

## Dermatological Effects of Different Keratolytic Agents on Acne Vulgaris

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Received date: March 24, 2016; Accepted date: April 18, 2016; Published date: April 25, 2016

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### Abstract

Acne vulgaris is a chronic inflammatory skin disease; it's one of the most common skin disorders and affects mainly adolescents and young adults. Keratolytic agents are widely used in treatment of acne from several years. In this study we aimed to evaluate and compare the cutaneous response of different keratolytic agents in management of acne vulgaris. Ninety patients were selected among those attending the outpatient dermatology clinic in AD-Dwadmi hospital during the period from October 2015 to February 2016. The selected patients had different forms of acne vulgaris, papulo-pustular, comedonal and post acne scar. Three types of keratolytic agents were used, glycolic acid 50%, salicylic acid 20% and jessner solution. In papulopustular lesions, the three agents were effective with non-significant difference between them; however, there was more excellent results with jessner solution (70 % of patients) then glycolic acid (50%) and lastly salicylic acid (40%). According to the clinical efficacy of used keratolytic agents in comedonal lesions, all lines were found to be effective and there was non-significant difference between the 3 studied groups, however there was more excellent results with salicylic acid (80%) then glycolic acid (60%) and lastly Jessner solution (50%). According to the clinical efficacy of all keratolytic agents in acne scar lesions, there was significant difference between the 3 studied groups. Both jessner and salicylic acid were non effective, however glycolic acid was moderately effective (30% showed excellent results and 40% showed good results). Minimal complications were noticed with all the agents used. More erythema was recorded with jessner solution. However there was significant difference between all keratolytic agents as regards the incidence of visible exfoliation where glycolic acid showed least visible exfoliation (only 40% of cases) followed by jessner solution (66.7%) and lastly salicylic acid (80%).

**Keywords:** Acne vulgaris; Salicylic acid; Glycolic acid; Jessner solution

### Introduction

Acne vulgaris is chronic inflammatory skin disease; it's one of the most common skin disorders. The presence of facial and shoulder lesions, pustules, pimples and sometime abscess accompanied by disease can produce a psychological burden on the patients [1]. Combination of several factors such as hormonal changes, excessive production of sebum and accumulation of exfoliates; allow bacterial growth resulting in the inflammation of the skin [2]. Acne affects mainly adolescents and young adults, with up to 90% of adolescents affected by acne at some stage. In addition, 5% of adults suffer from persistent or late onset acne [3]. Regarding to the prevalence of acne, studies show that more than 20% of adolescents with acne seek help from medical professionals. Instead, individuals either do not treat their acne or self-treat with over the counter products [4].

Salicylic acid belongs to  $\beta$ -hydroxy acids Pka3 which is most widely used in common skin disease like acne, psoriasis, warts, corn and calluses. It used mainly for its keratolytic, bacteriostatic, fungicidal, and photoprotective properties by different concentrations vary from 0.5% to 60% in topical preparation [5]. It exerts its function by reduce the rate of keratinocyte proliferation and inhibits cholesterol sulfotransferase enzyme which is responsible for cholesterol sulfate formation within keratinocytes, also salicylic acid directly solubilizes the stratum corneum by dissolving the intercellular cement [6].

There are five main alpha hydroxy acids, which is a group are known as "fruit acids". Glycolic acid (pKa 3.83) is the smallest molecule produced from sugar cane. So, it is the best to penetrate the epidermis and it has the greatest utility with valuable keratolytic action [7]. Lactic, malic, tartaric and citric acids are also used and comes from sour milk, tomato juice, grapes, and citrus fruits respectively. Glycolic acid is used to increase collagen, mucopolysaccharide, and hyaluronic acid production and increase skin thickness by concentrations range from 20% to 70% either in the free acid form or in the partially neutralized form. Glycolic acid is effective in treatment of inflammatory and non-inflammatory lesions of acne due to its antimicrobial and antioxidant action, also it can correct the hyperkeratinization found in acne [8].

Jessner solution is prepared by Max Jessner and composed of 14% salicylic acid, 14% lactic acid, and 14% resorcinol in 95% ethanol. The solution is stable for up to 6 months, but due to salicylic acid photosensitivity it must kept in amber glass containers. The presence of salicylic acid and resorcinol gives the solution keratolytic and anti-microbial activity also, lactic acid provide epidermolysis action so, the solution suitable for comedonal acne, post-inflammatory hyperpigmentation, mild melasma, and photoaging [9].

The aim of this study was to evaluate and compare the cutaneous response of different keratolytic agents in management of acne vulgaris.

## Patients and Methods

### Patients

Ninety patients with acne vulgaris were selected among those attending the outpatient dermatology clinic in AD-Dwadmi hospital during the period from October 2015 to February 2016. The selected patients had different forms of acne vulgaris include papulo-pustular, comedonal and post acne scar. patients who had history of photosensitivity, keloid formation, poor wound healing, immunosuppression, kidney or liver disease, recurrent herpes simplex, , dermabrasion or isotretinoin therapy in the past year were excluded from this study. The selected 90 patients were divided into 3 groups according to the used keratolytic agents, each group contains 30 patients as follows:

- Group I: This group include 30 patients treated with glycolic acid 50%.
- Group II: This group include 30 patients treated with salicylic acid 20%.
- Group III: This group include 30 patients treated with jessner solution.

According to the predominant acne lesion, each group was subdivided into 3 subgroups as follows:

- Ten patients with predominate papulo-pustular lesions.
- Ten patients with predominate comedonal lesions.
- Ten patients with acne scar lesions.

### Methods

Medical history was taken from each patient to complete the exclusion criteria mentioned above.

Clinical examination was done for each patient and the numbers of lesions were evaluated after every session, adverse effects and benefits were explained to all patients and agreement was obtained from every patient. Each patient received eight weekly sessions and therapeutic regimen as the following:

**Pretreatment instructions:** To ensure accurate evaluation of efficacy and safety of each of the keratolytic agents used, all patients were prohibited from treatment of acne for at least four weeks before the first session; prevent topical retinoin, hydroquinone derivatives or any other preparations used in treatment of acne. In addition, before 24 hours from starting session, the patients instructed to stop using make up, moisturizer, conditioner or spray.

#### Preparation and application of keratolytic agents

**Glycolic acid (50%):** 50 grams of glycolic acid crystals were dissolved in distilled water to form 100cc of 50% solution (wt./vol.) and saved in appropriate bottles.

**Application:** Glycolic acid was applied on the face rapidly after degreasing the skin by scrubbing with cotton gauze soaked in alcohol 75% (to promote more uniform penetration) starting with forehead then cheeks followed by the nose, and chin using cotton applicator within about 30 seconds. After 2 to 4 minutes washing by copious water soaked gauze then splashed water to ensure complete removal of the acid.

**Salicylic acid 20%:** 20 gram of salicylic acid crystals were dissolved in 95% alcohol to form 100cc of 20% solution (wt./vol.) and saved in dark amber containers.

**Application:** The skin was degreased as mentioned above and salicylic acid was applied using square cotton gauze starting with forehead and cheeks then chin, nose and lower eyelids within 30 seconds. At that time, patient was suffering from a stinging and burning sensation which increased during the next 2 minutes, reached maximum at 3 min and then rapidly decreased to baseline over the next minute; this is considered the end point. After application of salicylic acid it leaves white precipitate on the surface of the face which called salicylic acid frost due to evaporation of hydroethanolic vehicle so, penetration of the active agent is diminished. At this point, the agent causes a superficial anesthesia to light touch and the patient is instructed to wash the face with water.

**Jessner solution:** 14 gram of resorcinol, 14 gram of salicylic acid, and 14 ml of 85% lactic acid mixed in enough 95% ethanol to bring the quantity to 100 cc and saved in dark amber containers.

**Application:** The skin was degreased as mentioned above and the solution was applied rapidly covering the entire face starting with forehead then cheeks followed by the nose then upper lip and chin within 30 seconds with a cotton applicator. If no frost appears a second coat of the solution was applied until frost appeared.

**Post application instructions:** The patient was instructed to avoid extensive sun exposure, prevent the use of any topical preparations except the sunscreens or moisturizers, wash the treated area very carefully two times daily with non-irritating soap and male patients could shave after 3 days from the session.

The results were evaluated by clinical investigator during the eight sessions and based on evaluation of efficacy of treatment and beginning of improvement were encountered through doctor opinion, where the mean value of two different physicians opinions in percent was calculated and registered before asking the patient. Also, patient's opinions were taken and the mean value of the two opinions (doctors and patients) was calculated as the efficacy of this particular treatment. Improvement from baseline was rated on a four-point scale by both patient and physician at each visit where excellent with total improvement greater than 74%, good with total improvement greater 49%, fair with total improvement from 50% to 20% and no response with total improvement less than 20%.

Safety was evaluated by the assessment of the appearance of any side effects like erythema, discomfort (burning, itching), visible exfoliation, post inflammatory hyperpigmentation, each visit on a four-point scale for severity assessment (severe= +++, moderate= ++, mild= +, none= -).

### Statistical analyses

All statistical analyses were performed using SPSS (version 19). Statistical differences among the experimental groups were assessed by ANOVA. Duncan's test was used as a follow-up test and significance was defined at  $p < 0.05$ .

### Results

According to the age distribution in studied patients, there was non-significant difference ( $P > 0.05$ ) between the three groups (glycolic acid group, salicylic acid group and jessner solution group). The mean age

was 21.03 ± 2.52, 24.23 ± 4.08, 22.56 ± 4.46 in glycolic acid group, salicylic acid group and jessner solution group respectively (Table 1).

Age	Studied groups			P value
	Glycolic acid 50% (n=30)	Salicylic acid 20% (n=30)	Jessner solution (n=30)	
Age in years (X ± SD)	21.03 ± 2.52	24.23 ± 4.08	22.56 ± 4.46	p>0.05

**Table 1:** Age distribution between studied groups.

According to the sex distribution in studied patients, there was non-significant difference (P>0.05) between the 3 studied groups. In the glycolic acid group there was 8 males (26.6%) and 22 females (73.4%),

in salicylic acid group there was 5 male (16.6%) and 25 females (83.4%) while there was 7 males (23.3%) and 23 females (76.7%) in Jessner group (Table 2).

Sex	Studied groups						Total (n=90)		p-value
	Glycolic acid 50% (n=30)		Salicylic acid 20% (n=30)		Jessner solution (n=30)		No.	%	
	No.	%	No.	%	No.	%			
Male	8	26.6	5	16.6	7	23.3	20	22.2	P>0.05
Female	22	73.4	25	83.4	23	76.7	70	77.8	
Total	30	100	30	100	30	100	90	100	

**Table 2:** Sex distribution between studied groups.

Table 3 shows that there was non-significant difference (P>0.05) between the 3 studied groups as regards the skin type. In the glycolic acid group, there were 14 patients (46.6%) of skin type III and 16 patients (53.4%) of skin type IV, while in salicylic acid group there

were 18 patients (60%) of skin type III and 12 patients (40%) of skin type IV. In Jessner group there were 17 patients (56.6%) of skin type III and 13 patients (43.4%) of skin type IV.

Skin type	Studied groups						Total (n=90)		p-value
	Glycolic acid 50% (n=30)		Salicylic acid 20% (n=30)		Jessner solution (n=30)		No.	%	
	No.	%	No.	%	No.	%			
III	14	46.6	18	60	17	56.6	49	54.4	P>0.05
IV	16	53.4	12	40	13	43.4	41	45.6	
Total	30	100	30	100	30	100	90	100	

**Table 3:** Skin type distribution between studied groups.

In papulopustular lesions, the three agents were effective with non-significant difference (P>0.05) between them, however there was more

excellent results with Jessner solution (70 % of patients) then glycolic acid (50%) and lastly salicylic acid (40%) (Table 4).

Clinical efficacy	Studied groups						Total (n=30)		p-value
	Glycolic acid 50% (n=10)		Salicylic acid 20% (n=10)		Jessner solution (n=10)		No.	%	
	No.	%	No.	%	No.	%			
Excellent	5	50	4	40	7	70	16	53.3	P>0.05
Good	3	30	2	20	2	20	7	23.3	
Fair	2	20	2	20	1	10	5	16.6	
No response	0	0	2	20	0	0	2	6.8	

<b>Total</b>	10	100	10	100	10	100	30	100
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**Table 4:** Clinical efficacy of used keratolytic agents in papulopustular lesions.

According to the clinical efficacy of used keratolytic agents in comedonal lesions, all lines were found to be effective and there was non-significant difference ( $P>0.05$ ) between the 3 studied groups, however there was more excellent results with salicylic acid (80%) than glycolic acid (60%) and lastly Jessner solution (50%) (Table 5).

Clinical efficacy	Studied groups						Total (n=30)		p-value
	Glycolic acid 50% (n=10)		Salicylic acid 20% (n=10)		Jessner solution (n=10)		No.	%	
	No.	%	No.	%	No.	%			
<b>Excellent</b>	6	60	8	80	5	50	19	63.3	P>0.05
<b>Good</b>	3	30	2	20	3	30	8	26.6	
<b>Fair</b>	1	10	0	0	2	20	3	10	
<b>No response</b>	0	0	0	0	0	0	0	0	
<b>Total</b>	10	100	10	100	10	100	30	100	

**Table 5:** Clinical efficacy of used keratolytic agents in comedonal lesions.

According to the clinical efficacy of all keratolytic agents in acne scar lesions, there was significant difference ( $P<0.05$ ) between the 3 studied groups. Both Jessner and salicylic acid were non effective, however glycolic acid was moderately effective (30% showed excellent results and 40% showed good results) (Table 6).

Clinical efficacy	Studied groups						Total (n=30)		p-value
	Glycolic acid 50% (n=10)		Salicylic acid 20% (n=10)		Jessner solution (n=10)		No.	%	
	No.	%	No.	%	No.	%			
<b>Excellent</b>	3	30	0	0	0	0	3	10	P1<0.05; P2>0.05; P3<0.05; PT<0.05
<b>Good</b>	4	40	0	0	0	0	4	13.3	
<b>Fair</b>	1	10	1	10	4	40	6	20	
<b>No response</b>	2	20	9	90	6	60	17	56.7	
<b>Total</b>	10	100	10	100	10	100	30	100	

**Table 6:** Clinical efficacy of used keratolytic agents in acne scar lesions.

Table 7 shows that there was non-significant difference ( $P>0.05$ ) between the 3 studied groups as regards the clinical efficacy of the used keratolytic agents in treating all acne lesions as a whole.

Clinical efficacy	Studied groups						Total (n=90)		p-value
	Glycolic acid 50% (n=30)		Salicylic acid 20% (n=30)		Jessner solution (n=30)		No.	%	
	No.	%	No.	%	No.	%			
<b>Excellent</b>	14	46.6	12	40	12	40	38	42.2	P>0.05
<b>Good</b>	10	33.3	4	13.3	5	16.6	19	21.1	
<b>Fair</b>	4	13.3	3	10	7	23.3	14	15.5	

No response	2	6.6	11	36.6	6	20	19	21.1	
Total	30	100	30	100	30	100	90	100	

**Table 7:** Clinical efficacy of used keratolytic agents in all acne lesions.

In the current study, minimal complications were noticed with all the keratolytic agents used. More erythema was recorded with Jessner solution. However, there was no significant difference (P>0.05) between all keratolytic agents as regards the incidence of discomfort, hyperpigmentation (Tables 8-10).

Erythema	Studied groups						Total (n=90)		p-value
	Glycolic acid 50% (n=30)		Salicylic acid 20% (n=30)		Jessner solution (n=30)		No.	%	
	No.	%	No.	%	No.	%			
None	9	30	11	36.6	4	13.3	24	26.6	P>0.05
Mild	16	53.3	15	60	18	60	49	54.4	
Moderate	4	13.3	4	20	6	20	14	15.5	
Severe	1	3.3	0	6.7	2	6.7	3	3.5	
Total	30	100	30	100	30	100	90	100	

**Table 8:** Comparison between keratolytic agents regarding incidence of erythema in studied groups of patients.

Discomfort	Studied groups						Total (n=90)		p-value
	Glycolic acid 50% (n=30)		Salicylic acid 20% (n=30)		Jessner solution (n=30)		No.	%	
	No.	%	No.	%	No.	%			
None	24	80	21	70	20	66.6	65	72.2	P>0.05
Mild	3	10	4	13.3	6	20	13	14.4	
Moderate	2	6.6	3	10	3	10	8	8.8	
Severe	1	3.4	2	6.6	1	3.4	4	4.6	
Total	30	100	30	100	30	100	90	100	

**Table 9:** Comparison between keratolytic agents regarding incidence of discomfort in studied groups of patients.

Hyperpigmentation	Studied groups						Total (n=90)		p-value
	Glycolic acid 50% (n=30)		Salicylic acid 20% (n=30)		Jessner solution (n=30)		No.	%	
	No.	%	No.	%	No.	%			
Negative	28	93.3	27	90	26	86.6	81	90	P>0.05
Positive	2	6.7	3	10	4	13.3	9	10	
Total	30	100	30	100	30	100	90	100	

**Table 10:** Comparison between keratolytic regarding incidence of hyperpigmentation in studied groups of patients.

Comparing the used keratolytic agents regarding the incidence of visible exfoliation, there was significant difference between the 3 studied groups. There was significant difference between glycolic acid group and salicylic acid group (P<0.05). There was significant difference between glycolic acid group and Jessner group (P<0.05), while there was non-significant difference between Jessner group and salicylic acid group (P>0.05). So, glycolic acid shows less visible exfoliation than the other two solutions (Table 11).

Visible exfoliation	Studied groups						Total (n=90)		p-value
	Glycolic acid 50% (n=30)		Salicylic acid 20% (n=30)		Jessner solution (n=30)		No.	%	
	No.	%	No.	%	No.	%			
Negative	18	60	6	20	10	33.3	34	37.7	P1<0.05; P2<0.05; P3>0.05; PT<0.05
Positive	12	40	24	80	20	66.7	56	62.3	
Total	30	100	30	100	30	100	90	100	

**Table 11:** Comparison between keratolytic agents regarding incidence of visible exfoliation in all groups of patients.

Comparing the 3 studied groups as regards the onset of difference (P>0.05) between them; however there was little more rapid improvement expressed in sessions, there was non-significant improvement with Jessner solution (Table 12).

Onset of improvement	Studied groups						Total (n=90)		p-value
	Glycolic acid 50% (n=30)		Salicylic acid 20% (n=30)		Jessner solution (n=30)		No.	%	
	No.	%	No.	%	No.	%			
2 sessions	5	16.6	2	6.6	4	13.3	11	12.2	P>0.05
3-4 sessions	7	23.3	5	16.6	10	33.3	22	24.4	
5-8 sessions	16	53.3	12	40	10	33.3	38	42.2	
No improvement after 8 sessions	2	6.8	11	36.8	6	20	19	63.5	
Total	30	100	30	100	30	100	90	100	

**Table 12:** Comparison between chemical peelers regarding the onset of improvement in studied groups of patients.

## Discussion

Acne vulgaris is one of the most common chronic recurrent diseases of the skin, caused by changes in the pilosebaceous units [10].

Acne vulgaris exhibits hyperkeratinization and formation of a plug of keratin and sebum in the earliest stage. Increase in sebum production and enlargement of sebaceous glands occur with increased androgen production at adrenarche. Increased sebum production provides an environment for the overgrowth of bacteria which can cause inflammation [11].

Keratolytic agents involves the topical application of a chemical agent in order to produce a controlled injury to specific depth, thus allowing subsequent regeneration of the skin and inhibit a build-up of dead skin cells which combine with skin oil to block pores. It also helps to unblock already clogged pores which can result in improved texture, provide more homogeneous pigmentation, and less wrinkling. It is a relatively low-cost, simple procedure, and healing thereafter is usually quite rapid [12].

This study aimed to evaluate and compare the efficacy of salicylic acid 20 %, glycolic acid 50 % and jessner solution in the management of acne vulgaris.

This work was carried out on ninety patients selected among those attending the outpatient dermatology clinics in AD-Dwadmi hospital during the period from October 2015 to February 2016. The selected patients had different forms of acne vulgaris; papulo-pustular, comedonal and post acne scar.

This study included 70 female and 20 male. The high number of females noted in this study may be attributed to the fact that females are usually more aware about their images, so they complain more and earlier.

In the current study the used agents were effective in papulopustular lesions with non-significant difference between them; however the excellent results were noted in 7 cases in jessner solution group, 5 cases in glycolic acid group and 4 cases in salicylic acid group.

These results were in accordance with the results of Kim et al.,[13] who reported that both jessner solution and glycolic acid were effective in the management of papulopustular lesions. Also Lee and Kim, [14] had reported the efficacy of salicylic acid in the treatment of papulopustular lesions.

In 2003, Cotellessa [9] explained the efficacy of jessner solution in the management of papulopustular lesions as it has keratolytic and anti-inflammatory action. In addition, Briden et al. [15] found that glycolic acid seemed to add distinct benefit to standard acne treatment regimens in all types of acne as it diminishes corneocyte cohesion with subcorneal epidermolysis leading to normalization of follicular keratinisation and opening of comedones , and lead to unroofing of pustules. However, in contrary to our results, Grover and Reddu [16] found that glycolic acid was not effective in the same issue.

In this study the used keratolytics were found to be effective in comedonal lesions, and there was non-significant difference between the 3 studied groups, however excellent results were noted in 8 cases in

salicylic acid group, 6 cases in glycolic acid group and 5 cases in jessner solution group.

These results were in accordance with the study of Bari et al., [17] who found that salicylic acid was the most effective agent in the treatment of comedonal acne. Also Strauss et al., [18] mentioned that both glycolic acid and salicylic acid keratolytics were equally effective in the treatment of comedonal acne. This was explained by Koppel et al. [19] as the efficacy of salicylic acid may be due to being lipophilic, keratolytic, and anti-inflammatory.

According to the clinical efficacy of used keratolytics in acne scar lesions, there was significant difference between the 3 studied groups. Both Jessner and salicylic acid were non-effective; however glycolic acid was moderately effective.

These results were in accordance with the results of James [10], who found that 70% glycolic acid was significantly effective in the treatment of post acne scars.

In contrary to result of this study, Artz and Dinner [20] showed that all superficial chemical peelers were non effective in the treatment of post acne scars.

In this study there was non-significant difference between the different keratolytic agents used regarding the incidence of erythema. However jessner solution showed more erythema than the other two solutions. This was in accordance with Carniol et al. [21], who stated that glycolic acid and salicylic acid and jessner solution are effective method in the treatment of many skin diseases as acne vulgaris with minimal side effects.

Also, Alam et al. [22] reported that AHAs have high efficacy and safety in different varieties of skin types without serious adverse effects.

In contrary to the previous report, Song et al. [23] reported that glycolic acid application caused increased sensitivity to UVA and UVB light, thus cause erythema.

In this study there was non-significant difference between the used agents regarding the incidence of discomfort between the 3 studied groups. This was in accordance with Khunger et al. [24], who stated that glycolic acid well tolerated safe and effective therapy in treatment of many types of skin lesions even in dark skinned individuals.

Comparing the used keratolytics regarding the incidence of hyperpigmentation, there was non-significant difference between the 3 studied groups. This was supported by Briden [25], who stated that glycolic acid, salicylic acid and Jessner solution exhibit great flexibility over a range of skin types and conditions so they can be used on most body regions with minimal to no complications.

## Conclusion

Keratolytic agents show rapid improvement in the treatment of acne vulgaris if compared with other lines of treatment which have been used previously as other topical and systemic agents used in treating acne. Glycolic acid 50%, salicylic acid 20% and Jessner solution are effective and safe in the treatment of papulopustular and comedonal acne, however, jessner solution is better in papulopustular lesions and Salicylic acid is better in comedonal lesions. Both salicylic acid 20% and jessner solution are ineffective in the treatment of post acne scar, however, glycolic acid 50% is moderately effective in the treatment of the same lesions.

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