# VITAMIN A ACID IN ACNE

S. K. PANJA,\* S. K. SEN GUPTA † AND S. BOSE ‡

## Summary

Topical Vitamin A acid 0.05% in lotion and cream forms were tried in 55 patients. All of them except one had some form of local reaction, which started usually after a week and showed maximum intensity in between second and third week. Improvement started after 4 - 6 weeks and clearing of lesions were noticed in 8 week's time. The occurence of local reaction was often beneficial to the patient and served as a guide for effective therapy. The single patient without any reaction did not improve at all.

Lotions seemed to be more effective than the cream preparations. 83.6 % patients showed excellent response with papulo-pustular and comedo acne, whereas response was poor in nodules and cystic lesions.

Vitamin A acid improved the complexion in majority of patients indicating its mild demelanising property observed in this study.

### Introduction:

Retinoic acid (Vitamin A acid) was originally obtained during attempts to synthesize retinol (Vitamin A alcohol) and it has been suggested that this substance may be formed in vivo and play an important part in Vitamin A metabolism. Experiments have shown that retinoic acid can replace the function of Vitamin A in deficient animals with exception of its action on vision and reproduction<sup>1</sup>,<sup>2</sup>.

Absorption studies in animals indicate that the acid is mostly found in bile whereas Vitamin A is mostly found in lymph. In order to deliver a high dose of Vitamin A to the skin without producing systemic effects various topical forms of Vitamin A have been assessed. There is evidence that retinoic acid has more effect than other Vitamin A compounds when used in this way.

Vitamin A acid has been under investigation as a topical treatment for acne for about 15 years. Its usefulness has been sharply defined in the past 6 years<sup>3</sup> and showed this to be markedly superior to sulphur resorcinol lotion or benzyl peroxide 5% lotion. Since then concentrated research conducted by more than 30 dermatologists showed the efficacy of topical retinoic acid in acne therapy<sup>4-16</sup>. Combined therapy with tetracycline and Vitamin A acid has claimed superior results in acne vulgaris<sup>17</sup>, 18. The present report presents the results obtained in a pilot study from the use of retinoic acid lotion and cream 0.05% in the treatment of acne

‡ Registrar in Dermatology, Libya Request for reprint:

Dr. S. K. Panja,

117, Vivekananda Road, Calcutta-700006

Received for publication on 2-3-1979

<sup>\*</sup> Head of the Dermatology Unit, Department of Medicine, Institute of Post Graduate Medical Education & Research & S. S. K. M. Hospital, Calcutta-20

<sup>†</sup> Registrar in Dermatology, N. B. U. Medical College, Calcutta

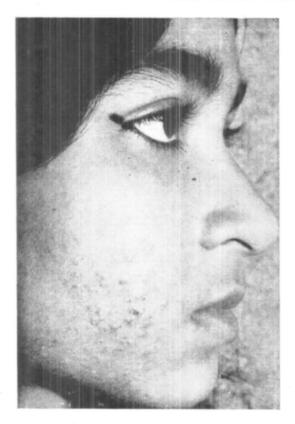


Fig. 1 Before treatment

### Materials and Methods

Treatment of acne vulgaris was carried out in patients attending the Dermatology Out - Patients Department of S. S. K. M. Hospital, Calcutta by topical application of vitamin A acid (re tinoic acid).

The preparation used were lotion in a propylene glycol base and cream in a vanishing base containing 0.05% of vitamin A acid, supplied by Clinical Research Department, Roche Products Ltd., India.

Cream was given for individual with normal or dry skin and lotion for those with oily skin. The patients were asked to apply the medicine twice daily, and to avoid sunlight as far as possible. All other medicaments were stopped and the patients were told to have their usual normal diet. The number of patients admitted to the trial was 70, out of which only 55 were studied as 13 did not return for follow-up and in 2 patients the treatment had to be abandoned as they found to have flare up of rosacea which they had in addition to the acne. All the patients had typical acne lesions showing various stages of the disease with papules, comedones, pustules, cysts and keloids.

For each patient a proforma was filled up. All patients were seen once a week. The number of lesions were counted and side - effects were noted. The details of the proforma is given in Table 1. The improvement was judged on the basis of clinical photographs and counting of comedones, papules, pustules and cysts.

#### Results

Among 70 patients studied, males were 43 and females 27. The age - sex distribution is shown in Table 2. duration of illness varied from less than 6 months to over 4 years. majority (53 patients) had acne for more than one year (Table 3). patients gave a positive family history of acne vulgaris. The average colours of the patients were dark and light. Most of them (63 patients) had tried some forms of anti-acne lotions and creams available in the market. Il had oral antibiotics - 7 patients had not used any medicine. 28 patients were found to have oily skin, and 28 normal skin. In 14 skin was found to be moderately oily only. Dry skin was not noted in any patient.

After application of retinoic acid, among the 55 patients studied, 54

	Table 1	VITAMIN	A ACID	IN ACI	and the same of th	* * per * - or * - ort bases QVE	-	Ш	]	(seethe) (
mitters meter:	pati	test sum:				ME	tengle age:	Cese Mi	stery; denuties	of some
lest treatment: (or	sparations)		*********			results	: excellent	gent 🗌	soderots 🗌	ner 🗌
acalization of lea	fone: face	nect _	num of t	for sack	itest [	l test [				
mas enducted:	face 🗌	mer 🗌	NAME OF T	Ne mack	chest [	tyck atters (	state)	*********		******
alour of the hale:			taleer of	the ages:		paleur at t	the side:		type of skin:	
ref		time .			trait [			normal		
ale .			yoth, or	97		. ten			#7	
ne .			irres			yellos .			Santi.	
Tues						black -		,	#las/	
		- 15 lestons - 10 lestons - 5 lestons w lestons			- severe - moderate - peor					
iff annihit,/day	Speed Pages	inites Mine cre	te Mis-	[RYTHERA	OS SQUIMATION	concept test local and general therapy	side effects (Tecs	e (dament) a	reasons for a	Ten ser
-										
	+						,			
-										
-	-	-								
	111									
mortson oith provi	ne fregimet:	better:	equel: [	1071	. 0	clinical eva	fuelter			in manufacture
Commence of the Commence of th	******									

TABLE II
(Age and Sex group)

Age in years	Total	Male	Female
15-20	54	32	22
21 - 25	16	11	5
	70	43	27

TABLE III
(Duration of acne)

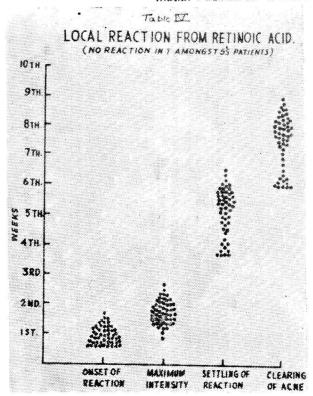
6 months or less	Yr.	Yrs	3 Yrs	4 Yrs	<4 Yrs
11	4	11	16	10	16

showed some amount of local reaction initially in the form of exacerbation of the old lesions with oedema, burning, tenderness, erythema and pustule formation with crusting. In 5 cases there was hypersensitivity to the application with extreme degree of local reaction and severe pain and tenderness over the part. This small group was about to

abandon the treatment but was persuaded to stick to the regime. Mild photosensitivity and itching were also noted in these patients. The evolution of the various stages of this reaction is shown in Table 4. The onset of reaction was noticed normally after a week and showed maximum intensity between 2nd and 3rd week of the treatment. The beneficial effect was visible at the end of 4-6 weeks and clearing of lesions occured in 8 weeks' time.

One patient who showed no reaction at all did not show any sign of improvement of the acne.

The application also opened up hidden papules, and comedones which constituted to part of the exacerbation mentioned. Both black and white comedones showed 80% reduction in their counts after 4 to 6 weeks. The counts had in fact started to show a decline from the end of the first week.



sisted after the subsidence of the reaction, but this cleared up satisfactorily within 1-2 weeks even while the patients continued the local application.

The reactions and clearing of lesions of acne vulgaris after vitamin A acid application are shown in figures 1, 2, and 3.

## Discussion

The beneficial effect of vitamin A acid stems from three actions:

(1) Prevention of formation of new comedones—

Retinoic acid produces an accelerated turnover rate of the epidermis and epithelium of the folicular canal and

Pustules showed 87.5' reduction although they started regressing after the subsidence of reaction. Nodules and cysts which were present in only 4 patients showed 56% and 50% reduction respectively. Keloids did not exhibit any change.

The rating scale for evaluating improvement, and the results of treatment are given in Table 5.

46 patients (83.6%) showed excellent results with complete clearing of acne lesions in 35 cases, in about 8 weeks' time. The improvement was maintained with no new lesions appearing for 3-6 months. Occasional pimples appearing thereafter were treated easily by repeating the application. Mild hyper-pigmentation and erythema per-

Fig. 2 Reaction





Fig. 3 After treatment

reduces the number of desmosomes, thereby loosening the attachment of the horny cells to one another. Thus it helps to prevent the formation of solid plug that comprise the comedones.

- (2) Expulsion of existing comedones. The reduction in the number of desmosomes of epidermal cells, and the increase cell turnover within the plugged follicle loosens the anchorage of existing comedones, and expels them from the follicle.
- (3) Breaking up of the hidden comedones: Retinoic acid increases the permeability of sebaceous glands, and permit escape of trapped lipids and fatty acids. What may appear to be an exacerbation of acne process is due to the result of the action of the drug on previously unseen lesions. An accele-

rated natural local inflammatory response provides early resolution of the deep lesions before they reach the skin surface.

Kligman et al do not consider that the topical effect of retinoic acid has anything to do with its physiological effects as a vitamin, but suggest that its action on skin may be related to its capacity to labilise lysosomes, thereby releasing proteolytic and hydrolytic enzymes capable of exciting inflammatory reaction, and thus explaining its unique mode of Vitamin A acid can convert comedones into inflammatory pustules by injuring the follicular epithelium, thereby allowing the escape of intra-follicular toxic substance (? fatty acid? bacterial product) which excites the accumulation of polymorphs. These inepithelium vade the with the formation of intrafollicular abscess culminating in the suppuration of

comedones.

TABLE V

Types of Results	Size of lesion reduced by	Actual result (cases)	Percen tage
Excellent	75 - 100%	46	83.6
Good	50 - 74.9%	6	10.9
Moderate	25 - 44.9%	1	1.8
Poor	<b>&lt;24.9%</b>	1	1.8
Exacer- bation	-	1	1.8

In this study the result obtained is very satisfactory. The comedones, papules and pustules showed considerable reduction in number. Contrary to other reports we have found significant reduction in number of pustules (87.5%) in pustular acne. Comedones and papules also show considerable clearing with 80% reduction in their numbers.

Too much of local reaction may give patients false impression of intolerance

to treatment resulting in discontinuation of therapy. None of our patients who came for follow-up expressed any desire to abandon the treatment because of local reaction. We believe that regular supervision helped us a lot in convincing the patients about the safety of the therapy and encouraging them to adhere to the regimen. In fact earlier the reaction started better was the improvement noticed in the end. The state of reaction often helped us to form a guideline to topical vitamin A acid therapy.

Many of our patients noticed lightening of their complexion resulting in a fairer complexion which was appreciated by all of them.

### Conclusion

From this study we can conclude that Vitamin A acid 0.05% is an excellent agent in the management of acne vulgaris with comedones and pustules. Retinoic acid not only expels the existing comedones but also opens up hidden ones, and prevents the formation of new comedones. The pustular lesions heal by quick crusting. Even some cysts and nodular lesions disappeared. The local reaction with retinoic acid, often is beneficial to the patient and can serve as a guide to the therapy. The change of complexion of the skin which became lighter by continued use of retinoic Acid application was due to partial loss of melanin pigment an additional demelanising property observed in our study. In our experience the lotion is more penetrative than the cream. This is probably due to propylene glycol base of the lotion which helps in its increased percutaneous absorption.

The only problem with retinoic acid is its local reaction which might discourage the patient from adhering to this therapy. Better pre-treatment approaches and regular supervision will help

to overcome this problem. Avoidance of prolonged exposure to the sun during the first month of treatment is advisable.

A low concentration, i.e. 0.025% of vitamin A acid preparation might possibly give good result with minimum reaction.

### Addendum

After completion of this pilot study, we felt that the main reason of abandoning Retinoic acid therapy is its intense local reaction within a fortnight of commencement of application. In later studies we used regularly 0.025% concentration and found this very much acceptable by the patients as the reactions were mild without altering the efficacy of the preparation. Combined treatment with long term low dose antibiotic therapy along with topical Retinoic acid preparation are indicated in severe cases with pustule, nodule and cyst formation.

### Acknowledgement

We are thankful to the Director. Institute of Post Graduate Medical Education & Research, Calcutta and the Surgeon Superintendent, S.S.K.M. Hospital for allowing us to study the clinical materials of the Institute and Hospital. Our thanks are also due to the Clinical Research Department, Roche Products Limited, India, for the generous supply of topical Retinoic Acid.

#### References:

- Dowling JE and Wald G: The role of Vit A acid, Vitams Horm. 18: 515, 1960.
- Thompson JN, Howell J Mec and Pitt GAJ: Vitamin A and Reproduction in Rats, Proc R Soc (series B), 159: 510. 1964.
- Kligman AM, Fulton JE and Plewig G: Topical Vitamin A acid in Acne Vulgaris: Arch Derm 99: 469, 1969.
- Pedace FJ and Stoughton R: Topical Retinoic Acid in Acne Vulgaris. Brit J Derm, 84: 465, 1971.

#### VITAMIN A ACID IN ACNE

- Peachey RD and Connor BL: Topical Retinoic Acid in the treatment of acne vulgaris, Brit J Derm, 84: 462, 1971.
- McGills TJ, Rapaport MJ, Reisner RM et al: Topical Vitamin A acid in the management of Comedone acne, Cutis, 7:144-150, 1971.
- Nurse DS: Vit A in acne Aust J Derm, 12:108, 1971.
- Cullen SI: Evaluation of Tretinoin in the treatment of acne vulgaris Cutis, 10:751, 1972.
- Bartlett BH: An open evaluation of Retinoic acid in acne: Aust J Derm 13:132, 1972.
- Marquis L and Jagavkar CK: Retinoic acid in the Treatment of Acne, Indian J Derm Ven, 40: 162, 1974.
- Shroff HJ & Shroff JC: Retinoic acid in the treatment of acne vulgaris, Indian J Derm Ven, 40:51, 1974.

- Haribhakti PB: Topical Retinoic acid in the treatment of acne vulgaris. Indian J Derm Ven, 39: 222, 1973.
- Kligman AM, Otto HM, Leyden JJ and Fulton JE: Postscript to vitamin A acid therapy for acne vulgaris, Arch Derm 107: 296, 1973.
- Singh G and Kumar B: Evaluation of Retinoic Acid in the Acne Vulgaris. Indian J Derm Ven Lepr, 42: 113, 1976.
- Yong CC: The use of topical Vitamin A acid in acne vulgaris in Singapore Indian J Derm Ven Lepr, 42: 203, 1976.
- Plewing G and Kligman AM: Acne Vulgaris, New York, Springer Verlog, 1975.
- Olson R: Treatment of acne with Vitamin A acid and tetracycline, Cutis, 7:285, 1971.
- Otto HM Marples RR, Kligman AM: Acne Vulgaris and Oral Therapy with Tetracycline and topical therapy with Vitamin A, Arch Derm, 106: 200, 1972.

### Announcement...

### Journal of Indian Association for Communicable Diseases

(Official Publication of Indian Association for Communicable Diseases)

The Journal of Indian Association for Communicable Diseases, earlier published from Mahatma Gandhi Institute of Medical Sciences, Sevagram, Wardha, will now be published from Maharani Laxmi Bai Medical College, Jhansi, (U.P.). The Journal publishes original contributions, review articles, technical comments/letters to the editor on all aspects of communicable diseases and book-reviews. The articles submitted for publication will be finalized within two months as regards their acceptance. Detailed guidelines for preparation of manuscripts can be obtained from Prof. R. N. Srivastava, Chief Editor, M. L. B. Medical College, Jhansi, (U.P.), – 284001, India.

(See Page 103 also)