
A comparative study of the effectiveness of tea tree oil and benzoyl peroxide in the treatment of acne vulgaris among Filipino teenagers and adults in Metro Manila

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Abstract

Introduction The researchers aimed to determine the efficacy of tea tree oil in comparison to benzoyl peroxide in treating mild acne. This study also aimed to identify the side effects of both treatment modalities.

Methods Using a randomized single blinded controlled clinical trial, teenagers and young adults with mild acne vulgaris were allocated to receive tea tree oil gel or benzoyl peroxide for four weeks. The effectiveness of the agents was measured using the Investigator's Global Assessment Scale. Post-treatment scores were compared with the baseline within groups. The difference was compared between the two study arms. Adverse reactions to the two agents were also noted.

Results Both tea tree oil and benzoyl peroxide groups showed a significant decrease in the post-treatment lesion counts compared to the baseline, however when the mean differences were compared between groups, the difference was not significant.

Conclusion Tea tree oil is comparable to benzoyl peroxide in treating mild acne vulgaris among teenagers and young adults.

Key words: Tea tree oil, benzoyl peroxide, mild acne vulgaris

Acne vulgaris is a common dermatological condition associated with psychological problems such as depression, anxiety and low self-esteem. Although acne is not life-threatening, it can

be a contributory factor in the cutaneous and emotional scars that last a lifetime, causing physical, social and psychological suffering, as well as reducing self-esteem and creating emotional distress due to the perceived disfigurement.¹ Due to better understanding of the pathogenesis of acne, new therapeutic modalities have been designed to improve the tolerability of patients to treatments. Studies reported that topical treatments such as benzoyl peroxide, salicylic acid, and a low-dose retinoid are favored in the treatment of mild acne.^{2,3} However, benzoyl peroxide can cause concentration-dependent cutaneous irritation or dryness, and bleaching of clothes, hair and bed linen. Both benzoyl peroxide and tretinoin can induce irritant dermatitis. Meanwhile, antibiotics cause bacterial resistance and

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cross-resistance and, therefore, are advised not to be used as monotherapy.²

Tea tree oil has anti-inflammatory activity *in vitro*, which was the basis of its use in the treatment of various skin diseases such as cuts, insect bites, boils, and dermatophytosis. Previous studies have also suggested the efficacy of 5% tea tree oil in the treatment of acne vulgaris.⁴ The researchers aimed to determine the efficacy of tea tree oil in treating mild acne in comparison to benzoyl peroxide. This study also aimed to identify the side effects of both treatment modalities.

Methods

This was a randomized single-blind trial among teenagers and young adults with mild acne vulgaris from Quezon City where eligible subjects were allocated to receive topical tea tree oil or benzoyl peroxide for four weeks. Efficacy was measured with the Investigator's Global Assessment Scale (IGA) by evaluators blind to the treatment. The study was approved by the Ethics Review Committee.

Men and women from a community in Barangay Doña Imelda, 18 to 29 years old, with acne problems and not under any treatment for acne were recruited. Pregnant women and those with comorbid diseases, allergy to treatments and participating in a similar study were excluded. A sample size of 25 per group inclusive of a 20% dropout was computed based on the Z-value for alpha error of 1.96, difference of 1.2, and assumed standard deviation of 2.⁴

Those who agreed to join the study and gave their consent were brought to the Dermatology outpatient clinic. A dermatologist checked their acne condition using Combined Acne Severity Classification (CASC); scale this entailed counting the number of comedones and papules. The presence of fewer than 20 comedones, or fewer than 15 inflammatory lesions, or total lesion count fewer than 30 was considered as mild acne vulgaris. Those who qualified were randomized via random letter assignment using Microsoft Excel to receive the intervention tea tree oil (TTO) gel or the control benzoyl peroxide (BPO). The patient's acne condition was then described using the USFDA Investigator's Global Assessment (IGA) scale.

The subjects were taught how to apply the treatment, the frequency, amount, and duration of the treatment. The participants documented the frequency of the application of the treatment every

night using a checklist; the participants underwent an initial trial for three days to check for adverse reactions to the assigned treatment. They were instructed to report any adverse reaction via text messaging. Any reported adverse reactions (referring to unwanted, uncomfortable, or dangerous effects that a drug may have, and can be considered a form of toxicity)⁵ were to be referred to the Dermatology OPD. Participants who did not report any serious reactions proceeded to the 4-week clinical trial with their assigned treatments. Their IGA grade scores were determined after four weeks. Treatment was considered successful if there was at least a two-grade reduction from the baseline IGA score; reduced, if the lesion count decreased but did not reach a two-grade reduction, and; no reduction, if there was no decrease in the number of lesions from the baseline.

An independent T-test was used to determine if there was a significant difference between the age and baseline lesion count of the TTO and BPO group; a chi-square was used to determine if there was a significant difference between the sex distributions of the groups. A paired T-test was used to determine if there was a significant difference between the post-treatment and baseline lesion counts in each group. An independent T-test was used to determine if the difference in lesion count between the TTO and BPO groups was significant. A p-value of < 0.05 was considered significant.

Results

Out of the 70 participants of the study, only 58 subjects were able to complete the study (31 in the TTO and 27 in the BPO groups). There was an 11% drop out rate in the TTO group while dropout rate in the BPO was 22%, thus intention-to-treat analysis was done. Multiple imputation using SPSS 20 was used to handle the missing cases. As seen in Table 1, the TTO and BPO groups were comparable in terms of age, sex, and baseline lesion count.

Table 1. Demographic characteristics of the treatment (TTO) and control (BPO) groups.

	TTO	BPO	p-value
Mean age	23.7 (2.41)	24.1 (2.34)	0.55
Sex			
Female	17	18	0.81
Male	18	17	
Baseline lesion count	19.6 (6.26)	21.8 (6.37)	0.16

Both TTO and BPO groups showed a significant decrease in the post treatment lesion count compared with the baseline count as seen in Table 2. When the mean differences of the groups were compared, the difference of the means was not significant (Table 3).

Table 2. Effectiveness of TTO and BPO based on number of lesions.

	Baseline	Post Treatment	Difference	p-value
TTO	19.9	14.4	5.5	< 0.01
BPO	22.1	14.3	7.8	< 0.01

Table 3. Intergroup comparison of the mean difference in the number of lesions.

	TTO	BPO	p-value
Difference	5.5	7.8	0.24
% change	27.64	35.29	0.38

Although there was a difference noted between the results of the original and the imputed data, the interpretation of the results remained unchanged despite a 25% dropout (Table 4). The result indicates that that TTO is less likely to reduce acne lesion count compared to those treated with BPO although this

is not statistically significant ($p = 0.6$). Those given TTO have a 1.38 chance of developing a side effect compared to those who were treated with BPO (Table 5).

Discussion

Acne vulgaris is a multifactorial inflammatory disease involving the pilosebaceous follicles.⁶ The combination of keratin, sebum and microorganisms, particularly *Propionibacterium acnes* leads to the release of pro-inflammatory mediators and the accumulation of lymphocytes, neutrophils, and foreign body giant cells. This, in turn, causes the formation of inflammatory papules, pustules, and nodulocystic lesions.⁷ Treatment is based on the severity of the acne. There is no standard treatment for acne but there are several treatment modalities that provide promising effects in treatment of acne in some patients. Benzoyl peroxide, retinoids, and antibiotics are usually used to treat mild to moderate acne.⁸ For mild severity, comedones are usually treated with topical retinoids and physical extraction while papular and pustular are treated with antimicrobials, topical retinoids and benzoyl peroxide. A study revealed that despite scarcity of research on benzoyl peroxide, it is considered as standard treatment.⁹ Benzoyl peroxide has mild keratolytic effect and antimicrobial activity which is attributed to its oxidative property. Tea tree oil has a broad spectrum of antimicrobial activity attributed to its composition of cyclic monoterpenes,

Table 4. Effectiveness of TTO in reduction of lesions.

	Without reduction in lesions	With reduction in lesions	RR	p-value
Original data				
TTO	8	23	0.91	0.51
BPO	5	22		
Imputed data				
TTO	11	24	0.89	0.60
BPO	8	27		

Table 5. Comparison of adverse reactions of TTO and BPO.

	TTO (n = 35)	BPO (n = 35)	RR	NNH	p-value
Drying of skin	11	8	1.38	7.5	0.27
Itchiness	11	8	1.38	7.5	0.27

specifically, terpinen-4-ol, the main antimicrobial component of tea tree oil.

Using the IGA scale, all participants were classified as Grade 2 at baseline but they remained at Grade 2 even after treatment. One possible reason is that the length of the treatment course might have been too short to incur a 2-Grade reduction from the baseline score. Both TTO and DPO showed a statistically significant decrease in the number of lesions and these results are consistent with previous studies.^{10,11}

Tea tree oil is derived from the leaves of *Malaleuca alternifolia*. It has a broad spectrum of antimicrobial activity attributed to its composition of cyclic monoterpenes, specifically, terpinen-4-ol, the main antimicrobial component of tea tree oil. There is also the presence of other components, such as α -terpineol, which have antimicrobial activity similar to those of terpinen-4-ol. As a common ingredient of healthcare and cosmetic products, tea tree oil concentrations range from 2% to 5% in commercially available products.¹²

According to a study, tea tree oil is 3.5 times more effective than the placebo in the total acne lesion count, and 5.8 times more effective in the acne severity index of the study's participants.¹³ Thus, there was a significant difference between 5% tea tree oil gel and placebo regarding improvement of the total acne lesion count. One study also concluded that tea tree oil is an effective treatment of mild to moderate acne vulgaris.¹⁴ The study showed a significant reduction of propionibacterium and follicular casts on the skin surface after treatment of two days with only slight reductions in mean acne grade and mean inflamed lesion count. The non-specific antibacterial action of BPO therefore may be utilized in short course treatments to reduce carriage of antibiotic-resistant microorganisms and in turn, improve the long-term efficacy of antibiotic acne treatments. A similar study done showed that both TTO and BPO significantly reduce inflamed lesions. However, BPO performed better than TTO.¹⁵

The results of this current study showed that TTO has a 1.38 risk of developing a side effect compared to those who were treated with BPO which contrasts with a previous study.¹⁵ There are several factors that may have affected the results of the study such as the preparation of the treatment modalities; TTO was given in a form of oil and BPO was prepared as a cream. The adjunct

ingredients used in the previous studies and this current study may have differed.

Several studies also showed contradicting results on the side effects of tea tree oil. A clinical study on the toxicity effects of TTO from its leaves (TTO-L) were evaluated by a skin irritation assay and liver function evaluation. TTO-L and two major components terpinen-4-ol and 1,8-cineole were used to evaluate skin toxicity by a single topical application. The results revealed no significant erythema, irritation and very slight edema upon application of TTO.¹⁵ However, tea tree oil was shown to cause both irritant and allergic reactions.

Since irritant reactions may frequently be avoided through the use of a lower concentration of the irritant, this bolsters the case for discouraging the neat oil in promoting the use of well-formulated products. The most definitive work indicates that allergic reactions are caused mainly by oxidation products that occur in aged or improperly stored oil.¹⁶

The investigators conclude that the efficacy of TTO and BPO in treating mild acne vulgaris is comparable, thus TTO can be considered as an effective alternative treatment to BPO. Post-treatment, the retained Grade 2 baseline IGA Grade of all participants may be due to the short duration of treatment (4 weeks), which did not allow for the maximum capacity of the treatment modalities to cure acne lesions. Other factors that may be considered are the stress level and hormonal changes of the participants. Likewise, the increased risk of side effects of TTO, which include dryness of skin and pruritus, must also be taken into consideration. Despite not having a reduction of at least 2 grades in the IGA classification of all participants, the results still revealed that there is significant reduction in the number of acne lesions when the efficacy of TTO ($p < 0.01$) and BPO ($p < 0.01$) are analyzed separately. Therefore, the researchers recommend TTO as an alternative treatment for mild acne.

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