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RESEARCH ARTICLE

A Randomized Standard Controlled Clinical Trial of Unani Topical Formulation in the Management of Dermatomycoses

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Abstract

Dermatomycoses are the human's oldest recognized and reported infections, which are the fastest growing infections of the skin, hair, and nails. These infections are a global concern due to their ever-increasing prevalence of about 25-27 %, high rate of relapse/recurrence, and resistance. The study was conducted in search of safer and more effective natural medicine. The effect of the standard drug, Terbinafine cream as control is compared with the test drug, Unani formulation in the paste form for local application, containing Kaththa (*Acacia catechu*), Hena (*Lawsonia innermis*), Mazu (*Quercus infectoria*), Kibreet (*Sulphur*), and Suhaga (*Borax*). The data on the effect of the control and test drugs on the various features of the dermatomycoses shows that the Unani formulation is almost similar to the standard drug in terms of Mycological cure and Clinical cure statistically. Hence, Unani formulation can be used in the treatment of dermatomycoses.

Keywords: Dermatomycosis, Fungal, Infection, Medicine, Tinea, Unani

1. Introduction

Dermatomycoses, the fungal infections of the skin, hair, and nails[1] are named according to their site. *Tinea capitis, Tinea barbae, Tinea faciei, Tinea corporis, Tinea cruris, Tinea manuum, Tinea unguium, Tinea pedis*, and *Tinea inter digitalis* for the fungal infection of the scalp, beard area, face, body, inguinal area, hands, nails, interdigital spaces, respectively. Similar descriptions of these diseases are mentioned in many classical literatures on Unani medicine. The clinical features of lesions of fungal infections of the skin are annular lesions with or without papulo-vesicular margins, clear center, scaling, erythema, itching, and burning[1].

The earliest description was given by Buqrat (Hippocrates), Father of Unani Medicine in 460 BC as 'Aphthae', which are mouth sores that modern mycologists identified as thrush[2]. Various Unani Literature described Qooba, Daad, Khashoonat, etc., as similar to Dermatomycosis a millennium ago. They mentioned Khashoonat, Sauda, Murra Sauda, Ratubate haad, Khoone-fasid and/or Khoone ghaleez, or Balghame Shore as the cause of it[3–8]. In the early modern era, it was thought to be caused by germs[9], later attributed to fungi, belonging to 03 genera; Trichophyton, Microsporum, and Epidermophyton[10–14].

Tinea causing fungi have been identified, reported, and named as Dermatophytes, which are Geophilic, Zoophilic, and Anthrophilic in nature. Geophilic Dermatophytes are associated with soil, which transmit through exposure to infected soil[15]. Zoophilic Dermatophytes are associated with animals and their transmission occurs by direct contact with an infected animal or indirectly by fomites or inorganic objects[16]. Anthropophilic Dermatophytes are related with humans and its transmission occurs by direct contact with infected humans and sometimes indirectly by fomites[17].

Predisposing factors are hot-humid climate, prolonged contact with animals, living in poor hygiene conditions, low socioeconomic status, promiscuity, immunosuppressive

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treatments, prolonged sports activities, wearing air-tight shoes, and use of public swimming pools[18–20].

2. Materials and Methods

Study was conducted after the approval of the Institutional Ethics Committee and Registration at the Clinical Trial Registry of India, vide Reg. No. CTRI/2020/04/024609. Patients were randomized into Groups A and B, who were given the control or the test drug. At the end of treatment, all collected data of the effect of both drugs were compared with the baseline.

Clinically diagnosed patients with fungal infection of the skin, attending the OPD of the Ajmal Khan Tibbiya College Hospital, Aligarh, Uttar Pradesh, India were subjected to a detailed clinical history and physical examination for screening. The patients fulfilling the inclusion and exclusion criteria were taken into account for the enrolment of the study after getting informed signed consent.

Patients of every sex above the age of 12 years to 65 years with the infection of dermatomycoses, having its clinical features viz. annular lesions with or without a clear center, active margins of papulo-vesicles, scaling, erythema, itching, and or burning, were subjected to microscopically KOH positive examination before their enrollment in the study.

The patients below 12 and above 65 years of age or lactating and pregnant women, or having other skin diseases like eczema, psoriasis, scabies, secondary infections of the skin, known allergic to any ingredient of the study drugs, systemic diseases requiring long-term treatment or not willing to give written consent were excluded from the study.

The safety of the test and control drugs is assessed clinically on the basis of side effects or adverse reactions reported by patients and the efficacy is measured by the improvement in clinical and mycological parameters.

3. Clinical Parameters

Clinical parameters for an overall assessment of efficacy were graded on a physician's 4-point scale and recorded at baseline and subsequent visits till the end of the study. Pre and post-treatment scores of individual patients were compared to assess the efficacy of the study drugs.

3.1 Methodology for Grading of the Lesions

The precise method of scoring various clinical findings/lesions is very difficult and has no standard. Therefore, the investigator has to rely on the patient's expression for scoring the lesions, which is shown in Table 1.

4. Mycological Parameters

At the end of the 6th week of treatment, the lesions were scrapped and examined. On the basis of the presence or absence of fungal hyphae, the results were reported as positive or negative for fungal hyphae and analyzed

Table 1. Grading of the lesions

	"0" Grade	"1" Grade	"2" Grade	"3" Grade
Annular lesions	Nil	Present scantly	Present in reasonable numbers	Present in extremely large numbers
Papulo-vesicular margins	Nil	Present scantly	Present in reasonable numbers	Present in extremely large numbers
Scaling	Nil	Visible on magnification, scantly present	Visible with naked eye, present reasonably	Widely present
Erythema	Nil	Present scantly	Present reasonably	Present extremely
Itching	Nil	Present occasionally	Does not disturb the normal activity	Disturbs patient's normal activity
Excoriation	Nill	Present scantly	Present reasonably	Present extremely
Burning	Nil	Present occasionally	Does not disturb the normal activity	Disturbs patient's normal activity

for mycological clearance. Negative results among the patients of previously positive findings before treatment were considered cured Mycologically.

5. Observations and Results

5.1 Annular Lesions

7(13.46%), 22(42.30%), 21(40.39%), and 2(3.85%) patients had 3, 2, 1 and 0 graded annular lesions on 4-point scale before treatment, respectively in Group A, which were observed as 0(0%), 0(0%), 7(13.46%), and 45(86.54%) patients after treatment. In Group B, these patients were 8(15.38%), 28(53.85%), 15(28.85%), and 1(1.92%) before starting treatment, respectively, and at the end 0(0%), 0(0%), 6(11.54%), and 46(86.46%) (Figure1).

5.1.1 Effect of Change in Annular Lesions

The mean score of annular lesions in the control Group A before treatment was 1.65, which decreased by 92.12% to 0.13 after treatment, while in Group B, it decreased by 93.44% from 1.83 to 0.12 as shown in Table 2. It indicates that there is no significant difference in effect.

5.2 Effect of Change in Papulo-Vesicular Margins

2(3.85%), 13(25%), 30(57.69%), and 7(13.46%) patients had 3, 2, 1, and 0 graded papulo-vesicular margins on the 4-point scale before treatment, respectively in Group A, which reduced to 0(0%), 0(0%), 3(5.77%), and 49(94.23%) patients at the end of treatment. In Group B, the patients were 3(5.77%), 23(44.23%), 21(40.38%), and 5(9.62%) before treatment, respectively, which became 0(0%), 0(0%), 5(9.62%), and 47(90.38%) at the end (Figure 2).

As shown in Table 3, the mean score of populo-vesicular margin decreased by 94.95% in the control Group A from 1.19 to 0.06 and by 93.15% from 1.46 to 0.10 in the test Group B. There is no significant variation of effect statistically. This means that the test drug is showing almost the same effect in reducing the populo-vesicular margin as the standard drug.

Table 2. Effect of change in annular lesions

Group	Baseline score	End score	% of Change	Mean	Std. Deviation	Std. Error Mean	t- value	Significance,
A	1.65	0.13	92.12%	1.519	.727	.101	15.062	.000
B	1.83	0.12	93.44%	1.712	.723	.101	17.066	.000

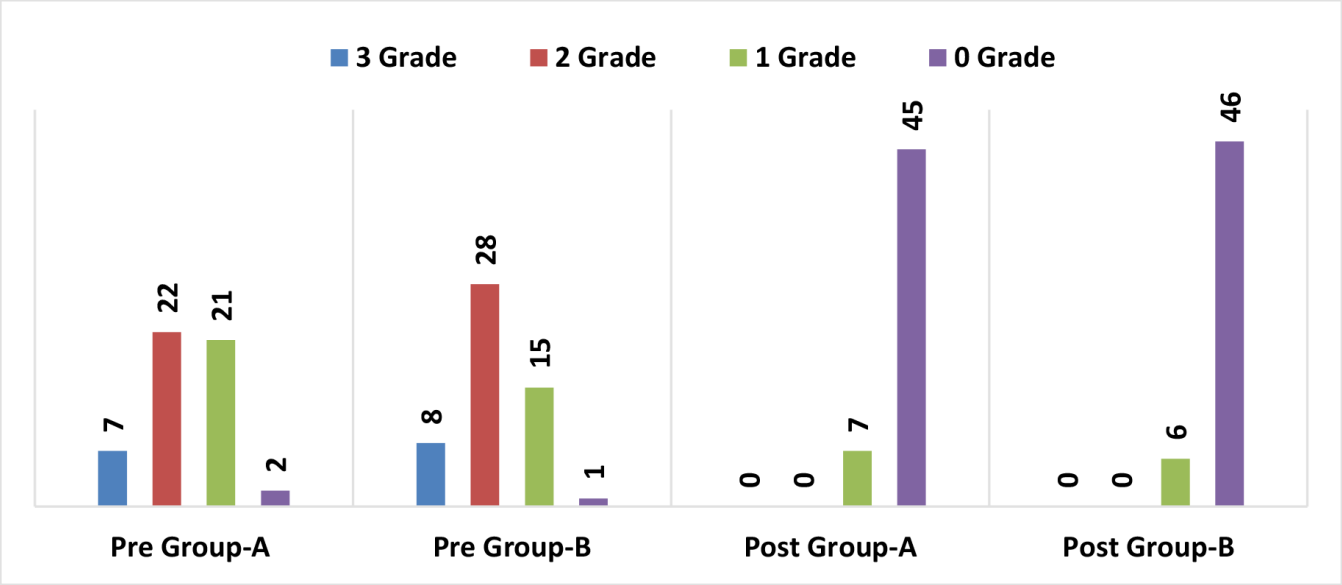

Figure 1. Number of patients with annular lesions, pre and post treatment papulo-vesicular margin.

Table 3. Effect of change in papulo-vesicular margin

Group	Baseline score	End score	% of Change	Mean	Std. Deviation	Std. Error Mean	t- value	Significance,
A	1.19	0.06	94.95%	1.135	.658	.091	12.441	.000
B	1.46	0.10	93.15%	1.365	.715	.099	13.774	.000

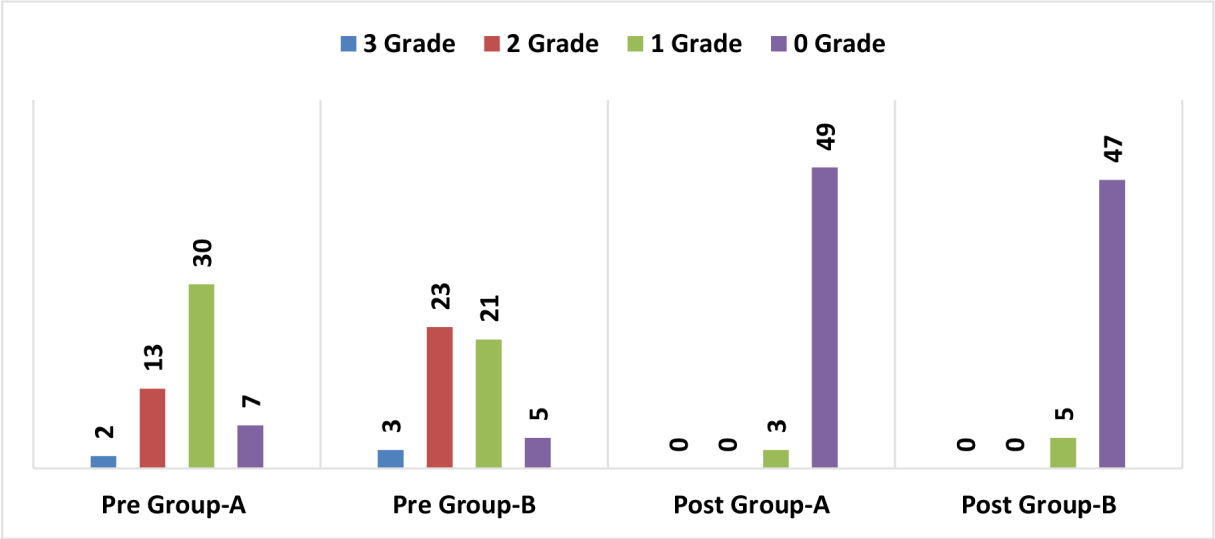

Figure 2. Number of patients with papulo-vesicular margin, pre- and post-treatment.

Table 4. Effect of change in scaling

Group	Baseline score	End score	% of Change	Mean	Std. Deviation	Std. Error Mean	t- value	Significance,
A	1.77	0.25	85.87%	1.519	.641	.089	17.080	.000
B	1.87	0.19	89.83%	1.673	.706	.098	17.081	.000

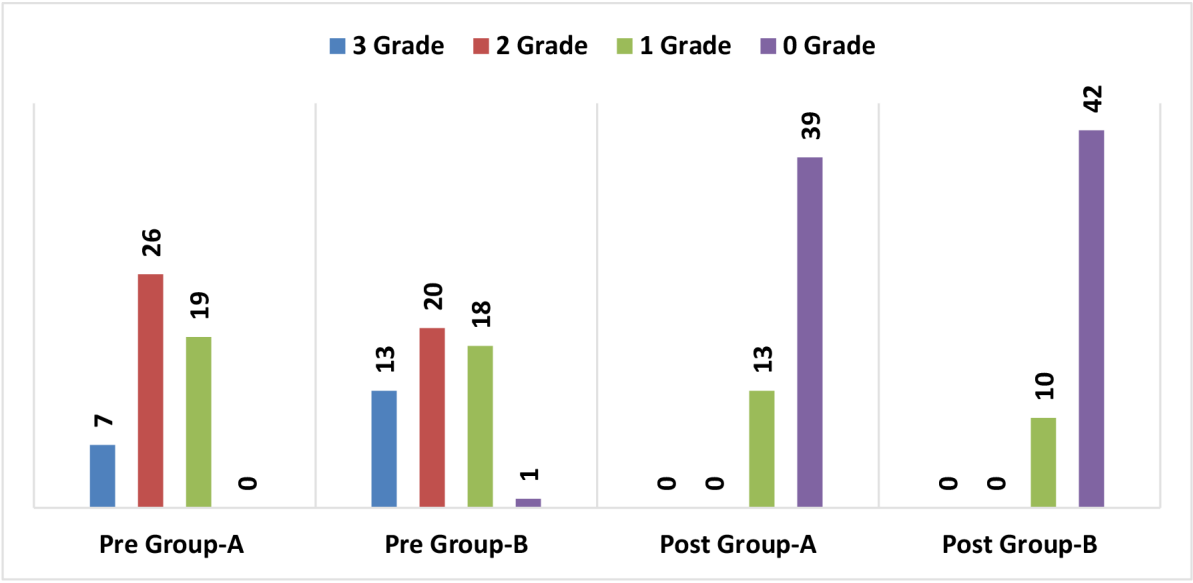

Figure 3. Number of patients with scaling, pre- and post-treatment.

5.3 Scaling

In Group A, 7(13.46%), 26(50%), 19(36.54%), and 0(0%) patients had 3, 2, 1, and 0 graded scales on 4-point scale before starting treatment, respectively, and 0(0%), 0(0%), 13(25%), and 39(75%) patients at the end of treatment. In Group B, 13(25%), 20(38.46%), 18(34.62%), and 1(1.92%) patients had 3, 2, 1, and 0 graded scales before treatment, respectively, and 0(0%), 0(0%), 10(19.23%), and 42(80.77%) patients at the end of treatment (Figure 3).

5.3.1 Effect of Change in Scaling

The mean score of scaling was 1.77 among controlled Group A, which reduced 85.87% to 0.25 after treatment and in patients of test Group B was 1.87 before treatment, which became 0.19 after reduction by 89.83%. It shows slightly better result of test drug as compared to standard medicine statistically as shown in Table 4.

5.4 Erythema

10(19.23%), 17(32.69%), 15(28.85%), and 10(19.23%) patients in Group A had 3, 2, 1, and 0 graded lesions before treatment, respectively, which became 0(0%), 0(0%), 3(5.77%), and 49(94.23%) patients after treatment. In Group B, 13(25%), 16(30.77%), 14(26.92%), and 9(17.31%) patients had 3, 2, 1, and 0 graded lesions before treatment, respectively, which became 0(0%), 1(1.92%), 7(13.46%), and 44(84.62%) patients at the end (Figure 4).

5.4.1 Effect of Change in Erythema

The mean score in the control Group A before treatment was 1.52, which was reduced by 96.05% to 0.06. In test Group B, it was 1.63 which lessened to 0.17 by a reduction of 89.57%. It indicates that the control drug is better than the test drug in reducing erythema as shown in Table 5.

5.5 Itching

The number of patients with the complaints of itching in 3, 2, 1, and 0 grades were 13(25%), 27(51.92%), 11(21.16%), and 1(1.92%) respectively, at the beginning, which became 0(0%), 2(3.85%), 10(19.23%), and 40(76.92%) patients at the end of treatment in Group A. In Group B, they were 18(34.62%), 23(44.23%),

Table 5. Effect of change in erythema

Group	Baseline score	End score	% of Change	Mean	Std. Deviation	Std. Error Mean	t- value	Significance,
A	1.52	0.06	96.05%	1.462	1.019	.141	10.346	.000
B	1.63	0.17	89.57%	1.462	1.019	.141	10.346	.000

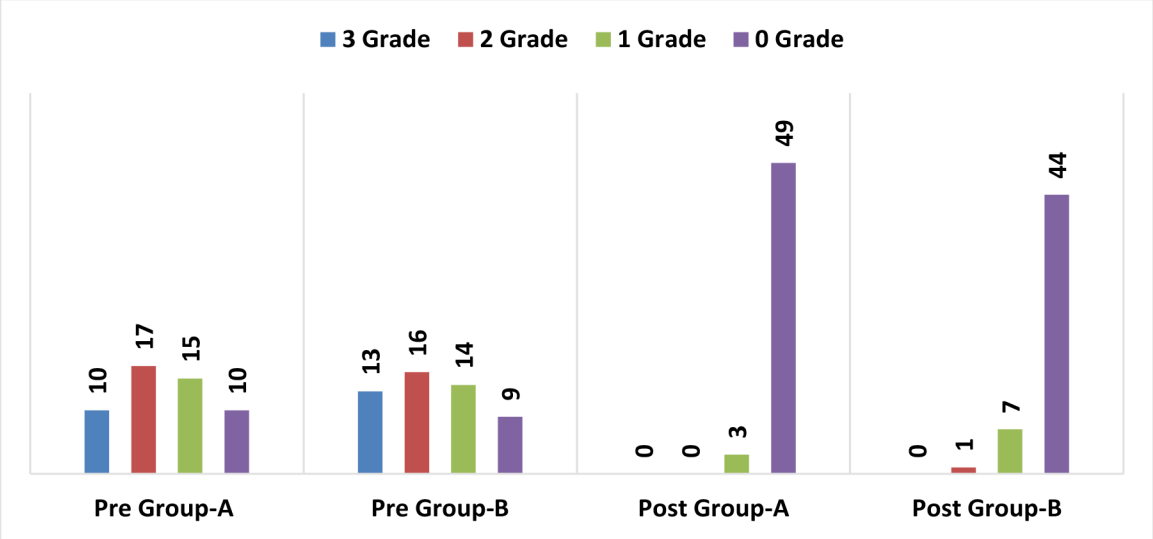

Figure 4. Number of patients with erythema, pre- and post-treatment.

10(19.23%), and 1(1.92%) before starting treatment, respectively, and 0(0%), 3(5.77%), 13(25%), and 36(69.23%) patients at the end of treatment (Figure 5).

5.5.1 Effect of Change

The mean score in control Group A reduced by 86.5% from 2.0 to 0.27 as shown in Table 6. While it decreases by 82.54% in Group B, the score went down from

Table 6. Effect of change in the itching

Group	Baseline score	End score	% of Change	Mean	Std. Deviation	Std. Error Mean	t- value	Significance,
A	2	0.27	86.50%	1.731	.598	.083	20.875	.000
B	2.12	0.37	82.54%	1.750	.682	.095	18.492	.000

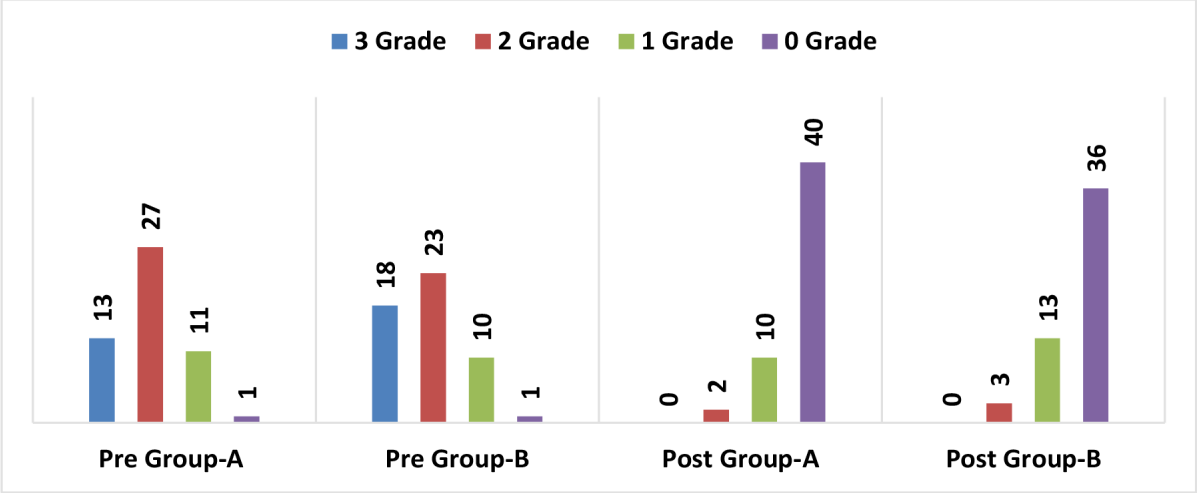

Figure 5. Number of patients with itching, pre- and post-treatment.

Table 7. Effect of change in excoriation

Group	Baseline score	End score	% of Change	Mean	Std. Deviation	Std. Error Mean	t- value	Significance,
A	0.44	0	100%	.442	.826	.115	3.860	.000
B	0.6	0.08	86.60%	.519	.779	.108	4.804	.000

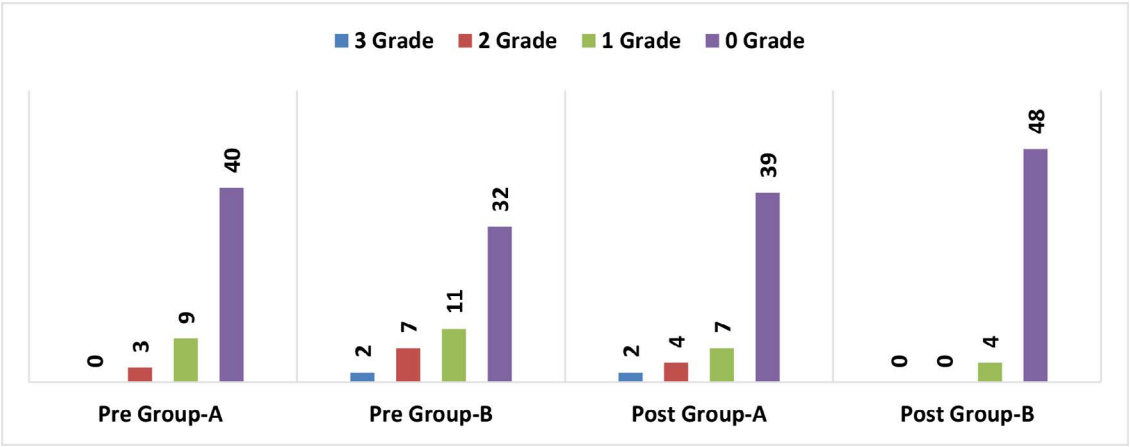

Figure 6. Number of patients with excoriation, pre- and post-treatment.

Table 8. Effect of change in burning

Group	Baseline score	End score	% of Change	Mean	Std. Deviation	Std. Error Mean	t- value	Significance,
A	0.19	0	100%	.192	.658	.091	2.108	.040
B	0.15	0.02	86.66%	.135	.444	.062	2.186	.033

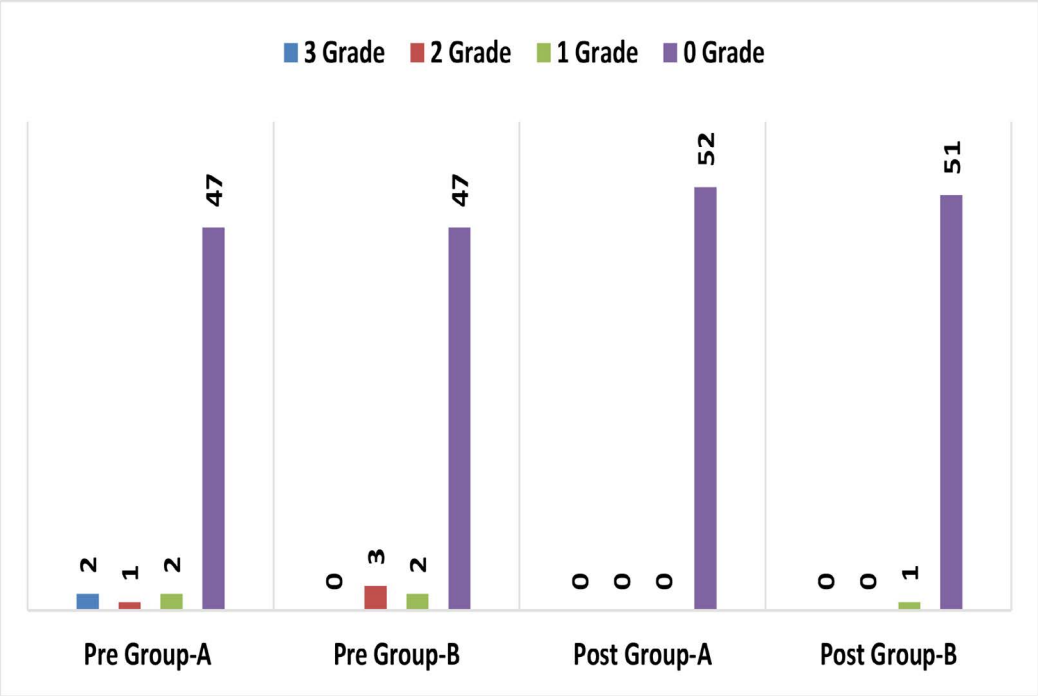

Figure 7. Number of patients with burning, pre- and post-treatment.

2.12 to 0.37. It shows that the control drug is better as compared to the test drug in controlling the itching.

5.6 Excoriation

0(0%), 3(5.77%), 9(17.31%), and 40(76.92%) patients had 3, 2, 1, and 0 graded feature of excoriation, before treatment, respectively, and 2(3.85%), 4(7.69%), 7(13.46%), and 39(75%) patients at the end of treatment in Group A. In Group B, they were 2(3.85%), 7(13.46%),11(21.15%), and 32(61.54%) before starting treatment, respectively, and 0(0%), 0(0%), 4(7.69%), and 48(92.31%) patients at the end of the treatment (Figure 6).

5.6.1 Effect of Change in Excoriation

The mean score was 0.44 before treatment, which decreased to zero by clearing 100% excoriation after treatment among Group A, while in the test Group B, it was 0.60, which decreased to 0.08 after treatment by relieving it 86.66% clinically (Table 7).

5.7 Burning

2(3.85%), 1(1.92%), 2(3.85%), and 47(90.38%) patients had 3, 2, 1, and 0 graded complaint of burning, at starting treatment, respectively, which became 0(0%), 0(0%), 0(0%), and 52(100%) patients at the end of treatment. In Group B, 0(0%), 3(5.77%), 2(3.85%), and 47(90.38%) patients had 3, 2, 1, and 0 graded complaint of burning, before starting respectively, which became 0(0%), 0(0%), 1(1.92%), and 51(98.08%) patients at the end of treatment (Figure7).

5.7.1 Effect of Change in Burning

The mean burning score in the control Group A as shown in Table 15 was 0.19, which is relieved 100% to becomes zero, whereas the mean score in the test Group B was 0.15, which decreased to 0.02 after 86.66%

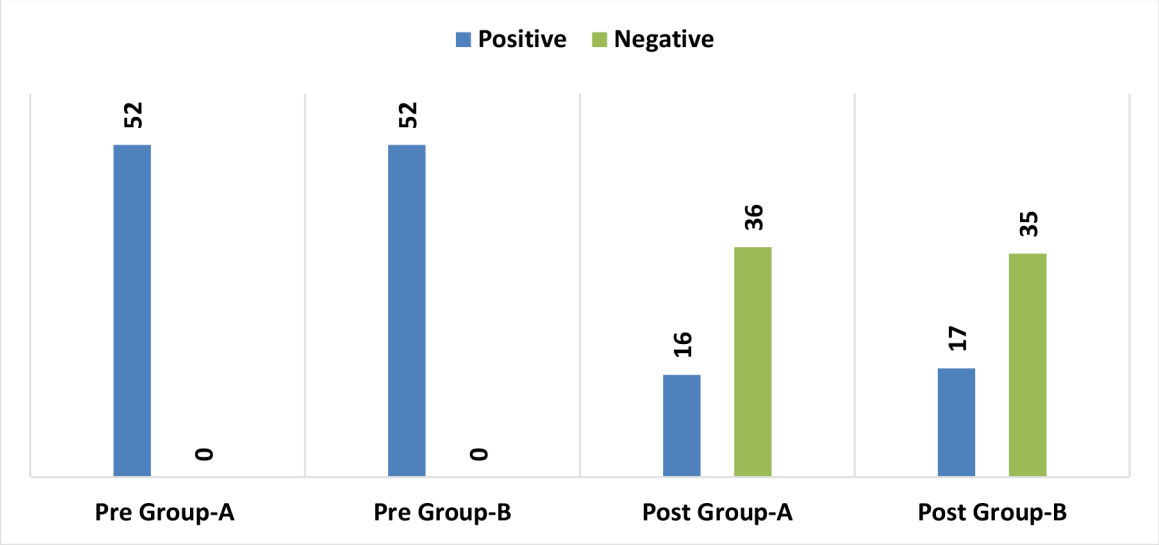

Figure 8. Number of patients with fungal hyphae, pre- and post-treatment.

reduction. It shows that the control drug has better results in reducing burning than the test drug (Table 8).

6. Fungal Hyphae

All the enrolled patients were positive for fungal hyphae on KOH examination as per selection criteria before starting the treatment in Groups A and B. In Group A, 36 (69.23%) patients became negative after completion of treatment and only 16 (30.77%) patients out of 52 were remained positive. In Group B, 35 (67.31%) patients became negative after completion of treatment, while only 17 (32.69%) patients remained positive of fungal hyphae (Figure 8).

7. Conclusion

The statistical analysis of collected data on the effects of the control and test drugs among patients with dermatomycoses shows that the Unani formulation is almost identical to the standard drug in terms of mycological cure and clinical efficacy.

In view of statistically significant beneficial effect of test drug, it is concluded that this Unani formulation could be a better therapeutic alternative to available drugs without adverse effects and with fewer chances of resistance but further extensive research and multicenter clinical trials on larger sample sizes are needed for a better understanding of the outcomes. Additionally, the details explored in this review may be helpful in awareness and further planning of studies on dermatomycoses.

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