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Clinical evaluation of efficacy and safety of a polyherbal formulation in acne vulgaris

Dr. Azad Hussain Lone*, Dr. Tanzeel Ahmad. *, Dr Mohd Anwar.*, Dr. Gh Sofi and AH Naiyar*****

* Dept. of Medicine, National Institute of Unani Medicine, Bangalore-91, India

**Lecturer, Dept. of Pharmacology, National Institute of Unani Medicine, Bangalore-91

*** Dept. of Pharmacology, Ajmal Khan Tibbiya College, Aligarh Muslim University, Aligarh, India

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Corresponding Author:

Dr Azad Hussain Lone,

E-mail: drazadnium@rediffmail.com

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Abstract

Background: Acne vulgaris is the most common disorder treated by dermatologists. Acne is a disease of the pilosebaceous unit characterized by the formation of the open and closed comedones, papules, pustules, nodules and cysts.

Objective: The objective of the study was to assess the safety and efficacy of a Polyherbal Formulation in comparison to benzoyl peroxide in the management of Acne Vulgaris.

Materials and Methods: A randomized, single blind, standard controlled study was carried out at outpatient department of Medicine, National Institute of Unani Medicine, Bangalore. 50 diagnosed patients of acne vulgaris were included in the study after obtaining their informed consents. The patients were divided randomly into polyherbal and benzoyl peroxide groups with 25 patients in each group. In polyherbal group, Polyherbal formulation was administered locally whereas patients of benzoyl peroxide group received standard drug topically for a period of 45 days. The severity of acne vulgaris and efficacy of the treatment was assessed by Cook's acne grading scale.

Results: At the end of study, the whole data was tabulated and analyzed by suitable statistical tests. Both the herbal formulation and standard drug were equally effective and statistically significant ($p<0.05\%$) in the treatment of acne vulgaris. There was no significant difference between the after treatment grading of polyherbal and benzoyl peroxide groups at 5% p level. Further the Polyherbal formulation was found safe and fairly well accepted by the patients.

Conclusion: The results concluded that the Polyherbal formulation can be used safely and effectively for the treatment of acne vulgaris

Keywords: Acne vulgaris, Comedones, Benzoyl Peroxide, Polyherbal Formulation, Cook's acne grading scale.

Introduction:

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous units and is characterized by seborrhoea, the formation of comedones, erythematous papules and pustules, less frequently by nodules, deep pustules, or pseudocysts and, in some cases, is accompanied by scarring [1,2]. It is believed to be the most common disease of the skin. The condition usually starts in adolescence, peaks at the ages of 14 to 19 years and frequently resolves by mid-twenties. Acne develops earlier in females than in males, which may reflect the earlier onset of puberty in females. The most severe forms of acne vulgaris occur more frequently in males, but the disease tends to be more persistent in females [3].

Acne vulgaris is one of the commonest skin diseases with point prevalence reaching 100% among adolescents. Although it is usually a condition of adolescent, acne affects 8% of 25-34 year olds and 3% of 30-44 year old age group [4,5,6,7]. The peak incidence of acne is in the mid to late teens. As many as 80 to 90% of all adolescent will have some type of acne and 30% will require medical treatment [8]. Acne is a polymorphic disease, which occurs predominantly on the face (99% of sufferers) and, to a lesser extent, occurs on the back (60%) and chest (15%). In young men, it affects mainly the face, and in older males the back is also significantly affected. Seborrhoea is a frequent feature [1,9].

The pathophysiology of acne is associated with four etiological factors, including: increased production of sebum, abnormal keratization of pilosebaceous duct, colonization with follicular microflora (*Propionibacterium acnes*) and inflammatory and immune response of the body. *Propionibacterium acnes* is the principal microorganism found within the pilosebaceous gland. Its role in acne pathogenesis may be related to its ability within the pilosebaceous unit to create and exist as a biofilm [10,11].

The mainstay for the treatment of acne is use of topical and or systemic antibiotics, retinoids but the long term use of drugs produce significant side effects like erythema, peeling, burning and drying of the skin. Moreover the development of antibiotic resistance to *P.acnes* may limit the use of topical antibiotics. There is a dire need to develop other therapeutic modalities including herbal medicines for the treatment of acne vulgaris. Fortunately physicians of Indian System of Medicine like Unani and Ayurveda have been practicing many herbo- mineral drugs for the treatment of acne since antiquity. Thus the present study was conducted to validate the safety and efficacy of a Polyherbal Formulation (Zimade Mohasa- a cream) on modern scientific parameters. The formulation was selected

for the study from the Hamdard Pharmacopoeia of Eastern Medicine and was procured from the department of Pharmacy NIUM. Its ingredients are Iris florentina, Azadirachta indica leaves, Acacia speciosa bark, Abrus precatorius and Lake salt 50 grams each [12]. This polyherbal cream acts topically as a detergent, astringent, anti-inflammatory and antibacterial agent. In an experimental trial, Azadirachta indica exhibited antibacterial activity against a variety of micro-organisms such as Staphylococcus, Enterococcus, Pseudomonas, Escherichia, Klebsiella, Salmonella and Mycobacterium [13]. Various clinical trials conducted using Polyherbal formulations showed that there was a significant improvement in acne at the end of the treatment [14,15,16].

Materials and Methods:

The present study was conducted in the department of Medicine, National Institute of Unani Medicine (NIUM), Bangalore from March 2009 to October 2010. It was a randomized, single blind, and standard controlled clinical trial. The diagnosed patients of acne vulgaris were enrolled in the study from outpatient department of Medicine and Dermatology, NIUM after obtaining their written informed consents. The patients were clinically assessed and diagnosed on the basis of history and dermatological examination. All the findings were recorded on the case record proforma, designed for the study. A total of 50 diagnosed patients of acne vulgaris qualifying the inclusion criteria were selected and were randomly allocated into polyherbal and benzoyl peroxide groups with the help of Lottery method but 10 patients were lost to follow up leaving behind 20 patients in each group who completed the treatment protocol. The patients of both sexes and age (12-30 years) were included in the study while patients with other variants of acne like acne fulminans, acne rosacea, acne necrotica, pregnant and lactating women, patients with any systemic illness, diabetic patients, patients below 12 and above 30 years of age and patients of other concomitant diseases were excluded from the study. Routine investigations like complete haemogram, urine and stool examination, Random blood sugar, Liver function test, and Renal function test were done before treatment in order to exclude the other systemic ailments. The patients of polyherbal group were advised to apply polyherbal cream to the area affected by acne at night and then wash the area with lukewarm water in the morning. Patients of benzoyl peroxide group were advised to apply Benzoyl peroxide cream once at night. The duration of treatment was 45 days and follow up was done weekly. The severity of acne vulgaris and efficacy the drug was done by employing Cook System of Acne Grading [17]. It is a commonly used grading scale of acne involving evaluation of the overall severity of acne on 0-8 Scale anchored to photographic standards. The patients were clinically assessed weekly and all lesion counts were performed at baseline and at 1, 2, 3, 4, 5 and 6th weeks. The response of both test and standard drugs at the end of study was noted on five point scale as follows: Excellent response - improvement of three grades; Good response- improvement of two grades; Poor response - improvement of one grade; No response - no change in grade and Worse grade - increase in grade.

Statistical analysis: At the end of study, the whole data was tabulated and analysed by using the registered SPSS program (Version 17, Manufacturer is SPSS Inc., 233 South Wacker Drive, 11th Floor. Chicago). For quantitative data, Man Whitney U Test and Wilcoxon Signed rank test were used whereas for qualitative data, Chi Square test was applied. The level of significance was considered at p<0.05 and highly significant at p<0.01.

Results:

The demographic observation in the study showed the highest incidence (42.5%) of acne in the age group of 17-21 years while the least (7.5%) was seen in the age group of 27-31 years. 25(62.5%) patients were females and 15(37.5 %) patients were males and 1/3 patients had onset of acne in the age group of 12-16 years. Most of the enrolled patients were students and 67 % were from middle income group. A positive family history was recorded in 24(60%) patients. Premenstrual flare up of acne was recorded in 45% females and was the most aggravating factor recorded. As far as the dietary habits are concerned 18(45%) patients were non-vegetarians and 12 (30%) were vegetarians and 10(25%). were having mixed dietary habits. Regarding the site of lesion, the commonest site observed was face (55%), followed by face and back (22%), face and chest (17.5%) and only 7.5% patients showed lesions on face and shoulders. (**Table-1**)

Parameter	No of patients	Percentage
Age		
12-16	12	30%
17-21	17	42.50%
22-26	8	20%
27-31	3	7.50%
Gender		
Male	15	37.50%
Female	25	62.50%
F/H		
Present	24	60%
Absent	16	40%
Site of lesion		
Face	22	55%
Face and back	8	20%
Face and chest	7	17.50%
Face and shoulder	3	7.50%

Table-1: Demographic Data

Effect of Test and Control drugs on Cook's Acne Grading:

In the polyherbal group, 1(5%) patient showed grade 8, 6(30%) patients showed grade 6, 10 (50%) patients showed grade 4, 3(15%) patients showed grade 2 and no patient showed grade 0 at base line grading while in benzoyl peroxide group, 2(10%) patients showed grade 8, 7 (35%) patients showed grade 6, 8(40%) patients showed grade 4,

3(15%) patients showed grade 2 and no patient showed grade 0 at base line grading. The base line grading of acne vulgaris of polyherbal and benzoyl peroxide group was compared by Man Whitney test. There was no statistical significance between two groups at 5% level. At the end of treatment, there was remarkable response in acne grading in both groups. 5(25%) patients showed grade 0, 12(60%) patients showed grade 2, 2(10%) patients showed grade 4, only 1(5%) patient showed grade 6 and no patients showed grade 8 after treatment in polyherbal group. (**Table -2**) Similarly in benzoyl peroxide group, 6(30%) patients showed grade 0, 10(50%) patients showed grade 2, 2(10%) patients showed grade 4, 2(10%) patient showed grade 6 and no patients showed grade 8 after treatment. (**Table -3**)

Grade	Baseline	1 st wk	2 nd wk	3 rd wk	4 th wk	5 th wk	6 th wk
	No of Pts	Pts.	Pts.	Pts.	Pts.	Pts.	No of pts
0	0	0	0	0	1	3	5(25%)
2	3(15%)	3	5	8	9	11	12(60%)
4	10(50%)	10	8	6	7	4	2(10%)
6	6(30%)	6	6	5	2	2	1(5%)
8	1(5%)	1	1	1	1	0	0

Table -2; Cook System of Grading in Test group

Grade	Baseline	1 st wk	2 nd wk	3 rd wk	4 th wk	5 th wk	6 th wk
	No of Pts	Pts.	Pts.	Pts.	Pts.	Pts.	No of pts
0	0	0	0	0	1	4	6(30%)
2	3(15%)	3	4	6	6	8	10(50%)
4	8(40%)	8	6	6	5	4	2(10%)
6	7(35%)	7	8	6	6	3	2(10%)
8	2(10%)	2	2	2	2	1	0

No= Number, Pts. =Patients

Table -3; Cook System of Grading in Control group

The improvement in acne grading in both groups was analysed by employing Wilcoxon Syned rank test for paired data. There was a strong evidence of a difference between the base line grading and grading at the end of study with $p<0.001$. The assessment of improvement in acne grading, recoded on a five point scale, showed that in polyherbal group, excellent response was seen in 6(30%) patients, good response in 11(55%) patients, poor response in 2(10%) patients and no response in 1(5%) patient. While in benzoyl peroxide group, excellent response was observed in 6(30%) patients, good response in 9(45%) patients, poor response in 4(20%) patients and no response in 1(5%) patients. (**Table-4**) The overall efficacy of the polyherbal formulation and standard drug was compared by Chi Square test. There was no significant difference between the after treatment grading of polyherbal and benzoyl peroxide groups at 5% level. However the test of significance between two proportions of poor response in polyherbal and

benzoyl peroxide groups showed that the proportion of poor response in benzoyl peroxide group was significantly greater than proportion of poor response in polyherbal group.

The safety and cutaneous tolerance of polyherbal formulation and standard drug was evaluated by erythema, dryness, scaling, burning and pruritus. In polyherbal group, no obnoxious adverse effects were observed during and after the study. But 20% patients of benzoyl peroxide group felt dryness, feeling of warmth, mild irritation, itching, redness or swelling of skin.

Response	Test group	Control group
	No of Patients	No of Patients
Excellent	6(30%)	6(30%)
Good	11(55%)	9(45%)
Poor	2(10%)	4(20%)
No Response	1(5%)	1(5%)
Worse	0	0

No= Number, Pts. =Patients

Table- 4; Assessment of Improvement

Discussion:

The present study was carried on 40 patients of acne vulgaris aged between 12-30 years to compare the safety and efficacy of Polyherbal cream with Standard drug in acne. In this study, the peak incidence was observed in the age group of 17-21 years. This finding corroborates with the findings of a pioneer epidemiological study on acne in which a peak was found in the incidence between 14-17 years in case of females and between 16 -19 years in case of males [26].

The patients in both polyherbal and benzoyl peroxide groups were clinically assessed by using Cook System of Acne grading. The response of the drugs was assessed and recorded on a five point scale and was statistically analyzed. There was a significant reduction in acne grading in both groups. After comparing the response of test and control drugs, no significant difference between the responses of two groups was observed at 5% p level. In polyherbal group, there was a significant improvement in acne grading at $p<0.001$. This improvement may be attributed to various pharmacological activities of the ingredients of Polyherbal cream. These herbs possess anti-inflammatory, detergent, absorbent, emollient, antiseptic and antimicrobial properties [18,19,20,21]. These herbs might have inhibited the proliferation and growth of follicular microflora and resolved the inflammatory process that led to the overall improvement in acne vulgaris at the end of treatment. This is in consonance with the pharmacological actions described in classical literature of Indian system of medicine and has been proved in various clinical and experimental studies [13,14,15,16]. Further significant improvement in acne flare was noticed to be earlier and therefore greater compliance of the treatment. The test drug was found safe and fairly well accepted by the patients as no adverse effects were observed in polyherbal group.

In benzoyl peroxide group, there was a significant ($p<0.001$) improvement in acne

grading after the completion of treatment. Benzoyl peroxide is comedolytic [22] and bactericidal [23] to *P. acnes*. It is the oldest and most widely used topical agent for the treatment of non-inflammatory and inflammatory acne vulgaris. This chemical's main mechanism of action is characterized by the cleavage of oxygen-oxygen bonds, which result in the production of benzoyl free radicals [23]. This triggers a cascade of events, resulting in the formation of more free radicals. These free radicals act as exfoliating agents, which clear pores and increase skin turnover: this helps treat the non-inflammatory comedones of acne. The free radicals also destroy bacteria in both aerobic and anaerobic conditions [24]. The response of standard drug was same as that of polyherbal formulation but the local adverse reactions like dryness, redness and irritation of skin, itching and bleaching of clothes was observed in benzoyl peroxide group. These findings coincide with the side effects described by M Sagransky and his colleagues [25].

Conclusion:

Since the therapy for acne vulgaris has limitations in western medicine, herbal remedies can offer an alternative therapy for acne, the present study showed that the Polyherbal cream has an encouraging potential in acne treatment with practically no side effects. In the light of above discussion, it may be concluded that Zimade Mohasa is safe and cost effective in the treatment of acne vulgaris. However, long term studies to determine the relapse rate and effect of Polyherbal cream on acne scarring need to be carried forward.

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