Original Research Article "A COMPARATIVE STUDY OF EFFICACY OF TOPICAL CLINDAMYCIN 1% GEL V/S TOPICAL DAPSONE 5% GEL IN THE TREATMENT OF ACNE VULGARIS"

Dr. Akhil Shah¹, Dr.Parikshit Sharma², Dr.Jitendra Raghuwanshi³, Dr. Aayushi Mehra⁴, Dr. Ishan Bansal^{5*}, Dr. Janak Bhindia⁶

¹Professor, Department Of Dermatology, Index Medical College Hospital & Research Centre, Indore,(MP)452016

²Professor & HOD, Department Of Dermatology, Index Medical College Hospital & Research Centre, Indore, (MP)452016

³Junior Resident, Department Of Dermatology, Index Medical College Hospital & Research Centre, Indore (MP)452016

⁴Junior Resident, Department Of Dermatology, Index Medical College Hospital & Research Centre, Indore (MP)452016

⁵Skin Specialist civil hospital Talwandi sabo district Bathinda Punjab 151302 ⁶Junior Resident, Department Of Dermatology, Index Medical College Hospital & Research Centre, Indore

Corresponding Author: Dr. Ishan Bansal

Skin Specialist civil hospital Talwandi sabo district Bathinda Punjab 151302

Abstract

AIM : To compare Efficacy of Clindamycin 1% gel v/s Dapsone 5% gel in the Treatment of Mild to moderate acne vulgaris .

METHODOLOGY: An prospective observational study was conducted in Dermatology department of IMCHRC Indore for a period of 18 months. All the adult patients with complaints suggestive of Patients of Mild to Moderate acne vulgaris. A total of 100 patients were involved in the study.

RESULTS we can infer that when used as monotherapy, topical dapsone gel was found to be more effective in reducing the grade of acne when compared to topical clindamycin gel. The probable reason for this is the additional anti-inflammatory action of dapsone compared to the only anti bacterial action of clindamycin.

Although dapsone gel was marketed as a novel drug, we in our study did not find any statistically significant results in favour of dapsonegel.

CONCLUSION:In conclusion, topical dapsone gel was found to be more effective in reducing the grade of acne when compared to topical clindamycin gel.However, more research on this topic with more number of patients & longer follow ups are required for assessing the effects of the drug on the quality of life.

1. INTRODUCTION

Despite being regarded as a benign condition, it can have a severe psychological impact on patients, particularly in those who have permanently disfiguring scars⁽¹⁾

Adult acne, however, was truly believed to be a contagious disease that could transfer from one person to another in the absence of any medical research or adequate information⁽²⁾.

The pilosebaceous units (hair follicles and the sebaceous glands that surround them), which are a frequent skin disorder known as acne vulgaris (AV), are affected ⁽³⁾.

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE1, 2024

Acne vulgaris is the eighth most common skin disorder, with an estimated prevalence of 9.38% in people of all ages, according to the Global Burden of Diseases⁽⁴⁾.

Clinically, it is differentiated by pleomorphic types of lesions such papules, comedones, pustules, nodules, and cysts. It is an inflammatory disorder .

The most typically impacted areas are the face, chest, and back. Scarring, pigmentary changes, and post-inflammatory macules can all happen.

It is typically a self-limiting illness⁽⁵⁾. Due to its protracted course, pattern of recurrence and relapse, and signs like severe outbreaks or slow start, acne is regarded as a chronic disease⁽⁶⁾.

Acne is caused by the sebaceous glands being oversensitive to a normal level of androgens in the blood, which P. acnes and inflammation exacerbate.

Cutibacterium acnes causes acne vulgaris to appear throughout adolescence when dehydroepiandrosterone (DHEA) is naturally circulating in the blood (DHEA)⁽⁷⁾.

Over 95% of adolescentboys and 85% of adolescent girls suffer with acne at some point in their lives. Nearly 20% of these adolescents have moderate-to-severe acne, and up to 50% of them still have acne as adults⁽⁶⁾.

Acne problems were directly caused by excessive oil production, pores getting clogged by gummy skin cells, germs, and irritation⁽⁸⁾.

Acne can be categorised as mild, moderate, or severe depending on how many and what type of skin lesions there are.

There are many therapeutic alternatives, ranging from topical to systemic medications, for the treatment of acne.

Disease severity, patient choice, and tolerance are taken into account while choosing a treatment (9).

Salicylic acid, benzoyl peroxide, antibiotics, combinations of antibiotics, retinoid medicines, sulfone pharmaceuticals, and azelaic acid are among the topical treatments frequently used on acne patients⁽¹⁰⁾.

The standard treatment for mild to moderate acne is the use of a topical retinoid and antibiotic in a set combination.

Topical retinoid however, also have side effects such itchiness, erythema, and photosensitivity that might affect how well patients adhere to their treatment plans⁽¹¹⁾.

Leprosy and a number of inflammatory dermatoses, such as dermatitis herpetiformis, pyoderma gangrenosum, bullous lupus erythematosus, and linear immunoglobulin, have been treated with Dapsone, a sulfone derivative, when administered orally⁽¹²⁾.

Acne may be reduced by Dapsone, which is known to have antibacterial and anti-inflammatory properties⁽¹⁰⁾. Dapsone was licenced by the FDA for acne patients in 2005, but only if they had a negative G6PD deficiency test; however, after a phase IV trial, the FDA eliminated this requirement, increasing feasibility⁽¹³⁾.

Sulfone is a component of topical % Dapsone gel, which also includes a sophisticated solvent micro particulate delivery method that allows stratum corneum penetration⁽¹⁴⁾. The goal of developing topical Dapsone 5 %, manufactured in an aqueous-based gel carrier, for the treatment of acne vulgaris was to reduce acne lesions through the drug's anti-inflammatory properties while avoiding toxicities related to systemic Dapsone use⁽¹²⁾

Dapsone may provide physicians with a novel multimodal monotherapy for treating acne due to its simultaneous anti-inflammatory and anti-microbial actions⁽⁵⁾. With or without other systemic treatments, topical clindamycin is a well-proven therapy option for mild to

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE1, 2024

moderate acne. It has been shown to be equally effective as topical erythromycin, topical benzoyl peroxide, and systemic tetracycline.

Although side effects from topical treatment are uncommon, there have been occasional instances of pseudomembranous colitis linked to topical clindamycin that have been documented^(15,16).Other adverse effects include localised skin irritation (redness and desquamation), which is mostly caused by the medication production method's carrier. When antibiotics are used alone, bacterial resistance rises as well, which reduces their effectiveness in treating acne^(17,18).

There aren't many research directly comparing topical Dapsone and topical clindamycin. With this in mind, the current study was conducted to compare the effectiveness of topical Dapsone with the widely used treatment method clindamycin gel in the patient population suffering from acne vulgaris. In this study, the effectiveness of % clindamycin and % Dapsone gel in treating individuals with Grade I and II acne vulgaris was compared.

AIM: To compare Efficacy of Clindamycin 1% gel v/s Dapsone 5% gel in the Treatment of Mild to moderate acne vulgaris

2. MATERIAL AND METHODS

An prospective observational study was conducted in Dermatology department of IMCHRC Indore for a period of 18 months. All the adult patients with complaints suggestive of Patients of Mild to Moderate acne vulgaris, A total of 100 patients were involved in the study. The study was formally started after getting the clearance from the institutional ethical committee. All the adult patients of mild to moderate acne aged between 14-40 years With GAGS score 0-30, included in the study. 50 patients selected from OPD with symptoms of mild to moderate acne of both sexes were entered in this case group and 50 patients with other cutaneous diseases served as controls. The study included a total of 100 patients (50 cases and 50 controls). The research protocol was approved by the Institutional ethics and scientific review committee. Subjects with nodulocystic acne, acne fulminans, acne conglobate, GAGS score > 30, subjects using anti-acne medication in last 30 days before study entry ,subjects with hormonal imbalance, truncal acne, pregnant and lactating women h/o drug allergy to dapsone, clindamycin & patients not giving consent for the study were excluded from the study. Informed consent taken from the patients for enrollment in the study. Detailed history and clinical examination was conducted and the details were entered in a proforma. History include age, occupation, , treatment details for acne (on the contour drug). Personal history and drug history for any allergies, chronic illness, hypertension, diabetes mellitus was taken. Family history of acne was taken. Investigation details like Complete blood count (CBC) including peripheral blood smear& were done. Clinical examination was done. General, physical, and systemic examinations were carried out and recorded.

3. RESULTS

Table 1: Comparison of age group of patients with drug used

Table 1. Comparison of age group of patients with urug useu						
		Gro	oup			
	Group A: C	Clindamycin gel			Chi Square	
Age Group	Count	ColumnN %	Count	ColumnN %	Value	P Value
14-20	24	48.00%	16	32.00%		
21-25	14	28.00%	20	40.00%		
26-30	8	16.00%	12	24.00%		
31-35	4	8.00%	1	2.00%		
36-40	0	0.00%	1	2.00%	6.259	0.181
Total	50	100%	50	100%	0.237	0.101

Table 2: Comparison of Gender of patients with drug used

		Gro	oup			
		oup A: ycin 1% gel	Group B: Dapsone 5%		a. . a	
Gender	Count	ColumnN %	Count	ColumnN %	Chi Square Value	P Value
Female	32	64.00%	29	58.00%		
Male	18	36.00%	21	42.00%		
Total	50	100%	50	100%	0.378	0.539

Table 3: Comparison of Duration of Acne with drug used

	Table 5. Comparison of Duration of Ache with drug used						
	Group						
	Group A: Clindamycin 1%gel		Group B: Dapsone5% gel		Chi Square	P	
Duration	Count	ColumnN %	Count	Column N %	Value	Value	
< 6 month	5	10.0%	5	10.0%		-	

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE1, 2024

6 - 12 Months	30	60.0%	24	48.0%		
12 - 18 Months	7	14.0%	8	16.0%	1.926	0.749
18 – 24 Months	5	10.0%	8	16.0%	1.920	0.7.19
> 24 months	3	6.0%	5	10.0%		
Total	50	100%	50	100%		

Table 4: Distribution of patients according to Grades of acne on subsequent follow ups

Table 4. Distribution of patien		Count	Column N %
	None	0	0.0%
	Minimal	13	13.0%
Acne Grade (Day 1)	Mild	41	41.0%
	Moderate	46	46.0%
	None	11	11.0%
	Minimal	26	26.0%
Acne Grade (Week 4)	Mild	41	41.0%
	Moderate	22	22.0%
	None	34	34.0%
	Minimal	26	26.0%
Acne Grade (Week 8)	Mild	34	34.0%
	Moderate	6	6.0%
	None	54	54.0%
	Minimal	24	24.0%
Acne Grade (Week12)	Mild	21	21.0%
	Moderate	1	1.0%

Table 5: Comparison and association of Grades of acne onsubsequent follow ups with drug used

		Group					
		Group A: Clindamycin 1% gel		Group B: Dapsone 5% gel		Chi square	
		Count	Column N %	Count	Column N %	value	p value
Aona	None	0	0.0%	0	0.0%		
Acne Grade	Minimal	7	14.0%	6	12.0%	0.101	0.951

ISSN: 0975-3583, 0976-2833 VOL15, ISSUE1, 2024

(Day 1)	Mild	20	40.0%	21	42.0%		
	Moderate	23	46.0%	23	46.0%		
	None	5	10.0%	6	12.0%		
Acne	Minimal	11	22.0%	15	30.0%		
Grade (Week4)	Mild	21	42.0%	20	40.0%	1.458	0.692
	Moderate	13	26.0%	9	18.0%		
	None	16	32.0%	18	36.0%		
Acne	Minimal	11	22.0%	15	30.0%		
Grade (Week8)	Mild	19	38.0%	15	30.0%	2.859	0.600
	Moderate	4	8.0%	2	4.0%		
	None	23	46.0%	31	62.0%		
Acne	Minimal	12	24.0%	12	24.0%		
Grade (Week12)	Mild	14	28.0%	7	14.0%	8.617	0.211
	Moderate	1	2.0%	0	0.0%		

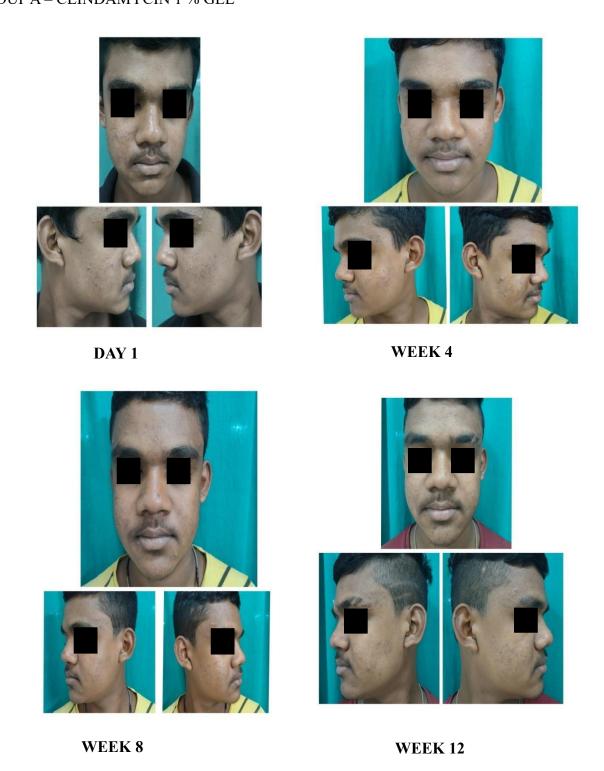
ISSN: 0975-3583, 0976-2833 VOL15, ISSUE1, 2024

	Group					
	_	Clindamycin ⁄₀ gel	Group B: D	apsone5% gel		
	Mean	Standard Deviation	Mean	Standard Deviation	t Value	p Value
GAGS Score (Day 1)	16.6	9.0	16.7	8.3	0.035	0.972
GAGS Score (Week 4)	12.7	9.8	10.2	8.3	1.467	0.146
GAGS Score (Week 8)	7.6	7.8	5.9	6.6	1.215	0.227
GAGS Score (Week 12)	5.0	5.9	2.5	4.1	2.423	0.017

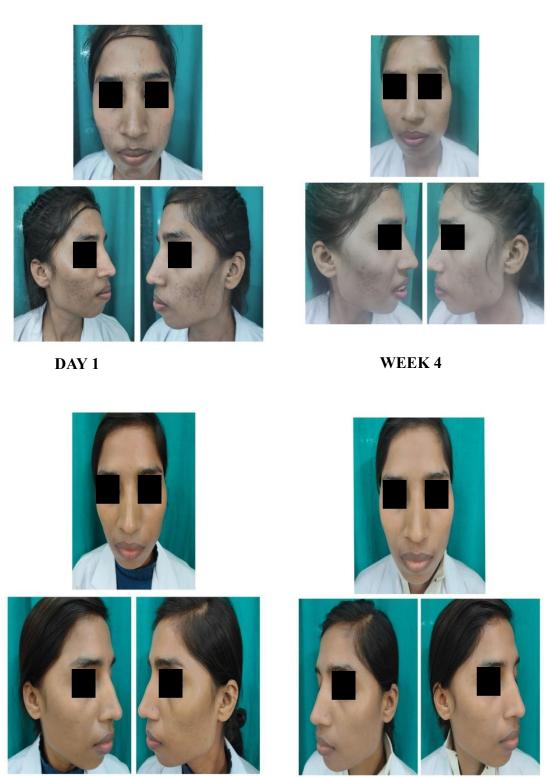
Table 6: Comparison and association of types of side effects withdrug used

		Gro				
	_	Clindamycin ogel	Group B: Dapsone5% gel		Chi square	n valua
	Count	ColumnN %	Count	ColumnN %	value	p value
Irritation	1	2.0%	4	8.0%	1.895	0.169
Burning	2	4.0%	5	10.0%	1.099	0.295
Pruritis	2	4.0%	0	0.0%	.344	0.558
Erythema	1	2.0%	4	8.0%	.122	0.727
Oily Skin	0	0.0%	1	2.0%	3.093	0.079

IMAGESGROUP A – CLINDAMYCIN 1 % GEL



GROUP B – DAPOSNE 5 % GEL



WEEK 8

WEEK 12

4. DISCUSSION

Acne is common problem in adolescents and young adults. Acne and its associated problems affects as many as 85% of adolescents and young adults. Both topical Clindamycin 1% gel gel and topical dapsone 5% gel are used in treatment of mild to moderate acne vulgaris

Group A: Clindamycin 1% gel participants were advised for topical application of Clindamycin 1% gel gel and Group B: Dapsone 5% participants were advised for topical application of Dapsone 5% gel. Patients were followed up for 12 weeks.

The key findings of the study are discussed below

Age and Gender

In present study, most of the study participants in this study belongs to 14-20 years of age, followed by 21-25 years of age group. Least number of participants belongs to 36-40 years of age group. Mean age of the participants was 22.1 ± 5 years. Study participants were divided into 2 groups Group A: patients advised to use Clindamycin1% gel and Group B: patients advised to use dapsone 5%. Most of the participants belongs to 14-20 years of age group in both group A and group B.

mean age in Group A: Clindamycin 1% gel and Group B: Dapsone 5%

was 21.70 ± 4.8 years and 22.40 ± 5.2 years respectively. In Group A: Clindamycin 1% gel, 14-25 years of age group consists of maximum 76% of patients rest 24%. Belonged to > 25 years of age. And in Group B: Dapsone 5%, most of the patients were in 14-25 years of age group 72%, rest 28 % belonged to > 25 years of age. Similar findings were reported in a study conducted by Balvinder Brar et al ⁽⁴⁰⁾ Age distribution showed 80% of patients were of age group 14 to 24 years. While, 20% were above 24 years of age. Age group distribution showed 73% patient were between 14-24 years of age, while rest 27% were above 24 years of age. Preeti Yadav et al ⁽⁴⁶⁾ conducted similar findings as their study and reported 77% participants were in the age group of 13-19 years.

In this study, 61% of the participants in this study were females and 39% were males. 64% of the Group A: Clindamycin 1% gel participants were females and 36% were males while in Group B: Dapsone 5% 58% were females and 42% were males. In a study conducted by Balvinder Brar et al ⁽⁴⁰⁾ it was found that in Dapsone group 56% were females and 44% were males while in Clidamycin group 54% were females and 46% were males.

Duration of Acne:

54 (54%) of patients in this study had 6-12 months of long history of acne followed by 12-18 months 15 (15%). Only 8 (8%) of patients had > 24 months of long history of acne. Group A: Clindamycin 1% gel 60% had 6-12 months of acne history and in Group B: Dapsone 5% 48% had 6-12 months of acne. It is almost equally divided in both groups A and B.

Acne Grade:

Present study, Results from both Groups A: Clindamycin 1% gel and Group B: Dapsone 5% were recorded in tabulated form and statistically analyzed considering significant p value <0.05.

It was reported that among both the groups number of participants with moderate grade of acne were maximum (23 in each group A and group B) on day 1. And no statistical difference among the groups was foundwith p value of 0.951.

After 4 weeks of treatment, it was found that there was decrease in the number of moderate number of cases among both the groups and increase in the number of patients in mild and minimal grades. Total 5 patients were cured with Clindamycin 1% gel therapy and 6 patients were cured with Dapsone 5% therapy. However no statistical difference was found among the groups with p value of 0.692.

After 8 weeks, Total 16 patients were cured with Clindamycin 1% gel therapy and 18 patients were cured with Dapsone 5% therapy. However no statistical difference was found among the groups with p value of 0.600.

After 12 weeks of treatment, Total 23 patients were cured with Clindamycin 1% gel therapy and 31 patients were cured with Dapsone 5% therapy. However no statistical difference was found among the groups with p value of 0.600.

It was found that there was gradually increase in the number of cured patients on subsequent follow-ups among both the group. And no significant difference was noticed.

In a study conducted by Durai PCT et al ⁽³⁷⁾, similar findings was observed. They reported more number of patients with moderate grade of acne than mild. But they had no statistical significant result through all follow-ups which is similar to our study.

Comparison of efficacy of Dapsone 5% gel vs Clindamycin 1% gel gel with various studies.

S No.	Study	Cured with Dapsone 5% gel after 12 weeks	Cured with Clindamycin 1% gelget after 12 weeks
1	Richa Verma et al (43)	50%	55.5%
2	Balvinder Brar et al (40)	50%	46.6%
3	Present Study	62%	46%

GAGS Score:

In this study, GAGS score mean was highest on day 1, which is subsequently decreases with treatment and on week 12 it decrease to 7. Mean of GAGS Score had no significant difference between both groups from day 1, week 4 and week 8 with P values of 0.972, 0.146 and 0.227 respectively. After 12 weeks, statistical significant difference was observed between both groups with p value of 0.017. On comparison of baseline finding with the subsequent follow ups, it was found that among both groups significant improvement was observed.

In a study conducted by Andrew F. Alexis et al ⁽⁴¹⁾, similar findingswas observed. They also had significant decrease in GAGS Score from day 0 to week 12. Charles W Lynde ⁽⁴⁵⁾ in their study also reported similar findings with our study and had decrease in mean of GAGS Score from Day 0 to week 12. Zoe D. Draelos ⁽⁴⁷⁾ also reported similar findings as our study. **Side effects:**

Dapsone is an antibacterial agent of the sulfone family that is widely used to treat diseases

such as leprosy, malaria, pneumonia, or toxoplasmosis in immunocompromised patients ⁽⁴⁹⁾. Dapsone is also used topically to treat many skin conditions, including acne vulgaris ⁽⁵⁰⁾. Dapsone is frequently reported as a cause of methemoglobinemia, with an estimated incidence of up to 20% after oral administration. Trials have confirmed that topical dapsone gel 5% is effective and safe as monotherapy and in combination with other topical agents in mild tomoderate acne vulgaris. ⁽⁵¹⁾ In this study, no patients reported to have any such illness.

In this study, 13% of the patients had any of the side effect and 87% of the participants had no side effects. Irritation, burning, pruritis, erythema, and oily skin were mostly associated side effects. Group B: Dapsone 5% had more number of side effects than Group A: Clindamycin

1% gel. but no statistical significant association was seen between both groups with any of the side effects. In a study Andrew F. Alexis et al ⁽⁴¹⁾, they also reported side effects such as burning, erythema, dryness, peeling and oily skin and had subsequent increase in frequency of this side effects from day 0 to week 12.

5. CONCLUSION

In conclusion, we can infer that when used as monotherapy, topical dapsone gel was found to be more effective in reducing the grade of acne when compared to topical clindamycin gel. The probable reason for this is the additional anti-inflammatory action of dapsone compared to the only anti bacterial action of clindamycin.

Although dapsone gel was marketed as a novel drug, we in our study did not find any statistically significant results in favour of dapsonegel.

However, more research on this topic with more number of patients & longer follow ups are required for assessing the effects of the drug on the quality of life.

6. REFERENCES

- 1. Leung AK RW. Acne. J R Soc Heal. 1991;111:57–60.
- 2. Claire Carusillo. History of Acne [Internet]. 2016. Available from: https://repeller.com/history-of-acne/
- 3. Dawson AL DR. Acne vulgaris. BMJ. 2013;346:f2634.
- 4. Vos T, Flaxman AD, Naghavi M, Lozano R MC, Ezzati M et al.
- 5. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: A systematic analysis for the global burden of disease study 2010. Lancet. 2012;380:2163–96.
- 6. Verma R, Yadav P, Chudhari M, Patel J, Umrigar D. Comparison of efficacy of two topical drug therapy of acne vulgaris 1% clindamycin versus 5% dapsone: A split face comparative study. Natl J Physiol Pharm Pharmacol. 2022;12(0):1.
- 7. Moradi Tuchayi S, Makrantonaki E, Ganceviciene R, Dessinioti C, Feldman SR, Zouboulis CC. Acne vulgaris. Nat Rev Dis Prim [Internet]. 2015;1(September):15029. Available from: http://dx.doi.org/10.1038/nrdp.2015.29
- 8. Motosko CC, Zakhem GA, Pomeranz MK HA. Acne: a side- effect of masculinizing hormonal therapy in transgender patients.
- 9. Br J Dermatol [Internet]. 2019;180(1):26–30. Available from: doi: 10.1111/bjd.17083. Epub 2018 Oct 14. PMID: 30101531.
- Sanyukta KAnwal. India- Acne Statistics [Internet]. Statista.
 Available from: https://www.statista.com/aboutus/our-research-commitment/2598/sanyukta-kanwal
- 11. Oge' LK, Broussard A MM. Acne Vulgaris: Diagnosis and Treatment. Am Fam Physician [Internet]. 2019;100(8):475–84. Available from: pmid: 31613567.
- 12. Guruputra KS, G H, GA P, JJ N, SV D, MN P. A double blind randomized study to compare efficacy of 5% Dapsone gel vs combination of Adapalene-clindamycin gel in the treatment of mild to moderate Acne vulgaris. J Dermatology Cosmetol. 2018;2(4):202–5.
- 13. Kubba R, Bajaj AK, Thappa DM et al. Acne in India: Guidelines for managementIAA consensus document. Indian J Dermatol Venereol Leprol. 2009;75(1):1–62.
- 14. Del Rosso JQ. Newer topical therapies for the treatment of acne vulgaris. Cutis. 2007;80(5):400–10.

- 15. Brar BK, Kumar S, Sethi N. Comparative evaluation of Dapsone 5% gel vs Clindamycin 1% gel in mild to moderate acne vulgaris. Gulf J Dermatology Venereol. 2016;23(1):34–9.
- 16. Zhu YI SM. Dapsone and sulfones in dermatology: overview and update. J Am Acad Dermatol. 2001;45(3):420–434.
- 17. Tan AU, Schlosser BJ PA. A review of diagnosis and treatment of acne in adult female patients. Int J Womens. 2018;4:56–71.
- 18. Shalita AR, Smith EB BE. Topical erythromycin v clindamycin therapy for acne: A multicenter, double-blind comparison. Arch Dermatol. 1984;120:351–5.
- 19. Chu A, Huber FJ PR. The comparative efficacy of benzoyl peroxide 5%/erythromycin 3% gel and erythromycin 4%/zinc1.2% solution in the treatment of acne vulgaris. Br J Dermatol. 1997;136:235–8.
- 20. Worret WI FJ. Topische Therapie mit Benzoylperoxid, Antibiotika und Azelainsäurebei der Akne (Acne therapy with topical benzoyl peroxide, antibiotics and azelaic acid). J Dtsch
- 21. Vos TF. -Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: A systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380(9859):2163–96.
- 22. SS. P. Epidemiology of acne vulgaris . Indian J Dermatol. (Thesis Abstr VII). 1983;28:109–10.
- 23. Pandey SS, Kaur P SG. Has acne urban bias? Indian J Dermatol Venereol Leprol. 1980;46:80–2.
- 24. M. CE, Griffiths MD, Jonathan Barker, Tanya Bleiker, Robert Chalmers D, Creamer, editors. Rook's Textbook of Dermatology.9th ed.
- 25. Lim LS JV. Plasma androgens in acne vulgaris. Br J Dermatol.
- 26. Tithof PK, Elgayyar H CT et al. Polycyclic aromatic hydrocarbons present in cigarette smokes causes endothelial cell apoptosis by a phospholipase A2 dependent mechanism. FASEB J. 2002;16:1463-4.
- 27. L. C. Implications of the role of diet in acne. Semin Cutan Med Surg. 2005;24:84-91.
- 28. Pochi PE SJ. Sebum production, causal sebum levels, titratable acidity of sebum and urinary fractional 17-ketosteroid excretion in males with acne. J Invest Dermatol. 1964;43:383–8.
- 29. Ingham E, Eady A GC et al. Pro inflammatory levels of interleukin 1 α like bioactivity are present in the majority of open comedones in acne vulgaris. J Invest Dermatol. 1992;98:895–901.
- 30. Nagy I, Pivarsci A K et al. Distinct stains of Propionibacterium acnes induce selective β-defensins-2 and in terleukin-8 expression human keratinocytes through Toll-like receptors. JInvest Dermatol. 2005;124:931-8.
- 31. Elias PM, Brown BE ZV. The permeability barrier in essential fatty acid deficiency: evidence for a direct role for linoleic acid in barrier function. J Invest Dermatol. 1980;74:230–3.
- 32. Doshi A, Zaheer A SM. A comparison of current acne grading systems and proposal of a novel system. Int J Dermatol. 1997;36:416–8.
- 33. Holland DB JA. The role of inflammation in the pathogenesis of acne and acne scarring. Cutan Med Surg. 2005;24:79–83.
- 34. Cotterill JA CW. Suicide in dermatological patients. Br J Dermatol. 1997;137:246-50.
- 35. Wu SF, Kinder BN TT et al. Role of anxiety and anger in acne patients: a relationship with severity of disorder. J Am Acad Dermatol. 1988;18:325-33.
- 36. Lowell A Goldsmith, Stephen I Katz, Barbara A Gilchrest, AmyS Paller DJL, editor.

- Fitzpatrick's Dermatology in General Medicine. 8th ed.
- 37. Archieves of Dermatology. 2003;139:668–70.
- 38. Canavan TN, Chen E, Elewski BE. Optimizing Non-Antibiotic Treatments for Patients with Acne: A Review. Dermatol Ther (Heidelb). 2016;6(4):555–78.
- 39. Durai PC, Nair DG. Acne vulgaris and quality of life among young adults in South India. Indian J Dermatol. 2015 Jan- Feb;60(1):33-40. doi: 10.4103/0019-5154.147784. PMID:25657394; PMCID: PMC4318060.
- 40. Purdy S, de Berker D. Acne vulgaris. BMJ Clin Evid 2011;2011:1714.
- 41. Kraft J, Freiman A. Management of acne. CMAJ. 2011 Apr 19;183(7):E430-5. doi: 10.1503/cmaj.090374. Epub 2011 Feb 28.PMID: 21398228; PMCID: PMC3080563.
- 42. Brar, BK, Kumar S, Sethi N Comparative evaluation of Dapsone 5% gel vs Clindamycin 1% gel gel in mild to moderate acne vulgaris. The Gulf Journal of Dermatology and Venereology Volume 23, No.1, April 2016.
- 43. Alexis AF, Burgess C, Callender VD, Herzog JL, Roberts WE, Schweiger ES, Stockton TC, Gallagher CJ. The Efficacy and Safety of Topical Dapsone Gel, 5% for the Treatment of Acne Vulgaris in Adult Females With Skin of Color. J Drugs Dermatol. 2016 Feb;15(2):197-204. PMID: 26885788.
- 44. Piette WW, Taylor S, Pariser D, Jarratt M, Sheth P, Wilson D. Hematologic safety of dapsone gel, 5%, for topical treatment of acne vulgaris. Arch Dermatol. 2008 Dec;144(12):1564-70. doi: 10.1001/archdermatol.2008.518. PMID: 19075138.
- 45. Yadav P, Verma R, Chudhari M, Patel J, Umrigar D. Comparison of efficacy of two topical drug therapy of acne vulgaris 1% clindamycin versus 5% dapsone: A split face comparative study. Natl J Physiol Pharm Pharmacol 2022;12(06):817-822.
- 46. Lucky AW, Maloney JM, Roberts J, Taylor S, Jones T, Ling M, Garrett S; Dapsone Gel Long-Term Safety Study Group. Dapsone gel 5% for the treatment of acne vulgaris: safety and efficacy of long-term (1 year) treatment. J Drugs Dermatol. 2007 Oct;6(10):981-7. PMID: 17966175.
- 47. Lynde CW, Andriessen A. Cohort study on the treatment with dapsone 5% gel of mild to moderate inflammatory acne of the face in women. Skinmed. 2014 Jan-Feb;12(1):15-21. PMID: 24720080.
- 48. Verma R, Yadav P, Chudhari M, Patel J, Umrigar D. Comparison of efficacy of two topical drug therapy of acne vulgaris 1% clindamycin versus 5% dapsone: A split face comparative study. Natl J Physiol Pharm Pharmacol 2022;12(06):817-822.
- 49. Draelos ZD, Carter E, Maloney JM, Elewski B, Poulin Y, Lynde C, Garrett S; United States/Canada Dapsone Gel Study Group.
- 50. Two randomized studies demonstrate the efficacy and safety of dapsone gel, 5% for the treatment of acne vulgaris. J Am Acad Dermatol. 2007 Mar;56(3):439.e1-10.doi: 10.1016/j.jaad.2006.10.005. Epub 2007 Jan 17. PMID: 17208334
- 51. Adityan B, Thappa DM. Profile of acne vulgaris--a hospital-based study from South India. Indian J Dermatol Venereol Leprol. 2009 May-Jun;75(3):272-8.
- 52. Turner MD, Karlis V, Glickman RS: The recognition, physiology,
- 53. and treatment of medication-induced methemoglobinemia: a case report. Anesth Prog. 2007, 54:115-117.
- 54. Zhu YI, Stiller MJ: Dapsone and sulfones in dermatology:overview and update. J Am Acad Dermatol. 2001, 45:420- 34. 10.1067/mjd.2001.114733.
- 55. Watton C, Smith K, Carter E: Methemoglobinemia as a complication of topical dapsone. N Engl J Med. 2015, 372