

Nigella Sativa Oil Lotion 20% vs. Benzoyl Peroxide Lotion 5% in the Treatment of Mild to Moderate Acne Vulgaris

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ABSTRACT:

BACKGROUND:

Acne vulgaris is the most common chronic inflammatory disease of the skin. Many patients fail to improve with the current anti-acne therapy due to the cost of therapy, adverse effects leading to noncompliance or lack of therapeutic benefits of current antibiotics (resistance).

OBJECTIVE:

To evaluate the efficacy and tolerability of *Nigella sativa* oil lotion 20% in comparison with well-known drug benzoyl peroxide lotion 5%.

METHODS:

This is a double-blind, active-controlled, randomized study to compare between *Nigella sativa* oil lotion 20% and benzoyl peroxide lotion 5%. 70 patients enrolled in this study, their age ranged between 12-23 years with less than 100 non-inflammatory lesions and less than 50 inflammatory lesion counts (according to the Combined Acne Severity Classification).

RESULTS:

62 patients complete the study. Patients on *Nigella sativa* lotion show a reduction of (-63.3%), (-64.6%) and (-63%) in the non-inflammatory, inflammatory and total lesion counts respectively while patients on benzoyl peroxide demonstrate a reduction of (-43.8%), (-50.9%) and (-45.9%) on the above lesion counts respectively. The difference between groups was statistically significant ($P < 0.0001$, $P < 0.016$, $P < 0.0001$). 97% of patients on *Nigella sativa* lotion show good to excellent improvement (more than 50% reduction in total lesion counts), while only 50% of patients on benzoyl peroxide lotion show good to excellent improvement. Patients on *Nigella sativa* lotion 20% had a milder and fewer side effects, than those who receive benzoyl peroxide lotion 5%. Both groups demonstrate statistically significant increase in lesion counts after 8 weeks from the end of therapy.

CONCLUSION:

Nigella sativa oil lotion 20% is more effective and safe than benzoyl peroxide lotion 5% in the treatment of mild to moderate acne vulgaris.

KEY WORDS: acne vulgaris, *nigella sativa*, benzoyl peroxide

INTRODUCTION:

Acne vulgaris is the most common chronic inflammatory disease of the skin to affect humans ⁽¹⁾. The reported prevalence of acne varies from 35% to over 90% of adolescents at some stage ⁽²⁾. Acne is a multi-factorial disease involving hormonal influences, altered keratinization, inflammation and immune changes ⁽³⁾. Current treatments of acne include topical and oral antibiotics, topical antimicrobial, topical and oral retinoids. All acne treatment has potential side effects some of which may be severe ⁽⁴⁾. Many patients fail to improve with these agents due to the cost, adverse effects leading to noncompliance (irritation) or lack of therapeutic

benefit (antibiotic resistance). The use of oral antibiotics and systemic retinoids increase both the cost and risk of adverse effects ⁽⁵⁾. To overcome the problems of conventional therapies many studies have been done to find new effective and safe treatment of acne vulgaris. One of these methods to overcome the problems of conventional therapy is the use of medicinal plants in the treatment of acne vulgaris ⁽⁶⁾. One of the well-known medicinal plants used is *Nigella sativa*, this plant have been used traditionally in Middle Eastern folk medicine as natural remedy for various diseases for over 2000 years ⁽⁷⁾. More than 150 studies conducted since 1959 confirmed the pharmacological effectiveness of *Nigella sativa* seed constituents ⁽⁸⁾. It has been shown that *Nigella sativa* seed and oil are effective antimicrobial ⁽⁹⁾, immunomodulatory ⁽¹⁰⁾, antioxidant ⁽¹¹⁾, anti-inflammatory ⁽¹²⁾ and antitumor activity ⁽¹³⁾.

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MATERIALS AND METHODS:

The present study is randomized, double-blind, active-controlled, parallel assignment, safety/efficacy trial, done between October 2006 and October 2007. The number of patients examined was 70 and their ages varied from 12-23 years, 38 were females and 32 males. Patients with mild to moderate facial acne vulgaris; defined as having comedones number below 100, and inflammatory lesion counts (papules and pustules) below 50 and no more than 5 nodules or cysts according to the combined acne severity classification⁽¹⁴⁾ were included in the study. Patient with severe acne excluded from the trial (those having more than 100 comedones and/or inflammatory lesions above 50). Pregnant and lactating women excluded from the trial, as well as, patient with known hypersensitivity to the drugs of the trial. *Nigella sativa* oil lotion (20%) prepared through the following methods: Firstly we prepare the solvent by adding 200 ml of ethylene glycol to 200 ml of ethyl alcohol and 600 ml distilled water in a ratio of 2:2:6^(15,16). *Nigella sativa* oil lotion 20% prepared by taking 80 ml from the above solution and adds to them 20 ml of *Nigella sativa* oil; the oil lotion putted in dark container. The active control of the present study is benzoyl peroxide lotion 5% (Ben-Oxide® lotion 5%, DOMINA pharmaceuticals, Syria). The study performed with 35 patients randomly allocated to each study arm. Oral consent was taken from the patients before the beginning of the study; group A given 20% *Nigella sativa* oil lotion, group B given benzoyl peroxide 5% lotion. Patients instructed to wash their face with a mild nonmedicated cleansers and wait 15 minutes until drying and then add the lotion to the entire face, the procedure done twice daily in the morning and

evening. No other lotions, creams, medicated powder, or solutions were allowed on the treatment area. The patients followed up each two weeks and assessment done with each visit to the following: number of comedones, number of inflammatory lesions (papules, pustules), total lesion count (comedones + papules + pustules) and ask the patients about any side effects of the treatment. The active treatments continue for two months, after that patients followed up for another two months to monitor disease flare up. The response of the patients to treatment classified as: excellent response: 75% reduction in lesion counts, good response: 50%-75% reduction in lesion counts, fair response: 25%-50% reduction in number of acne lesions and poor response: no response or less than 25% reduction in the number of acne lesions^(17, 18). The satisfaction of the patients to the treatment classified into: full satisfaction, partial satisfaction, no satisfaction. Statistical analysis done with statistical package for social sciences (SPSS version 12), both descriptive and analytic data used, and two-sided $P \leq .05$ considered statistically significant. Paired t-test used to compare means in the same group, while independent t-test used to compare means between two study groups. Chi-square test used for qualitative data.

RESULTS:

Out of 70 patients included in this study, 62 patients completed the treatment and follow up period. Those who stopped the treatment were for unknown reasons and considered as default. The number of female patients was 32 (51.6%); the number of male patients was 30 patients (48.4%). Their (mean age \pm SD) was (16.24 \pm 2.5), and their range between (12-23) years.

Table 1 : Patients demographic features

	Nigella sativa	Benzoyl peroxide	P. values
Patients	32	30
Men / Women	14/18	16/14
Age, years	16.7 \pm 2.9 ^Ω	15.7 \pm 2.0	0.135(n.s)*
Lesion counts			
Total	39.5 \pm 8.5	39.1 \pm 8.5	0.855(n.s)
Inflammatory	16.93 \pm 5.4	17.06 \pm 5.7	0.928(n.s)
Non-inflammatory	22.62 \pm 4.9	22.10 \pm 5.3	0.688(n.s)

Ω values shown as mean \pm SD unless otherwise indicated, * (n.s): not significant

Efficacy on comedones (non-inflammatory) lesion count

Regarding, *Nigella sativa* oil lotion 20%, the mean lesion count reduced to (8.38 \pm 2.64) after 8 weeks of treatment from the baseline mean count

(22.63 \pm 4.93), which was statistically significant ($P < 0.0001$). **Benzoyl peroxide** lotion 5% recorded a decrease of lesion counts from (22.10 \pm 5.31) to (12.43 \pm 4.00) after 8 weeks of treatment; this reduction was statistically significant ($P < 0.0001$).

Nigella sativa oil lotion was statistically more effective than **benzoyl peroxide lotion** at 6 weeks visit ($P < 0.003$) and at 8 weeks visit ($P < 0.000$). After 8 weeks of treatment, the mean difference between the two groups (4.05) and the class interval of the difference (2.3 – 5.7).

Efficacy on inflammatory lesion counts (papules and pustules)

Nigella sativa: the mean inflammatory lesion count at the start of therapy (16.94±5.46) was reduced to (6.19±3.41) after 8 weeks of treatment this reduction was statistically significant ($P < 0.0001$). **Benzoyl peroxide:** After 8 weeks, there was a reduction of (8.90±4.99) from the baseline lesion counts (17.07±5.72) this is statistically significant ($P < .0001$). At the end of 8 weeks, there was statistically significant difference in favor of **Nigella sativa** vs. benzoyl peroxide ($P < .016$). The point estimate of the difference (mean difference) between the two treatment is (2.7), the class interval of the difference (0.55-4.87).

Efficacy on total lesion counts (comedones, papules & pustules)

Nigella sativa oil lotion 20%: the baseline total lesion counts was (39.56±8.50) and after 8 weeks the mean lesion count was (14.56±4.28) which was statistically significant ($P < .0001$). **Benzoyl peroxide lotion 5%:** the baseline lesion counts were (39.17±8.52) and after 8 weeks the mean lesion count dropped to (21.33±7.03) and this statistically significant ($P < 0.0001$). **Nigella sativa oil lotion 20%** showed a significant difference from benzoyl peroxide lotion 5% at 6 weeks and at 8 weeks ($P < 0.002$ and $P < 0.0001$) respectively. After 8 weeks, the mean difference between the groups was (6.7) and class interval of the difference (3.83-9.70) in favor of **Nigella sativa** oil lotion.

The percent reduction in lesion counts

The following table shows the percent reduction in lesion counts of both **Nigella sativa** oil lotion 20% and benzoyl peroxide lotion

Table 2: Percent reduction of lesions counts for Nigella sativa lotion and benzoyl peroxide after 8 weeks of therapy

	Non-inflammatory (comedones)	Inflammatory lesion (papules and pustules)	Total lesion counts (comedones, papules, pustules)
Nigella sativa	63.3%	64.6%	63%
Benzoyl peroxide	44%	51%	46%
P value	0.0001	0.016	0.0001

Overall response to treatment

Regarding **Nigella sativa oil lotion 20%**, the overall response of the patients to treatment at the end of 8 weeks was as follows: four patients have excellent improvement (12.5%), 27 patients show good improvement (84.4%), fair improvement seen in one patient (3.1%). **Benzoyl peroxide lotion 5%:** one

patient only showed excellent improvement (3.3%), 14 patients had good improvement (46.7%), 13 patients showed fair improvement (43.3%), only two patients had poor improvement (6.7%). The comparison between the two drugs shows that there was a significant difference ($P < 0.0001$).

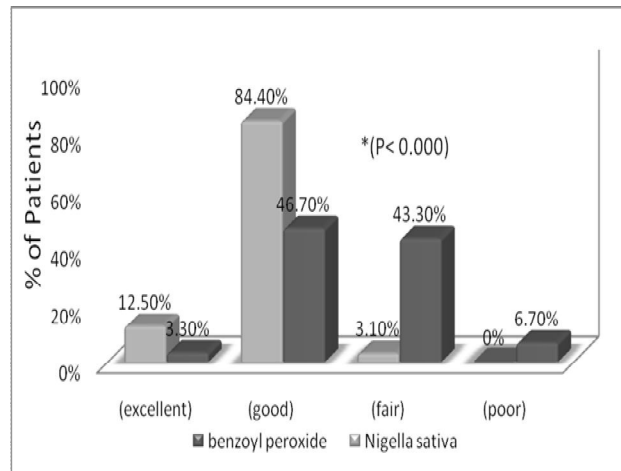


Figure 1: Overall response of patients treated with *Nigella sativa* oil lotion 20% and benzoyl peroxide lotion 5%. Excellent response > 75% improvement, Good > 50%, fair 25%–49%, poor < 24%. * ($P \leq 0.05$) significant with chi square test.

Patients’ satisfaction to treatments

Patients on *Nigella sativa* oil lotion 20%, 20 of them showed full satisfaction to treatment (63%), eight patients showed partial satisfaction (25%) and four patients showed no satisfaction to treatment (12%). Regarding benzoyl peroxide lotion 5%, 14 patients showed full satisfaction (47%), another 14 patients showed partial satisfaction (46%) and two patients showed no satisfaction (7%).

Total lesion counts after 8 weeks from the end of therapy

Nigella sativa oil lotion 20%: at the end of 8 weeks therapy, total lesion count was (14.56±4.28), after 8 weeks of stopping therapy the total lesion count was (17.09±4.76). The mean percent increase in total lesion count from the end of therapy was (18.71%). This increase in total lesion count was statistically significant ($P < 0.0001$). Regarding benzoyl peroxide lotion 5%, the total lesion count was (21.33±7.03) at the end of 8 weeks, after 8 weeks from the end, the total lesion count became (25.60±7.01). The mean percent increase in total lesion count from the end of therapy was (23.10%), this change in lesion count was statistically significant ($P < 0.0001$). The comparison between the two drugs was statistically not significant ($P < 0.19$).

Side effects reported in response to treatment

Of the 32 patients treated with *Nigella sativa* oil lotion 20%, two patients (6%) complained from mild irritation, burning sensation and slight erythema. Six (20%) patients out of 30 treated with benzoyl peroxide lotion 5% complained from irritation, burning sensation, erythema.

DISCUSSION:

The study done by Dr. Ali Ismail ⁽¹⁵⁾ was the first to show the efficacy of *Nigella sativa* oil in the treatment of mild to moderate acne vulgaris. The reduction in the papules and pustules count was 47.5% and 51.6% respectively. In this study, there was no report of any side effects to *Nigella sativa* oil lotion.

This study done to confirm the results of previous study, and to show the effectiveness of *Nigella sativa* oil lotion in comparison with a well-known drug used in the treatment of acne, which is benzoyl peroxide. The other difference with the previous study is the dose, we increase the dose to show any change in the effect in comparison with previous work (dose-response curve) and also we include the non-inflammatory lesion count to see the effect of *Nigella sativa* on comedone counts. Benzoyl peroxide, the active-control of our study is widely used by dermatologist and considered one of the two main pillars of acne treatment with retinoids ⁽¹⁹⁾. Benzoyl peroxide is a powerful antimicrobial agent that rapidly destroys *P. acnes*, also has a secondary comedolytic effect and is shown to be more effective than topical antibiotics with no known resistance to it ⁽²⁰⁾.

After 8 weeks of the study, *Nigella sativa* oil lotion effects on the non-inflammatory, inflammatory and total lesion counts were (-63.2%),(-64.6%) and (63%) respectively, these results, were statistically more effective than benzoyl peroxide, which had an effects of (-43.8%), (-51%) and (-46%) on the non-

inflammatory, inflammatory and total lesion counts respectively.

Both drugs showed statistically significant difference from the baseline lesion counts as early as 4 weeks of treatment for all the lesion counts. Ninety seven percent of patients on *Nigella sativa* lotion showed good to excellent improvement, in comparison with 50% in patients with benzoyl peroxide lotion.

Patient on *Nigella* oil lotion were more satisfied than those on benzoyl peroxide lotion and have fewer and milder side effects. After 8 weeks from the end of therapy, there was statistically significant increase in total lesion counts for both treatments.

This increase may be because lesions tend to recur even after discontinuing a successful treatment regimen⁽²¹⁾. In a study done by Thielitz et al.⁽²²⁾ tretinoin and combination of tretinoin with clindamycin showed a significant decrease in the lesion count after 12 weeks of therapy, but lesions were seen to recur after 4 weeks of discontinuation of the above therapies. Another study done by Thiboutot et al.⁽²³⁾, found that discontinuation of adapalene plus doxycycline or doxycycline alone showed also acne lesions flare up within 3 months follow up period. Recently, a study done by Thielitz et al.⁽²⁴⁾ showed that microcomedones recur after adapalene end of therapy within 3 months follow up period.

Regarding the benzoyl peroxide, our results are consistent with previous studies, which showed the effect of benzoyl peroxide on non-inflammatory lesion counts ranging from 11-70% and on inflammatory lesion counts ranging from 37-71%⁽²⁵⁾. *Nigella sativa* lotion (20%) showed more effect on inflammatory lesion than the previous study done by Ismail⁽¹⁵⁾, who used a concentration of 10%. In comparison with the other topical therapies, *Nigella sativa* oil lotion showed similar efficacy or even better effect than the conventional anti-acne therapies⁽²⁶⁾.

CONCLUSION:

Nigella sativa oil lotion 20% is more effective and safe than benzoyl peroxide lotion 5% in the treatment of mild to moderate acne vulgaris.

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