiotic therapy is best used in combination with a topical regimen that includes benzoyl peroxide and retinoid. Combination therapy improves efficacy and reduces bacterial resistance.^{18,19}

About 60% of our patients achieved good or excellent response and treatment was well tolerated. The therapeutic response observed with doxycycline over the years has remained stable with most of our patients achieving at least satisfactory response. The stability in response to therapy may suggest that antibiotic resistance rate in our patients is low. This needs to be confirmed further by *P. acnes* culture and sensitivity studies.

CONCLUSION

Awareness of local antibiotic therapeutic response and prescribing patterns is important due to increasing prevalence of antibiotic-resistant *P. acnes*. Strategies to minimize the potential for antibiotic resistance include judicious use of antibiotics and combination therapy. Studies are needed on local *P. acnes* resistant patterns to optimize the efficacy of our acne therapy.

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