International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

A Randomized Control Trial to Compare the Efficacy and Safety of 40% Mandelic Acid Peel with 30% Salicylic Acid Peel in Acne Vulgaris

Dr. M P Sankeerthana[1], Dr. Shea Sharma Bhaskara Babu[2], Dr. Jayakar Thomas[3]

Post-Graduate, Department of Dermatology, Venereology & Leprosy, Chettinad Hospital and Research Institute Kelambakkam, Chennai, Tamil Nadu, India
Contact Information: 09789900966
Corresponding Author Email: *sankeerthanamuppala[at]gmail.com*

Former Post-Graduate, Department of Dermatology, Venereology & Leprosy, Chettinad Hospital And Research Institute, Kelambakkam, Chennai, Tamil Nadu, India

Emeritus Professor, Director of Department, Department of Dermatology, Venereology & Leprosy, Chettinad Hospital And Research Institute, Kelambakkam, Chennai, Tamil Nadu, India

Abstract: ***Introduction**: Acne is a common inflammatory disorder of the pilosebaceous unit and the disease runs a chronic course. Multiple modalities of management are available for acne vulgaris which includes topical therapy, systemic therapy, chemical peels, microdermabrasion, intralesional steroids and light therapies. Chemical peel with salicylic acid is an excellent keratolytic agent used in acne. Mandelic acid which is a superficial chemical peel is gaining momentum for the treatment of Acne vulgaris. Hence this study is being done to compare the therapeutic efficacy and safety of 40 % Mandelic acid peel with standard 30% salicylic acid peel in Acne vulgaris. **Objective**: To assess the therapeutic effectiveness, safety and side effects of 40% Mandelic acid peel in Acne vulgaris and to compare it with the standard 30% Salicylic acid peel. **Study Design**: An open labelled, single blinded, randomized control comparative study. **Study population**: Patients with Acne vulgaris Grade I-III presenting to Department of Dermatology, Venereology and Leprosy, Chettinad hospital and research institute, Kelambakkam. **Duration of the study**: 1 year (February 2021 to February 2022). **Materials and Methods**: A total of 100 patients were included in this study. Patients were divided into 2 groups, Group A and Group B. Group A patients received 30% Salicylic acid peel every 2 weeks once for 8 weeks in OPD which was neutralised with water after frosting was seen followed by broad spectrum sunscreen application. Group B patients received 40% Mandelic acid peel every 2 weeks once for 8 weeks in OPD which was neutralised with water after 2 minutes of application followed by sunscreen application. Lesion reduction was calculated using MSI (Michaelson severity Index score), subjective and objective evaluation and photographic comparison on each follow up. **Results**: Out of 100 patients, 86 patients completed the study. Majority of the patients belonged to 18-22 years age bracket proving acne is a disorder of adolescents and young adults. Most of the patients in our study were females. Study population treated with 30% Salicylic peel had significant reduction in MSS index compared to patients treated with 40% Mandelic peel. The safety and tolerability was better seen with 40% Mandelic acid peel. Further studies with higher number of peeling sessions should be done to evaluate the true efficacy of 40% Mandelic acid in Acne vulgaris. **Conclusion**: Despite better safety and tolerability of 40% Mandelic acid amongst the study population, 30% Salicylic acid showed better efficacy in clearing acne lesions.*

Keywords: Acne vulgaris, Salicylic acid, Mandelic acid

1. Introduction

Acne vulgaris is dermatological condition characterised by inflammation of the pilosebaceous unit, with a chronic course. Acne vulgaris is the commonest dermatoses affecting all ethnicities, socioeconomic groups and races worldwide. Acne is highly prevalent in the adolescent age group [1].

Aetiology of acne vulgaris has diverse factors which includes excessive serum dihydroepiandrosterone (DHEA), genetics, stress, lifestyle factors and systemic therapy [1].

The complex pathomechanism of Acne vulgaris involves elevated levels of serum DHEA stimulating the sebaceous gland to produce sebum and also causes increased keratinisation at the infundibular epithelium leading to obstruction of the duct, proliferation of C.acnes thereby leading to the morphogenesis of acne [1]

Acne vulgaris clinically manifests in the form of comedones, papules, pustules, nodules or cysts depending on its severity. Acne vulgaris usually affects the seborrheic regions of the body viz face, shoulder and trunk [1, 2].

A holistic approach of treatment is usually needed for acne. Lifestyle modifications includes maintaining facial hygiene, healthy diet, regular exercise and smoking cessation [1].

Topical therapy for acne includes retinoids, antibiotics, benzoyl peroxide, nicotinamide, anti-androgens and azelaic acid and systemic therapy for acne vulgaris are Isotretinoin, antibiotics, oral contraceptives and anti-androgens [1].

Chemical peeling with salicylic acid, mandelic acid, glycolic acid, lactic acid, TCA peel, and Jessner's solution can be used for acne in varying percentages according to the severity, in patients whose response for topical and systemic therapy is poor. Salicylic acid is the most widely used chemical peel in Acne due its excellent keratolytic properties. Mandelic acid is an emerging peel with paucity of data in acne [1, 2]. Other modalities of treatment include light therapy, intralesional steroid, lasers and physical extraction of comedones [1]

As a result, the motive of this study is comparing the therapeutic effectiveness and tolerability of a 40 percent Mandelic acid peel to a typical 30 percent Salicylic acid peel in Acne vulgaris.

2. Materials and Methods

Study Design and Population
This was an an open labelled, single blinded, randomized control comparative study conducted at the Department of Dermatology, Venereology and Leprosy, Chettinad hospital and research institute, Kelambakkam.

The inclusion criteria was Patients with Grade I – III Acne vulgaris aged more than 18 years and exclusion criteria included patients less than 18 years of age, Pregnant women, Breastfeeding mothers and women planning for pregnancy, patients having allergy/hypersensitivity to formulations used, patients on topical therapy and/or oral retinoids for Acne vulgaris, those with irregular menstrual cycles and patients with Grade IV Acne vulgaris.

Patients over the age of 18 with Acne vulgaris (grades I-III) were included if they met the inclusion and exclusion criteria after obtaining the written and informed consent. On the initial session, the chosen patients were assessed for baseline lesion count, Michaelson Severity Index Score (MSI) and acne grade. Patients are then randomized into two groups.

Group A: Salicylic acid 30% peel was applied to these individuals every two weeks for an eight-week period. Before the procedure, photographs were taken. At every visit, the skin was degreased with acetone, the eyes were covered with eye pads, and the sensitive areas (nasal ala and angle of lips) were coated with Vaseline. The peel was applied on the lesions and then washed away with cold water when frosting appears. Sunscreen with a broad spectrum range (SPF 40+) was used. Every day, the patient was instructed to use a moisturiser and sunscreen. At each visit, the Michaelson severity index score was calculated. At each visit, erythema, dryness, and burning sensation were noted.

Group B: Mandelic acid 40% peel was applied to these individuals every two weeks for an eight-week period. Before the procedure, photographs were taken. At every visit, the skin was degreased with acetone, the eyes were covered with eye pads, and the sensitive areas (nasal ala and angle of lips) were coated with Vaseline. The peel was applied on the lesions and then washed off with cold water after 2 minutes of application. The time was calculated using a stop watch. Sunscreen with a broad spectrum range (SPF 40+) was used. Every day, the patient was instructed to use a moisturiser and sunscreen. At each visit, the Michaelson severity index score was calculated. At each visit, erythema, dryness, and burning sensation were noted.

Statistical Analysis
Data entry was done using Microsoft Excel 2013 and analysed using SPSS V16. Qualitative data was represented in frequency and percentages and Quantitative data was represented in mean and standard deviation. Non parametric statistics i.e. 'unpaired t test' was employed to determine the significant correlation between the two qualitative variables. 't test' was used to calculate the MSS Score between the two groups to find the significant association between quantitative variables. The results are represented using bar graphs and a pie chart. p value of <0.05 was deemed as statistically significant.

3. Results

A randomized control trial was conducted among patients diagnosed with Acne Vulgaris (Grade I-III) in a Tertiary Care Institution located in Chennai from 2021-2022. This study aimed to compare the efficacy and safety of 40% Mandelic acid peel (Group B) with 30% Salicylic acid peel (Group A). The study findings are as follows:

Group A (30% Salicylic Acid Peel)

1) Demographics:

Age: On Randomization, a total of 50 patients were subjected to 30% salicylic acid peel. The mean age of patients in Group A was 21.9 ±3.8 years. Majority 31(62%) belonged to 18 – 22 years. The minimum and maximum age were 18 and 35 years. The details of age distribution is shown in Figure 14.

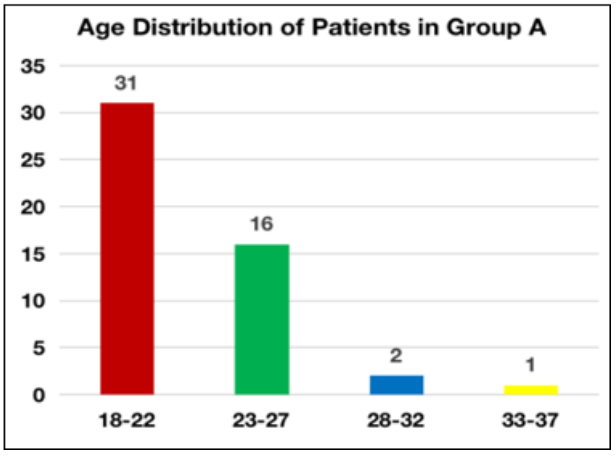

Figure 14: Study participants according to age group in Group A

Gender: A major proportion of the patients enrolled in Group A were Females 36(72%) as shown in Figure 15.

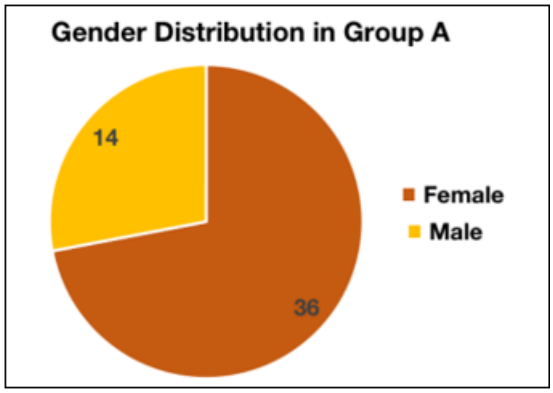

Figure 15: Gender Distribution of study participants in Group A

Occupation: Majority of patients i.e. 26 (52%) enrolled in group A were employed. Around 17(34%) patients were students and 7 (14%) were unemployed as mentioned in Figure 16.

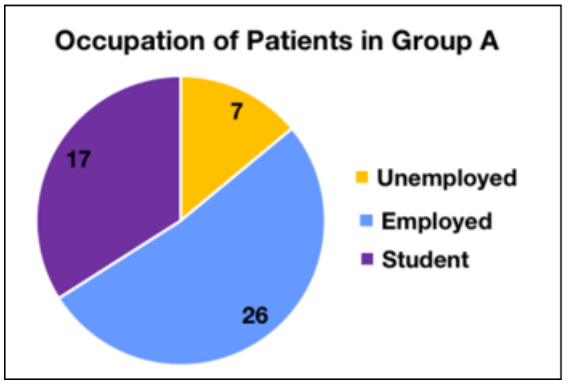

Figure 16: Distribution of study participant in Group A according to Occupation

Grade of Acne Vulgaris :A major set of patients in group A were having Grade II (48%) Acne Vulgaris followed by Grade I (34%) and the least being Grade III (18%) (Figure 17).

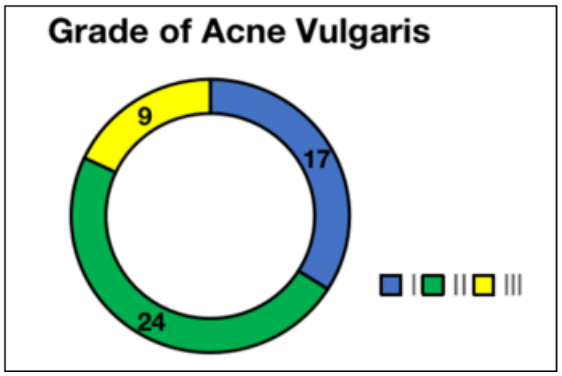

Figure 17: Distribution of study participants in Group A According to Grade

Group B (40% Mandelic Acid Peel)

Age: On Randomization, a total of 50 patients were subjected to 40% Mandelic acid peel. The mean age of patients in Group B was 23.4 ±4.9 years. Majority of them 25 (50%) belonged to 18 – 22 years. The minimum and maximum age were 18 and 39 years. (Figure 18)

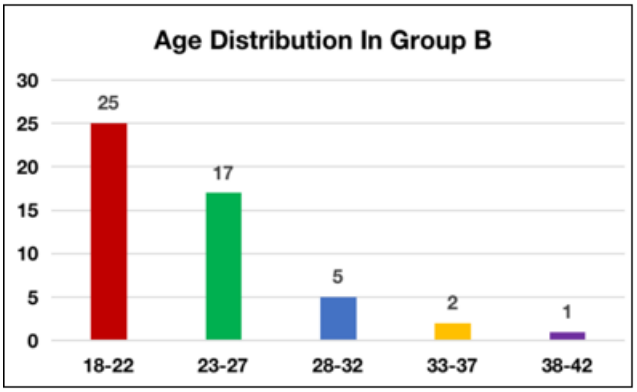

Figure 18: Age group of study participants in Group B

Gender: Major proportion of the study participants enrolled in Group B were also Females 40(80%). (Figure 19)

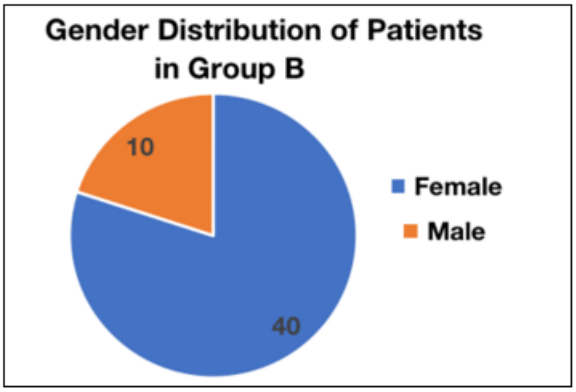

Figure 19: Gender distributions of study participants in Group B

Occupation: Majority i.e. 30 (60%) were employed, 10 (20%) were students and the rest 10 (20%) patients were unemployed as shown in Figure 20

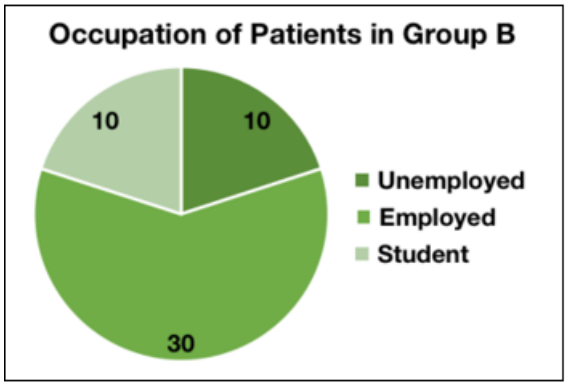

Figure 20: Study participants in Group B according to occupation

Grade of Acne Vulgaris: Most of the patients had Grade 2 (46%) Acne Vulgaris followed by Grade 1(30%). (Figure 21)

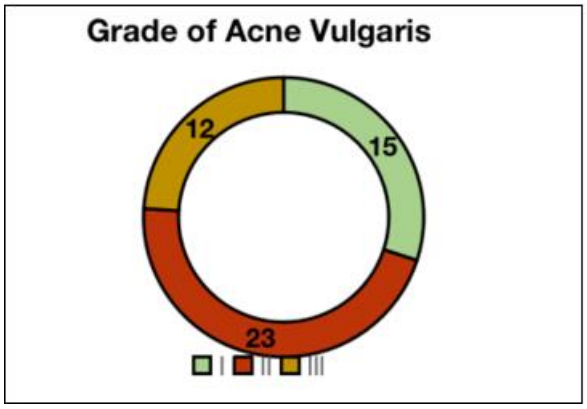

Figure 21: Study participants in Group B according to Grade

II. Side Effects

Burning, dryness and Erythema were the common side effects reported by the patients treated with both salicylic acid and mandelic acid. Among patients treated with salicylic acid, 19 (38%) reported with side effects as mentioned above. Among patients treated with mandelic acid, 16 (32%) reported with these side effects. Burning and erythema were more commonly observed in patients treated with mandelic acid. Whereas, Dryness was more commonly present in those treated with salicylic acid. (Figure 22)

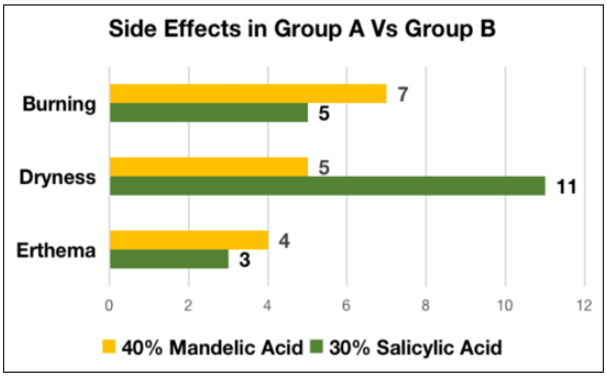

Figure 22: Side Effects in Salicylic acid Vs Mandelic acid

Table 5: Chi Square Test of Significance for Side Effects

Side Effects	Group			P-Value
	Salicylic Acid (n= 50)	Mandelic Acid (n= 50)	Total N= 100	
Erythema				
Present	3 (42.8%)	4(57.2%)	7	0.695
Absent	47 (50.5%)	46 (49.5%)	93	
Dryness				
Present	11 (68.7%)	5 (31.3%)	16	0.101
Absent	39 (46.4%)	45 (53.6%)	84	
Burning				
Present	5 (41.6%)	7 (58.4%)	12	0.538
Absent	45 (51.1%)	43 (48.9%)	88	

III. Michaelson Severity Index Score

Loss to follow up:

Table 6: Loss to follow up among patients in both groups

Group	Loss to follow up			
	Baseline	2 Weeks	4 Weeks	6 Weeks
A (n= 50)	50	50	47	44
B (n= 50)	50	50	47	42

Michaelson Severity Scoring Index was calculated at baseline, 2 weeks, 4 weeks and 6 weeks in both the groups. The mean and standard deviation of severity index at each visit for both the groups is given in the table below. There were significant mean differences observed in the Michaelson Severity Scoring Index at the baseline visit. Though there was reduction in number of lesions in subsequent visits, it was not found to be significant. (Table 7)

Table 7: Unpaired T test: Michaelson Severity Scoring Index (Group A Vs Group B)

Visits	Michaelson Severity Scoring Index		P-Value
	Salicylic Acid (n= 50) Mean ± SD	Mandelic Acid (n= 50) Mean ± SD	
Baseline Visit (1st Visit)	23.07± 8.8	27.4 ±8.3	0.012
At 2 weeks (2nd Visit)	16.4± 6.8	18.9± 6.1	0.063
At 4 weeks (3rd Visit)	11.4± 5.3	12.5± 4.8	0.266
At 6 weeks** (4th Visit)	5.8± 3.8	6.17± 3.5	0.693

3rd Visit: Loss to follow up at 3rd visit. Hence n = 47
** 4th Visit: Loss to follow up in Salicylic acid group: 6; n=44
4th Visit Loss to follow up in Mandelic acid group: 8; n=42
*P Value obtained from Unpaired t test; P<0.05 is statistically significant.

There is reduction in number of lesions in both groups. But in patients treated with salicylic acid the reduction is more than mandelic acid group as evident from the time trend. (Figure 23)

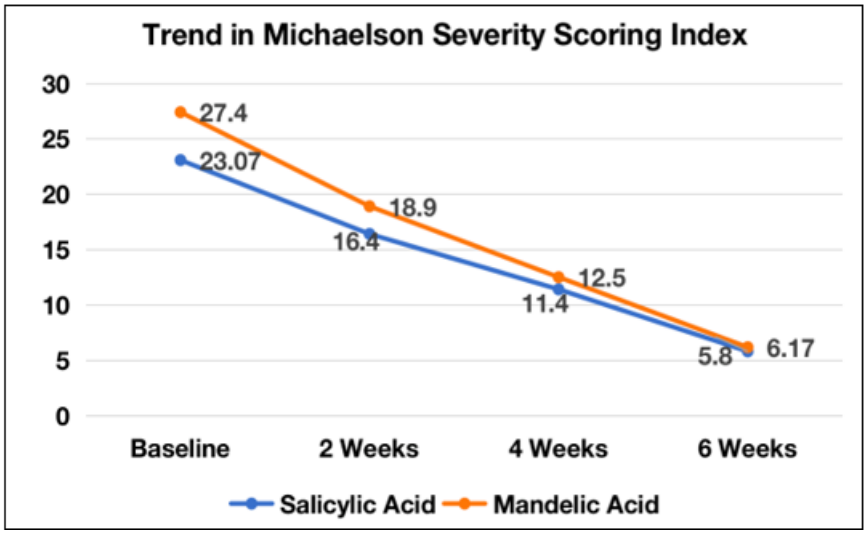

Figure 23: Trend in Michaelson severity scoring inmdex

Photographic Comparison

Group A (30% Salicylic Acid)

BASELINE

4TH VISIT

Group B (40% Mandelic Acid)

BASELINE

4TH VISIT

4. Discussion

This study is a randomized comparative study of efficacy and safety of 40% Mandelic acid with 30% Salicylic acid in Acne vulgaris (Grade I – III).

In a study conducted by Shishira R Jartarkar et al, 50 patients with Acne vulgaris were selected. One half (Group A) were treated with 20% Salicylic acid and other half (Group B) were treated with 30% Mandelic acid. Group A had a lesion reduction of 73.3% and Group B had 65.4% reduction in inflammatory lesions. The non-inflammatory lesion reduction in group A was found to be 39.4% and 27.9% in group B patients respectively.

In this study, most of the patients in group A (62%) and group B (50%) belonged to 18- 22 years of age group. Though the criteria is to include patients up to 60 years of age as a part of study, the oldest patient in this study was aged 39 years. The mean age of presentation in this study in group A is 21.9 years and in group B, it was found to be 23.4 years.

Acne vulgaris affects all genders equally. In this study, a female preponderance was seen as 72% and 80% in group A and group B respectively. A research made by Yi-Chien Yang et al revealed that acne affects females more than males and also the onset in females is said to be late. The findings also showed that acne lesions can last until middle age in both men and women. [3]

Adult acne varies from adolescent acne in terms of gender, according to a research by Nevena Skroza et al. Females are more impacted by adult acne, whereas men are more affected by adolescent acne. Cunliffe et al studied on the prevalence of adult acne and found that acne prevalence was greater in adolescent men compared to adolescent women [4,5].

In this study, 52% of the patients in group A were employed and 60% of employed patients were included in group B. 34% and 20% of patients were students in group A and group B respectively. The rest of the patients were unemployed. Job stress was linked to more severe forms of acne in women in a study, and women with localised acne lesions also reported to have a stressful job [6]. Shadi Zari et al studied on stress and acne showed that female medical students experience acne due to stress [7].

Most of the patients included in this study belonged to Grade II in both the groups. In group A, 48% of the patients and in group B 46% of patients had grade II acne vulgaris. Grade I was found to be the second commonest grade in both the groups and the least was found to be Grade III. In a study conducted by Nevena Skroza et al, the most common form of acne was "moderate acne," which was was seen in both male and female patients of adolescent and adulthood; the least common form was severe acne in all groups. Adult acne typically manifests itself morphologically as papules and pustular lesions on the chin. In contrast to acne occurring in the adolescent age bracket, adult acne usually develops over time and is mild to moderate in severity. [5].

A total of 14 patients out of 100 were lost on follow up during the study. In group A, among 6 patients that were lost, 3 were lost at 3rd visit and 3 during 4th visit. In group B, out of 8 patients that were lost on follow up, 3 were during the 3rd visit and 5 were lost on 4th visit. On follow up over phone, the reason cited by 11 out of 14 patients to lose on follow up was moving out of the city and 2 patients were diagnosed with Covid-19 and were quarantined for the same and 1 patient was unable to reach or contact.

Side effects that were most commonly reported in our study are erythema, burning or stinging sensation and dryness. Out of 50 patients in group A, 19 patients (38%) experienced side effects. The most common side effect experienced by patients treated with Salicylic acid peel was dryness. 10% of the patients experienced burning and 6% of patients had post peel erythema in group A. Out of 50 patients in group B, 14% experienced burning and 10% patients had dryness. Post peel erythema was the least common side effect reported in patients treated with 40% Mandelic acid peel (group B). Only 6% patients reported erythema in group B. In this study, the side effects were comparatively less in group B.

The side effects of Salicylic acid peel in this study were similar to the study conducted by Shishira J et al. Zhang et al studied on salicylic acid peel and has revealed that Salicylic acid peel reduces sebum secretion which could plausibly cause dryness in patients treated with Salicylic acid peel [129]. Lee HS et al has reported that erythema and dryness to be a common side effect of Salicylic acid peel in his study conducted on Asian patients [9,10]. Grimes et al revealed that patients treated with Salicylic acid peel also experienced peeling of the skin, crusting and also xerosis in dark skinned individuals [11].

The mean MSS index in this study in group A is 23.07±8 on the first visit and the mean MSS index on the 4th visit was 5.8±3.8. There was significant reduction in MSS index in group A. The mean MSS index in group B during baseline visit was 27.4±8.3 and the mean MSS index

during 4th visit was found to be 6.17±3.5. Though the MSS index decreased in group B, it decreased significantly in group A during the course of the study, making Salicylic acid a better peel agent for Acne vulgaris, even though the difference was not statistically significant.

In mild-to-moderate facial AV, a 45 percent Mandelic acid peel was shown to be equally efficacious as a 30 percent SA peel. The safety and tolerability of the Mandelic acid peel, on the other hand, was superior to that of the Salicylic acid peel in research done by Surabhi Dayal et al [12].

5. Limitations

This study had a few limitations. This study included patients for a shorter time period of 8 weeks. The study period if increased 12 to 16 might yield different results. Secondly, the study did not investigate the peel agent for Grade IV acne even though chemical peels are utilised in clinical practise for grade IV.

6. Conclusion

Acne vulgaris is a very frequent dermatosis that dermatologists see on a daily basis. Acne vulgaris is most common among teenagers, however it can afflict anybody of any age and both sexes. Acne vulgaris is a persistent, obstructive and inflammatory condition of the pilosebaceous unit. While acne is not life threatening, it can have a substantial psychological impact on persons of a specific age group due to scarring and facial disfigurement, lowering their quality of life. It is critical for primary care doctors to recognise and address the psychological consequences of acne.

In our study, most of the patients, i.e. 62% in group A and 50% in group B were in the age group of 18-22 years, proving the fact that acne vulgaris is a disorder of adolescents and young adults. This study also calculate gender distribution of acne and females outnumbered males in this study. 72% of group A patients were female and 80% of group B study population were females. The patients in this study come from a variety of occupational backgrounds.

Group A patients had a significant reduction in the lesion count than group B patients. The reduction was not statistically significant. The safety and tolerability was superior in group B patients than group A patients though statistically not significant. The most common side effect reported in group A patients was dryness. Dryness and burning were the common side effects in group B patients.

On basis of MSS index and clinical appearance, 30% Salicylic acid peel showed better results in clearing acne lesions in 4 sittings inspite of the fact that 40% Mandelic acid had better safety and tolerability in the study population.

Finally, chemical peels of a shallow to medium depth are effective supportive therapy in patients with acne vulgaris. They efficiently address the several elements that contribute to the onset of this common skin disease while also enhancing the efficacy of other topical treatments. Nonetheless, the advantages and drawbacks vary by racial group, and great care must be taken while dealing with dark-skinned patients.

Abbreviations

IPL- Intense Pulse Light, MSS-Michaelson Severity Scoring Index, OCPs- Oral Contraceptives, PDT- Photo Dynamic Therapy.

Data Sharing Statement

The data produced and analysed for this study are available from the corresponding author upon reasonable request.

Ethical Consideration and Confidentiality

The study was commenced after obtaining the approval from institutional human ethics committee. The study was registered in CTRI and the registration number for this trial is CTRI/2021/07/035095. The study participants were conveyed about the motive of this study. Confidentiality of the study participants was protected throughout the stages of the study.

Disclosure

The authors report no conflicts of interest in this work.

References

[1] Aydemir EH. Acne vulgaris. Turk Pediatri Ars. 2014;49(1):13-16. Published 2014 Mar 1. doi:10.5152/tpa.2014.1943
[2] Ghorpade A, Reddy B. Acne Vulgaris. Indian J Dermatol Venereol Leprol 1982;48:260-267
[3] Yang, Y. C., Tu, H. P., Hong, C. H., Chang, W. C., Fu, H. C., Ho, J. C., Chang, W. P., Chuang, H. Y., & Lee, C. H. (2014). Female gender and acne disease are jointly and independently associated with the risk of major depression and suicide: a national population-based study. BioMed research international, 2014, 504279. https://doi.org/10.1155/2014/504279
[4] Cunliffe W J, Gould DJ. Prevalence of facial acne vulgaris in late adolescence and in adults. Br J Med. 1979;1(6171):1109–1110
[5] Skroza, N., Tolino, E., Mambrin, A., Zuber, S., Balduzzi, V., Marchesiello, A., Bernardini, N., Proietti, I., & Potenza, C. (2018). Adult Acne Versus Adolescent Acne: A Retrospective Study of 1,167 Patients. The Journal of clinical and aesthetic dermatology, 11(1), 21–25.
[6] Dréno B, Thiboutot D, Layton AM, et al. Global Alliance to Improve Outcomes in Acne Large-scale international study enhances understanding of an emerging acne population: adult females. J Eur Acad Dermatol Venereol. 2015;29(6):1096–1106.
[7] Zari, S., & Alrahmani, D. (2017). The association between stress and acne among female medical students in Jeddah, Saudi Arabia. Clinical, cosmetic and investigational dermatology, 10, 503–506. https://doi.org/10.2147/CCID.S148499

[8] Zhang, L., Shao, X., Chen, Y., Wang, J., Ariyawati, A., Zhang, Y., Chen, J., Liu, L., Pu, Y., Li, Y., & Chen, J. (2022). 30% supramolecular salicylic acid peels effectively treats acne vulgaris and reduces facial sebum. Journal of cosmetic dermatology, 10.1111/jocd.14799. Advance online publication. https://doi.org/10.1111/jocd.14799

[9] Arif T. (2015). Salicylic acid as a peeling agent: a comprehensive review. Clinical, cosmetic and investigational dermatology, 8, 455–461. https://doi.org/10.2147/CCID.S84765

[10] Lee HS, Kim IH. Salicylic acid peels for the treatment of acne vulgaris in Asian patients. Dermatol Surg. 2003;29:1196–1199.

[11] Grimes PE. The safety and efficacy of salicylic acid chemical peels in darker racial-ethnic groups. Dermatol Surg. 1999;25:18–22.

[12] Dayal, S., Kalra, K. D., & Sahu, P. (2020). Comparative study of efficacy and safety of 45% mandelic acid versus 30% salicylic acid peels in mild-to-moderate acne vulgaris. Journal of cosmetic dermatology, 19(2), 393–399. https://doi.org/10.1111/jocd.13168