Acta Dermatovenerol Croat 2005;13(3):156-159 CLINICAL ARTICLE

# The Treatment of Acne Vulgaris with Low Dosage Doxycycline

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Received: April 24, 2005.
Accepted: June 1, 2005.

**SUMMARY** Doxycycline hyclate 20 mg bid is an effective maintenance dosage in patients with inflammatory acne. Twelve subjects aged 14 to 36, both men and women, completed a 16-week study to demonstrate the effectiveness of subantimicrobial dosing of doxycycline hyclate. Seventeen subjects were screened, and three withdrew before receiving any medication. The subjects were given doxycycline hyclate 100 mg daily for eight weeks. One subject withdrew due to unrelated side effects. Eleven subjects had a 50% reduction of lesions at eight weeks, which qualified them to enter the second eight-week phase of the study. This group received either doxycycline hyclate 20 mg bid or placebo. The six subjects receiving doxycycline hyclate 20 mg bid maintained their improvement, while the placebo group did not.

**KEY WORDS** acne vulgaris, subantimicrobial dosing of doxycycline, inflammatory acne

## INTRODUCTION

Antimicrobials have been the mainstay of acne therapy since their serendipitous introduction over a half-century ago (1). Initially, Marion Sulzberger suggested the concept of a loading dose, followed by maintenance therapy, to which he referred as "morbistatic therapy" (2). Clinicians, during the second half of the twentieth century, have vacillated between utilizing high doses throughout the course of treatment and employing lower doses, once diminution of inflammatory signs occur.

In recent years, doxycycline has become an increasingly important agent in the acne armamentarium, its efficacy having been established for treating this sebaceous gland disorder over three decades ago (3,4). The advent of the subantimicrobial dosage (SD doxy) concept has raised the

question, once again, of utilizing lower dosing, after initial improvement. To document this concept, we conducted the following clinical trial.

## MATERIALS AND METHODS

Seventeen patients, aged 14 to 36 years, having inflammatory acne of six-month duration or more, were screened for a prospective randomized clinical trial to evaluate the role of SD doxy 20 mg bid (Periostat®) as maintenance therapy for inflammatory acne*. To qualify, the subjects needed to have 15 to 40 facial inflammatory lesions (papules and pustules) with no more than 5 acne abscesses. They also were required to have a minimum score of 2 on the Clinician's Global Assessment Scale and to have no allergy to doxycycline.

Each participant received up to eight weeks of doxycycline hyclate 100 mg daily. If the number of inflammatory lesions were reduced by 50% at the fourth or eighth week, the subject could enter the second phase of the study, which required eight weeks of SD doxy 20 mg bid *vs*. matched placebo. Subjects were permitted to wash with a mild soap (Purpose®), but no other topicals or other antimicrobials were permitted during the course of the trial.

Once qualified, the subjects were evaluated at the end of 4, 8, 12, and 16 weeks, at which time lesion counts and global observations were made (5). Changes between baseline and subsequent visits were recorded. Photographs supplemented these observations.

## RESULTS

Seventeen subjects met the criteria and entered the study. Three subjects withdrew from the trial prior to receiving medication due to logistical problems. Two subjects did not improve sufficiently by the eighth week and were not randomized. One subject discontinued the trial early due to recurrent episodes of myoclonic twitching, a condition which she had developed several years before; this was unrelated to the study medication.

None of the eleven subjects achieved the 50% reduction in lesions until the eight-week visit, at which time they began the second phase of the trial: SD doxy 20 mg bid *vs.* placebo. None of the subjects completing the trial reported unwanted side effects.

The six subjects receiving SD doxy 20 mg bid were able to maintain the improvement during the ninth to sixteenth week of the trial, while the placebo group forfeited much of the improvement obtained during the first part of the trial (Figs. 1 and 2).

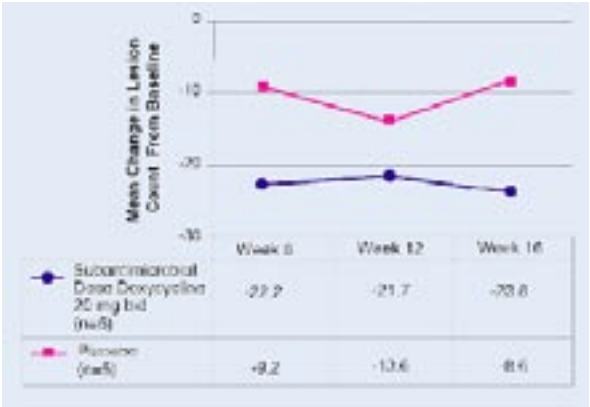
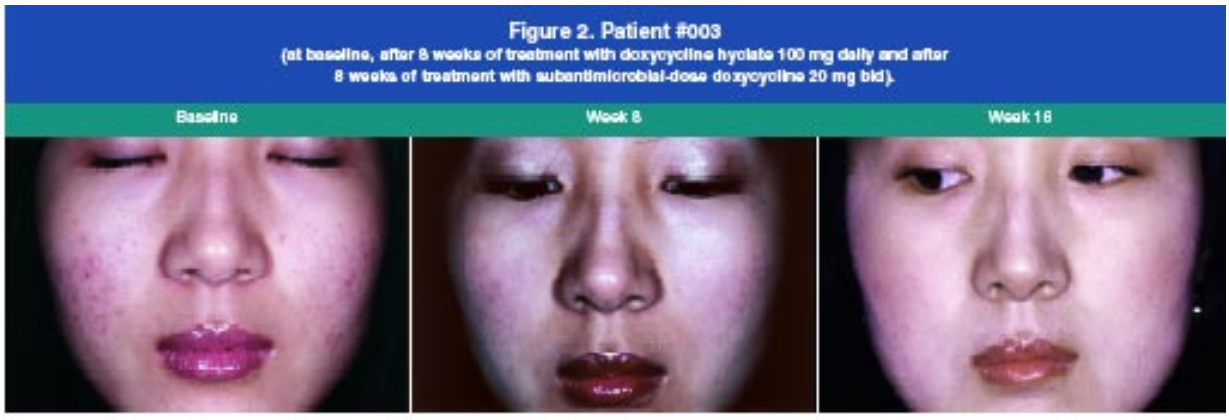



**Figure 1.** Mean changes in lesion count from baseline.




* clinical study funded in part through an unconditional research grant from CollageGenex Pharmaceuticals, Inc, Newton, Pennsylvania

Acta Dermatovenerol Croat
2005;13(3):156-159

## DISCUSSION

Doxycycyline has been known to be effective in the treatment of acne for several decades (4). The mechanism of action of this antibiotic, like other agents useful in the treatment of acne, vacillates between being unknown and being unclear (6). Whether the role of antimicrobials is that of an anti-chemotactic agent (7) or a pharmaceutical agent that attacks *Propionibacterium (P.) acnes* (8) is one that has baffled the finest dermatologic minds (6). The morphology and pathology of this sebaceous gland disorder are clear, but the suggestions of interleukins and tumor necrosis factor being involved remain speculative (9).

Added to the dilemma is the fact that antimicrobials produce resistant *P. acnes* (8) and possibly the overgrowth and resistant patterns of such bacteria as *Streptococcus pyogenes* (10). The tetracyclines are also implicated in causing candidiasis, particularly vaginal candidosis. Doxycycline has a good safety profile; the side effects of full doses of doxycycline, while not common, include esophagitis (11), pseudotumor cerebri (12), and onycholysis (13).

SD doxy 20 mg bid had previously been shown to be effective in treating inflammatory acne during a six month regimen, where acne lesions were reduced by at least 50% with a similar reduction of non-inflammatory lesions (comedones). It has no observable effect on *P. acnes,* nor did other resistant organisms emerge (9) due to the fact that the plasma concentration never reaches an antibacterial level. SD doxy 20 mg bid has also been found to reduce inflammation for up to 18 months with no significant unwanted effect. In addition, the SMD doxycycline 20 mg bid regimen seems to eliminate the possibilities of photosensitivity, gastrointestinal upset, and yeast production associated with higher dosing.

SMD doxycycline 20 mg bid has been studied extensively in periodontal disease, where it has been demonstrated to inhibit polymorphonuclear leukocyte-derived collagenase (MMP-8) and prevent the development of inflammatory cytokines. This halts the destruction of tissue that can occur with inflamed periodontal tissue. SD doxy 20 mg bid has been postulated to stop the production of inflammatory cytokines that up-regulate the reactions to *P. acnes*. These include IL-6, IL-1$\beta$, and TNF-$\alpha$. Other possibilities may be the prevention of the down-regulation of *P. acnes* reducing the free fatty acids that promote neutrophil activity through their potent chemokine activity (9).

This trial demonstrated that SD doxy 20 mg bid could maintain the benefits of full dose doxycycline hyclate (100 mg) daily for two months. Because no medicated facial washes or other topical treatments were used in the trial, the observed benefits of SD doxy 20 mg bid could be considered independent of any other therapy. While single modality still cannot be advocated, this study also demonstrated that SD doxy 20 mg bid could maintain the diminution of acne lesions without any adjunct of washes or other topicals, a concept first suggested by Sulzberger fifty years ago (2).

## CONCLUSIONS

SD doxy 20 mg bid permits the maintenance of improvement in patients with inflammatory acne for at least eight weeks, initially achieved by eight weeks of doxycycline 100 mg daily. No unwanted side effects were noted in this clinical trial.

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