

## **Anti-pruritic efficacies of doxycycline and erythromycin in the treatment of acne vulgaris: A randomized single-blinded pilot study**

Sir,

Pruritus is a significant symptom that is frequently experienced by patients with acne vulgaris and contributes significantly to patients' morbidity.<sup>1,2</sup> In our clinical experience, pruritus in acne

vulgaris can be effectively reduced with systemic antibiotics, such as doxycycline and erythromycin, which are commonly used as first-line systemic acne medications. However, it is not known if this effect results from a decrease in inflammation alone or if

there are additional anti-pruritic effects mediated by the antibiotics. A study on human keratinocytes demonstrated that tetracycline attenuates the protease-activated receptor 2 interleukin-8 axis in the modulation of proinflammatory responses.<sup>3</sup> This effect was not observed in the macrolides, including erythromycin and clarithromycin.<sup>4</sup> Because protease-activated receptor 2 has been shown by multiple studies to be an important itch receptor, doxycycline may possibly have a greater efficacy in relieving itch through the inhibition of protease-activated receptor 2, as compared to erythromycin.

The aim of this randomized single-blinded pilot trial was to evaluate the anti-pruritic efficacies of doxycycline and erythromycin in the treatment of acne vulgaris. Approval for the study was obtained from the National Healthcare Group Ethics Review Board and Health Sciences Authority, Singapore.

Patients with mild-to-moderate acne based on the Comprehensive Acne Severity Scale [Figures 1 and 2] and associated itch intensity of more than 2 on a 10-point numerical scale were recruited from the dermatology clinics at the National Skin Centre in Singapore.<sup>5</sup> Subjects were randomized to receive either oral doxycycline 100 mg daily or erythromycin 500 mg b.d. for 6 weeks. All subjects were instructed to stop the application of any topical agents during this period and to use the same type of mild cleanser (QV wash®) for facial washing up to a maximum of three times a day. At baseline and 6 weeks after treatment, an itch questionnaire was administered,<sup>6</sup> which included the average itch intensity over the prior 1 week on a 10-point numerical scale, frequency of itch (graded 1–7, ranging from 1 episode a month to more than 10 episodes daily) and itch quality-of-life assessment (16 questions, each graded 1–6 ranging from not affected to severely affected, giving a total score of 16–96). The severity of acne was also graded by a dermatologist blinded to the treatment arm (graded 0–5 on the Comprehensive Acne Severity Scale [Figure 3], from clear to very severe) at baseline and at 6 weeks. Analyses were performed on a per-protocol basis using the paired *t*-test (for within-group comparisons) and two-sample *t*-test (for between-groups comparisons).

Thirty-six subjects were recruited, of whom 29 completed the study and 7 were lost to follow-up. Of the 29 subjects, 14 received

erythromycin, while 15 received doxycycline. Both groups had comparable baseline characteristics [Table 1]. Grading of acne severity [Table 2] significantly improved in both groups ( $P < 0.01$ ), and there was no significant difference between the two treatment arms ( $P = 0.29$ ). Subjects in the doxycycline group experienced a significant reduction in itch intensity scores at 6 weeks ( $P = 0.03$ ) and this remained significant after adjusting for improvement in acne grading ( $P = 0.02$ ). The reduction in itch intensity scores was not statistically significant in the erythromycin group ( $P = 0.11$ ). Comparing the efficacies of doxycycline and erythromycin in reducing itch intensity scores, the difference was not statistically significant ( $P = 0.42$ ). The itch quality-of-life scores were significantly better in both groups ( $P = 0.03$ ), but the frequency of itch was not much different.

We were unable to find any previous reports of the anti-pruritic efficacies of systemic antibiotics in the treatment of acne. Doxycycline was found to significantly reduce pruritus in acne vulgaris and we postulate that in addition to a reduction in inflammation, attenuation of the protease-activated receptor 2 interleukin-8 pathway may contribute to this effect. A limitation of this study is the relatively high dropout rate (19%). Sample size is very small. Other factors like age of the patient, other comorbidities and general skin condition have not been taken into consideration.

In conclusion, our results revealed that doxycycline effectively reduces itch intensity in pruritic acne and this effect was independent of improvements in acne severity. Doxycycline may serve as a good antibiotic option for patients who experience itch in their acne lesions.

**Table 1: Baseline characteristics of 29 subjects who completed the study**

Oral antibiotics used	Doxycycline	Erythromycin
<i>n</i>	15	14
Male (%)	10 (67)	8 (57)
Age, median (range)	20 (16-24)	21 (16-38)
Baseline itch severity*, mean (SD)	4.9 (1.3)	5.5 (1.5)

\*Rated on a numerical rating scale of 0-10, with 0 being no itch and 10 representing the worst imaginable itch. SD: Standard deviation



**Figure 1:** Grade 2 (mild in severity) acne based on Comprehensive Acne Severity Scale. Easily recognizable, less than half affected area involved. Many comedones, papules and pustules



**Figure 2:** Grade 3 (moderate in severity) acne based on Comprehensive Acne Severity Scale. More than half affected area involved. Numerous comedones, papules and pustules

**Table 2: Differences in scores after 6 weeks treatments with doxycycline and erythromycin**

Grading of acne severity and itch scores	Doxycycline		Erythromycin	
	Score	P	Score	P
Improvement in facial acne severity grading* (SD)	1.1 (0.9)	<0.01	0.8 (0.1)	<0.01
Mean decrease in itch scores <sup>†</sup> (SD)	1.4 (2.3)	0.03	1.1 (2.6)	0.11
Mean decrease in itch scores after adjusting for improvement in acne severity grading (SE)	1.4 (0.6)	0.02	1.2 (0.6)	0.07
Reduction in itch frequency grading <sup>‡</sup> (SD)	0.3 (1.4)	0.37	0.3 (1.3)	0.41
Mean improvement in itch quality of life score <sup>§</sup> (SD)	13.8 (21.4)	0.03	13.9 (21.0)	0.03

\*CASS; graded 0-5, from clear to very severe. †Rated on a numerical rating scale of 0-10. ‡Graded from 1 to 7, ranging from 1 episode a month to >10 episodes daily. §Derived from a 16-item questionnaire, each graded on a scale of 1-6, giving a total score ranging from 16 to 96. SD: Standard deviation, SE: Standard error, CASS: Comprehensive Acne Severity Scale

**Figure 3: Acne quality-of-life questionnaire**

These questions concern the skin condition which has bothered you the most during the past week. On a scale of 0–6 (0 being never and 6 being frequent), during the past week, how often have you been bothered by:

- Your skin condition itching
- Your skin condition burning or stinging
- Your skin condition hurting
- Your skin condition being irritated
- The persistence/reoccurrence of your skin condition
- Worry about your skin condition (e.g., that it will spread, get worse, scar, unpredictable etc.)
- The appearance of your skin condition
- Frustration about your skin condition
- Embarrassment about your skin condition
- Being annoyed about your skin condition
- Feeling depressed about your skin condition
- The effects on your skin condition on your interactions with others (e.g., family, friends etc.)
- Your skin condition making it hard to show affection
- The effects of your skin condition on your daily activities
- Your skin condition making it hard to work or do what you enjoy

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There are no conflicts of interest.

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