



NEW REGIMEN OF DOXYCYCLINE IN THE TREATMENT OF MODERATE FACIAL ACNE

KEYWORDS

doxycycline, unidox solutab, treatment, moderate facial acne

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ABSTRACT *Studies have already proved the efficacy of antibiotics in acne patients, but long treatments produce unwanted side effects.*

The aim of our study was to evaluate a new therapeutic regimen: half a pill of Unidox Solutab (50 mg Doxycycline) / day, during dinner with food and enough water, 15 days / month, for three consecutive months. The oral treatment was combined with the daily use of a cleansing gel.

15 patients with moderate acne were recruited from a Private Office of Dermatological Care, Cluj-Napoca, Romania, following reading and signing the informed consent. Evaluation methods: Global evaluation of acne, Global evaluation of scars, Photographic assessment-if patients provided written consent.

The results of the study proved the efficacy of the new Unidox administration scheme. Inflammatory acne was reduced by more than 50%-by comparison with Day 0. Our study also showed the safety of the therapy, covering aspects regarding tolerance, compliance and adverse events rate.

I. INTRODUCTION

Acne vulgaris is a common skin disease, characterized by areas of seborrhea comedones, papules, pustules, nodules and scarring [1,2].

It affects globally approximately 650 million people, or about 9.4% of the population, as of 2010 [3]. Almost 90% of the people in the Western societies are affected during their teenage years and the condition may persist into adulthood [4]. Post-adolescent acne (after age 25) has an incidence of 54% in women and 40% in men [3]. Acne vulgaris has a lifetime prevalence of 85%. About 20% are moderate or severe cases [5].

Doxycycline is a useful antibiotic in acne due to its antibacterial and anti-inflammatory effects [1,6]. The recommended treatment consists of 1 pill per day (100 mg Doxycycline) for 3 months. Long antibiotic treatments in acne patients produce unwanted side effects [7,8].

The aim of our study was to evaluate a new therapeutic regimen: half a pill of Unidox Solutab (50 mg Doxycycline) per day, during dinner with food and enough water, for 15 days per month, for three consecutive months.

We have chosen half of the normal dosage of Doxycycline and half of the treatment time period to decrease the occurrence rate of the adverse reaction and the photosensitivity risk. Our oral treatment was combined with the daily use of a cleansing gel.

OBJECTIVES

The global approaches of our research work were:

- To evaluate the result of the studied regimen : Unidox

scheme of treatment (Doxycycline half of the normal dosage for half of the treatment period) in patients with moderate acne.

- To establish the efficacy of the drug, with reference to the acne improvement, from the doctor's point of view.
- To identify the adverse reaction rate of the studied drug.
- To evaluate the compliance of the acne patients to the treatment regimen.

II. MATERIAL AND METHOD

Study Group, Research Design and Method

The protocol of the study was approved by the Institutional Ethical Committee (IEC) of Iuliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca.

The study subjects were recruited from a Private Office of Dermatological Care, from Cluj-Napoca, Romania. Males and females with age range between 14 and 45 years old, suffering of moderate acne vulgaris were included in the study.

Out of the total number of 21 subjects, 6 did not meet the inclusion criteria. A number of 15 patients remained in the study, after reading and signing the informed consent. For the subjects under the age of 18 years old, the informed consent was signed by parents or legal representatives.

The subjects of this prospective trial were 7 males and 8 females. The included patients had the opportunity to decide if they wanted to be photographed during the trial or not. Only 10 patients (5 males and 5 females) signed for approval of digital photographs. With these subjects each visit (baseline – day 0 and evaluation – day 90) implied the use of the same digital camera, same parameters and lighting

conditions in order to photograph the acne status. The photographs were then analyzed by two doctors (blinded to the study), each one assessing the number of papules and pustules for each subject on Day 0 and Day 90.

Inclusion criteria:

- 1) Subjects over 14 years old, under 45 years old
- 2) Patients for whom the dermatologist decided that this was the best treatment protocol.
- 3) Acne severity: moderate acne at baseline (GEA > 2).

Exclusion criteria:

- 1) Patients outside the age range
- 2) Patients with mild or severe acne
- 3) Hypersensitivity to doxycycline or tetracycline
- 4) Pregnancy or breastfeeding
- 5) Acute or chronic renal failure
- 6) Liver diseases

Evaluation methods:

- Global evaluation of acne (GEA scale)
- Global evaluation of scars (ECCA – simplified version)
- Photographic assessment - if the patient gave his written consent to be photographed.
- Patients’ treatment questionnaire – results to be focused on in another study.

Treatment details

1 pill of Unidox solutab contains 100 mg Doxycycline.

Our treatment regimen included half a pill of Unidox Solutab (50 mg Doxycycline), 1 administration/day, during dinner time, with food and enough water. The treatment was 15 days in the first month, pause, 15 days in the second month, pause, then 15 days in the third (last) month of the study.

Oral treatment with Doxycycline was combined with local therapy consisting of a cleansing gel. For standardization purposes we recommended the use of the same cleansing face gel during the trial, for daily wash. Patients received the medication and the face wash gel for daily use. No other systemic or topical acne treatment was allowed during the treatment period (90 days).

III. RESULTS

a.) Demographic data

Our study included both female and male patients suffering of moderate acne. Regarding the age, the youngest patient in our study group was a 15 years old female, while the oldest was a 35 years old male patient. Mean female age was 22,75. Mean male age for study subjects was 23,14 years old. The mean age for both female and male subjects was 22,9 years old.

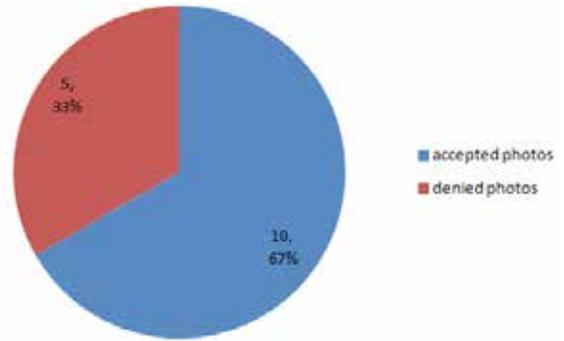
Taking into consideration the age of the patients we were able to assess the acne type: juvenile acne was present in 3 out of 8 female subjects (37,5% of females) and in 4 out of 7 male patients (57,1%). Mature acne was more common in female subjects (62,5% of the female patients) and less common in males (42,8%).

The evaluation of the urban and rural distribution of patients shows that 46,66% of the patients belonged to the rural community. We noticed a rather equal distribution, with 53,33% of the study subjects coming from an urban environment.

b) Acceptance of photographic acne assessment

We noticed the following trend: more than half of the patients accepted this evaluation method (67% of the total study subjects).

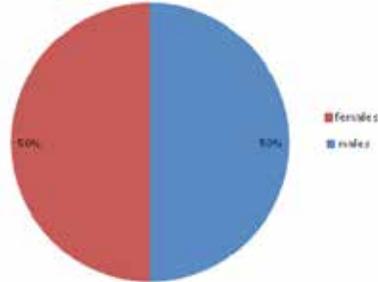
Figure1. Degree of patients' acceptance of the photographic evaluation method.



We also assessed the acceptance of photographic evaluation by taking into consideration the gender criteria.

Out of the 15 patients encompassed in the study, the 10 patients who accepted the photographic evaluation had an equal distribution regarding the gender: 50% were males and 50% were females.

Figure 2. Distribution of patients who accepted the photographic evaluation method on the basis of gender



c) Photographic assessment of acne at baseline (day 0)

The following photographs of the male patients were taken before the treatment administration, on day 0 (Baseline)

Figure 3. Males subjects on baseline – acne assessment on Day 0



Female subjects’ photographs, taken before the treatment administration, on day 0 (Baseline)

Figure 4. Females subjects on baseline – acne assessment on Day 0



d) Results of photographic assessment of acne after the

treatment (day 90)

Patients completed the treatment period and were evaluated by the doctor on Day 90. With the subjects who agreed to perform photographic evaluation, the same procedure was performed : same digital camera, same parameters and lighting conditions in order to capture the acne status after the treatment period.

To achieve a proper evaluation we had to define some assessment criteria. We used a general grading scale in order to evaluate the treatment results:

0=	no	improvement
1=	mild	improvement
2=	moderate	improvement
3=	good	improvement
4=	excellent	improvement

Figure 5. Effectiveness of the treatment on male patients – assessment on Day 90



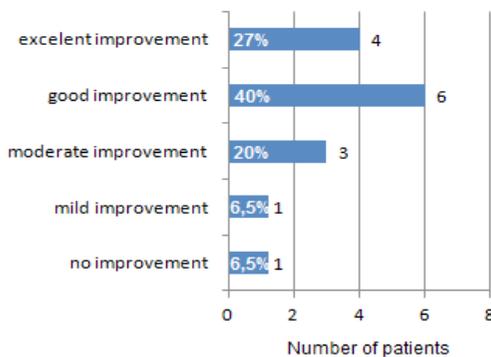
We noticed a significant improvement in all male subjects. The number of the acne lesions (pustules and papules) and the inflammatory acne was reduced by more than 50 % - by comparison with the pictures captured on Day 0 ($p < 0,05$).

Figure 6. Effectiveness of the treatment on female patients – assessment on Day 90



As in males, a significant acne improvement was noticed in all female subjects included in the study. The pustulous acne was decreased to more than 50%, compared to the initial status of the disease ($p < 0,05$).

Figure 7. Doctor's evaluation at 3 months- Improvement of acne lesions after the treatment



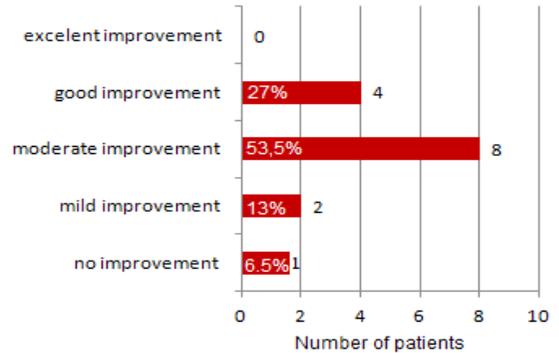
PARAMETER	VALUE
Mean(Average)	2.73
Standard deviation	1.16
Variance (Standard deviation)	1.35
Population Standard deviation	1.12

Variance (population standard deviation)	1.26
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More than half of the patients reached good results after the treatment – 27% of the total study subjects had excellent results with Unidox therapy, while 40% of the patients had good results and 20% of the subjects had moderate outcome in improving the acne lesions. 6,5% of the patients did not see any improvement and the same number reported the modifications were mild.

The first improvements were noticed with the acne lesions after 12 weeks of treatment (3 month of Unidox administration - 50 mg Doxycyclin/day).

Figure 8. Doctor's evaluation at 3 months- Improvement of acne scars after the treatment

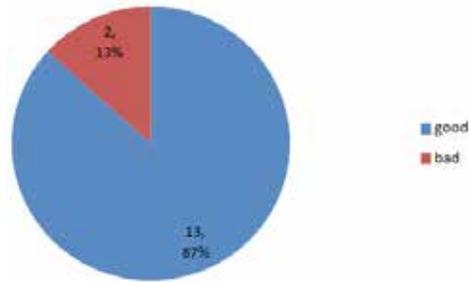
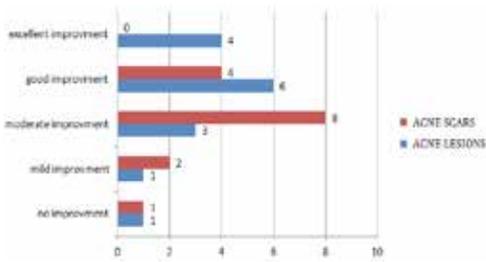


PARAMETER	VALUE
Mean(Average)	2.00
Standard deviation	0.84
Variance (Standard deviation)	0.71
Population Standard deviation	0.81
Variance (population standard deviation)	0.66

There were no excellent improvements in scars after the treatment, but good improvements were seen in 27 % of the cases and 53.5% of the patients had moderate improvement after the 12th week of treatment. For 1/5 of the total study subjects, there was no significant improvement of the acne scars: 13% of the patients recorded mild improvement, while 6,5% had no improvement of acne aspect by the doctor's evaluation.

The results of our study suggest that the acne lesions recorded significant improvement after the treatment. Comparing the two aspects of interest (acne lesions and scars), we noticed that the therapy had a better effect on acne lesions than on acne scars. Since Doxycycline has antibacterial and anti-inflammatory properties, it works better on inflammatory acne lesions than on scars.

Figure 10. Combined overview of the treatment results on acne lesions and scars

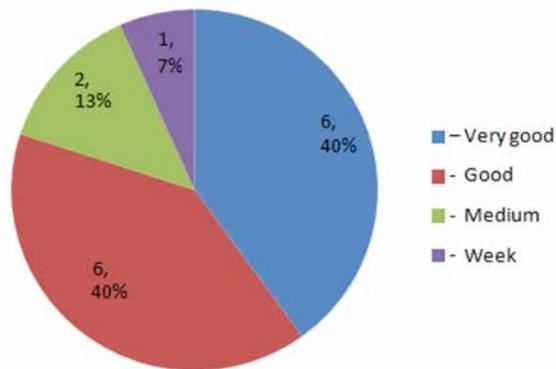


e) Overview of the tolerance

For statistical purposes we graded the patients' tolerance in: very good – 3 points, good – 2 points, medium – 1 point, week – 0 points.

Tolerance was good and very good in 80% of the cases, with equal distribution between the specified categories. Medium tolerance was encountered in 13% of the cases, and weak tolerance in 7%.

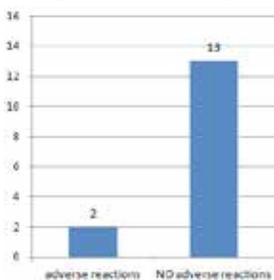
Figure 11. Tolerance of patients during the treatment period



f) Overview of the adverse events/reaction rate

2 patients out of 15 developed an adverse reaction, representing 13% of the total study subjects. One female reported stomatitis on the third month of treatment, while one male subject had a diarrhea episode (without fever) in the last month of the trial, which was treated by symptomatic medication. There was no discontinuation of the study drug, and all patients completed the therapy period as described in the treatment protocol details.

Figure 12. Adverse reactions which occurred during the treatment period



g) Overview of the patients' compliance during the treatment

Figure 13. Patients compliance during the treatment period

Regarding the compliance to the treatment during the therapy period, our results showed a good compliance in 87% of the study subjects. 13 patients out of 15 stated that the treatment regimen was easy to follow. 13% of the study subjects were not pleased, recording a bad compliance. They were, most probably, those who experienced an adverse event or reaction.

IV. DISCUSSION

Nowadays specialists still show a lot of interest in "acne as it" remains a very common disease that affects the majority of the population [3,11]. New oral and local therapies have developed in the past years and the research in this area seems to be improving, with the development of adjuvant acne treatments [6,12,13].

Our study has focused on antibiotic treatment of acne with Doxycycline (Unidox solutab). In literature, the usual instructions regarding the administration of the drug refer to 1) recommended administration: a dosage of 100mg/day for 6-12 months [7]. 2) Primary evaluation of the therapy efficacy could be seen after two weeks but for significant results it is recommended to continue the therapy for 3 months [3]. In 90% of the cases after three months of treatment we can notice the dimension reduction of the acne lesions and the inflammatory reactions are stopped [14]. 3) The treatment can be retaken anytime, if necessary [15].

Most of the available studies have already proved the efficacy of the drug [16-20]. A Double-Blind study showed that Doxycycline , 100 mg/day, was given orally as a single dose every morning for four weeks, with no concomitant internal or external therapy. Out of the 62 patients with inflammatory acne who received the treatment, 33% of the subjects had good or excellent response in reducing the inflammatory lesions, compared to 22% receiving placebo. The improvement produced by doxycycline was significant and generated no adverse reactions [17].

Our research focused on a sample of patients with moderate acne. The study group included 15 patients, 8 females and 7 males, who were treated with half a pill of Unidox Solutab (50 mg Doxycycline) per day, for 15 days per month, for three consecutive months.

Our study results showed that more than half of the patients reached good results after the treatment – 27% of the total study subjects had excellent results with Unidox therapy (50 mg/day), while 40% of the patients had good results on improving the acne lesions. 6,5% of the patients did not see any improvement and the same number said the improvement was mild.

13% of the total study subjects developed an adverse reaction to the drug. One female reported stomatitis in the third month of treatment, while one male subject experienced a diarrhea episode (without fever) in the last month of the trial, which was treated by symptomatic medication. The adverse reactions were minor and with no outcome for discontinuing the study drug. The rate of occurrence and the severity of the adverse reactions were under the circumstances described by the literature.

A study conducted by Skidmore et al, with 20 mg doxycycline given twice daily on moderate acne over a 6 month period, showed a statistically significant improvement of the patients' lesions [18]

The Hirschmann study focused on the same low-dose Doxycycline administration scheme. This study included patients with moderate acne during a 6-month course of 20-mg doxycycline twice daily compared with placebo. Among the 40 patients who completed the study, the mean reduction of inflammatory lesions and comedones was 52% in the doxycycline group versus 18% in the placebo group, a significant difference. This study suggested that the applied regimen may be the safest approach to antibiotic treatment of acne [19].

In our study the results obtained after 3 months of therapy with Doxycycline 50mg/day showed that the number of acne lesions (pustules and papules) and the inflammatory acne were reduced by more than 50 % - by comparison with the pictures captured on Day 0.

An interesting fact that needs to be pointed out is the issue that another study performed by Toosi et al, showed a reduction of 84% in papules and 90% in pustules at 20 mg doxy twice daily for 3 months, in 100 patients with moderate inflammatory acne [20]. This study revealed better results than ours, in acne reduction after the same time treatment period and with less than a half of the dosage of the same drug. The disadvantage of our study consisted

in the fact that we did not have a large treatment group, neither a placebo group.

V. CONCLUSIONS

The results of the study proved the efficacy of the new Unidox administration scheme: half a pill of Unidox Solutab (50 mg Doxycycline) per day, during dinner with food and enough water, for 15 days per month, for three consecutive months.

Improvements were noticed in the acne lesions after the first 12 weeks of treatment.

In both male and female subjects after 90 days of therapy, the number of the acne lesions (pustules and papules) and the inflammatory acne were reduced by more than 50 % - by comparison with photographic acne assessment performed on Day 0.

There were no excellent improvements in scars after the treatment, but good improvements were seen in 27% of the cases. We have to take into consideration that besides the oral antibiotic treatment, all patients used the same cleansing face gel during the trial.

Comparative assessment showed that the antibiotic therapy worked better on the inflammatory acne lesions than on the scars, most probably because Doxycycline has important antibacterial and anti-inflammatory properties.

The patients' tolerance was good and very good in 80% of the cases, with equal distribution between the specified categories.

Regarding the compliance to the treatment during the therapy period, our results showed a good compliance in 87% of the study subjects.

The following adverse reactions occurred: one case of stomatitis and a diarrhea episode, without fever, in another patient, both developed in the last month of the treatment. Adverse reactions were minor and were under the circumstances described by literature.

In conclusion, our study showed both the efficacy of the new Unidox administration scheme and the safety issues of therapy, covering aspects regarding the tolerance, compliance and adverse events/reaction rates. The good results obtained by both male and female patients with moderate acne encourage us to continue this therapy regimen and to apply it within a larger trial.

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