



## Comparison of Topical Retinoids Adapalene and Tretinoin in the Treatment of Grade I and II Acne

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### ABSTRACT

#### Introduction

Acne is a chronic, inflammatory disease of the pilo-sebaceous unit. It is multifactorial. Topical retinoids are widely used in acne and act by reducing sebum production and reducing inflammation. The widely used topical retinoids are Adapalene and Tretinoin.

#### Objectives

To compare efficacy of Topical Adapalene 0.1% and Tretinoin 0.04% in the treatment of Grade I and II acne with respect to clinical efficacy and side effects.

#### Subjects and Methods

Randomized prospective comparative trial was done over a period of 6 months with 25 patients in each group. Follow up was done at 4 and 8 weeks to assess improvement.

#### Results and Conclusion

Better improvement was seen in with Adapalene - 92% subjects had reduction in Grade compared to 76% in Tretinoin. Side effects were more with tretinoin (72%) than Adapalene (32%). Adapalene was a better choice in Grade I and II acne compared to Tretinoin.

**KEYWORDS : Acne, Adapalene, Tretinoin, Topical**

### Introduction

Acne vulgaris is a common condition seen in adolescents and young adults that is well recognized causing social and psychological issues. Acne is defined as a chronic, self-limiting inflammatory disease of the pilo-sebaceous unit, manifesting generally in adolescents with pleomorphic lesions like comedones, papules, pustules and nodules.<sup>1</sup> The disease is seen in all races affecting almost 90% with age of incidence between 14-17 years in women and 16-19 years in men.<sup>2</sup> The susceptibility to acne is determined by genetic factors.<sup>3</sup> The main factors in acne pathogenesis are – Seborrhea, Hypercornification, *P. acnes* and inflammation. Hormonal factors such as androgen levels, puberty, menstrual cycle and insulin resistance can influence seborrhea. Excessive sebum production is a pre-requisite for development of acne.<sup>4</sup> Comedones occur as a result of abnormalities in proliferation and ductal differentiation of keratinocytes. Number and size of follicular casts correlate with severity of acne and their presence is a measure of comedogenesis.<sup>5</sup> Studies have shown that there is an increase in cellular turnover in comedones.<sup>6</sup> Bacterial colonization of skin and pilosebaceous ducts by *Propionibacterium acnes* is seen more in adolescents.<sup>7, 8</sup> Inflammation in acne is mediated by CD 4<sup>+</sup> T cells. The secretion of IL-12, TNF –  $\beta$ , INF –  $\gamma$  is seen in acne prone skin, showing a Th1 type inflammatory response. Response of host to *P. acnes* is important as there is activation of both classical and alternate complement pathways.<sup>9, 10</sup>

Acne vulgaris is seen mainly on sebum rich sites of the body such as face, mid-chest, back, shoulders and upper arms. The clinical picture can vary from non-inflammatory to inflammatory lesions. Comedones are the characteristic non inflammatory lesion and can be open or closed. Papules and pustules are the inflammatory lesions, they are superficial and <5mm in diameter. They arise from micro-comedones and can develop into deeper lesions. Clinical grading of acne is: Grade I (Mild) - Comedones, occasional papules, confined to face

Grade II (Moderate) - Comedones, many papules, few pustules, confined to face

Grade III (Severe) - Predominantly pustules, nodules and abscesses. More extensive but confined to face.

Grade IV (Cystic) – Mainly cysts or abscesses, widespread scarring involving face and upper aspect of trunk.

Aims to acne treatment are to reduce the follicular bacterial population, remove follicular obstruction, reduce inflammation and decrease sebaceous gland activity thereby clear existing lesions, limit disease activity, prevent new lesions, prevent scars and improve quality of life. Acne treatment can be evaluated by overall or global assessment, separate evaluation of individual lesions and/ or predominant lesion type. Patients with mixed lesions should be prescribed therapy active against comedones and microcomedones, given that they are the precursors to inflammatory lesions and must be given topical retinoids.<sup>11</sup>

The Retinoids are synthetic forms of vitamin A or chemically related to it. They are used topically and systemically in acne treatment. Mechanism of action – reversal of hypercornification, unplugging of follicle, reduces *P. acnes* population, inhibits development of microcomedone, anti-inflammatory and reduces sebum production thereby acting on all major steps in acne formation. Tretinoin belongs to first generation retinoids. It decreases number and severity of acne. Side effects include stinging sensation, dryness, redness, itching, and photosensitivity. Adapalene is a third generation topical retinoid and is used as 0.1% cream or gel. It is anti-inflammatory and decreases cytokine levels. Side effects are similar to tretinoin.

### Materials and Methods

This study was a randomized prospective comparative study done in a medical college in Kanchipuram between May to August 2016. The sample size was 50 with 25 patients in Group A (Adapalene) and 25 in Group B (Tretinoin). Informed consent was obtained from all selected patients.

**Inclusion Criteria:** Patients with Acne of Grade I and II, age 15 years or above, with lesions on face alone, attending Dermatology Out Patient Department were chosen.

**Exclusion Criteria:** Pregnant and Lactating women, patients above the age of 40, with other dermatological disorders, patients with polycystic ovarian syndrome and those with contra-indications to treatment with Adapalene/ Tretinoin.

Initial acne was graded, lesion counts were taken and thorough dermatological examination was done. Group A patients were treated with Topical Adapalene 0.1% gel and Group B patients were treated with Topical Tretinoin 0.04% gel by self-application, once daily at bedtime. Patients were given clear instructions on how to apply the topical preparations and all necessary precautions were given. Grades were calculated at every 4 weeks and recorded at 0, 4 and 8 weeks. Reduction percentage was calculated based on reduction in lesion counts. Side effects were recorded at 4<sup>th</sup> and 8<sup>th</sup> week.

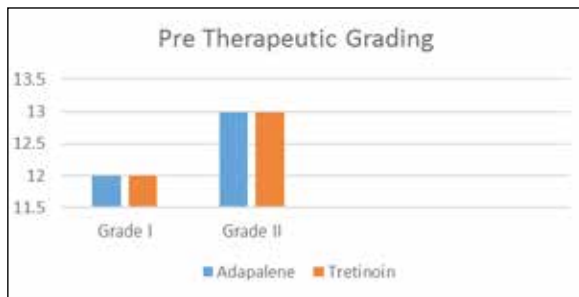
Ethical clearance was obtained from Ethical Committee.

Statistical analysis was done.

**Results**

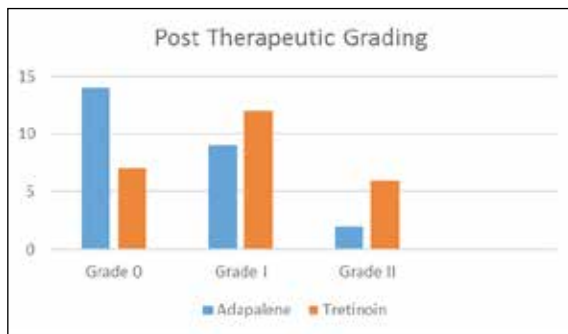
Of the 25 patients in Group A, 12 had Grade I Acne and 13 had Grade II Acne. Similar findings were noted in Group B.

**Graph 1. Pre- Therapeutic Grading of Acne in Group A and B**



**Post therapy –** In Group A, 14 patients (56%) had reduced to Grade 0(no acne), 9(36%) reduced to Grade I and only 2(8%) remained in Grade II. In Group B, only 7(28%) reduced to Grade 0 whereas 12(48%) were in Grade I and 6(24%) remained in Grade II.

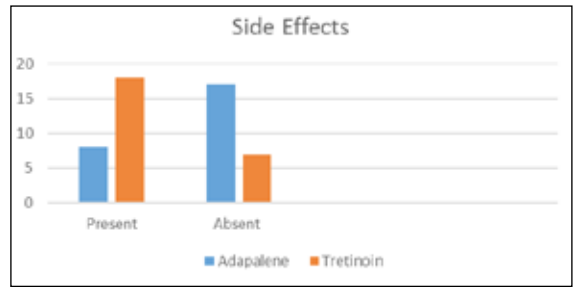
**Graph 2. Post Therapeutic Grading of acne in Group A and B**



**Side Effects-**

Out of 25 patients in Group A, side effects were seen in 8(32%) whereas in Group B, 18 patients (72%) had side effects. Most of the patients in Group A (68%) did not have side effects but only 28% patients in Group B were free of side effects. Dryness and photosensitivity with burning were seen more with tretinoin. Minimal burning sensation and mild itching was seen with Adapalene.

**Graph 3. Comparison of side effects between Group A and B**



**Table 1: Comparison of Comedones at Different period of Follow up between two groups**

Comedone	Group				P value
	Adapalene		Tretinoin		
	Mean	SD	Mean	SD	
Baseline	7	2	7	2	0.281
4 Weeks	6	1	6	2	1.000
8 Weeks	2	3	4	3	0.022*

Significant reduction in Comedone was observed in Adapalene group at 8 weeks compared to Tretinoin.

**Table 2: Comparison of Papules at Different period of Follow up between two groups**

Papule	Group				P value
	Adapalene		Tretinoin		
	Mean	SD	Mean	SD	
Baseline	3	3	3	2	0.840
4 Weeks	2	2	2	2	0.385
8 Weeks	1	1	2	2	0.02*

Significant reduction in papules was observed in Adapalene group at 8 weeks compared to Tretinoin.

**Table 3: Comparison of Pustule at Different period of Follow up between two groups**

Pustule	Group				P value
	Adapalene		Tretinoin		
	Mean	SD	Mean	SD	
Baseline	1	1	1	1	0.486
4 Weeks	0	1	0	1	0.368
8 Weeks	0	0	0	1	0.039*

Significant reduction in pustules was observed in Adapalene group at 8 weeks compared to Tretinoin

**Discussion**

In our study, there was a reduction in the number of all types of lesions i.e. comedones, papules and pustules in both groups. Group A showed better lesion reduction compared to Group B. More number of patients in Group A reduced in grade to Grade 0 and I compared to Group B. Grade II Acne was found in 24% patients in Group B versus 8% in Group A at the end of 8 weeks. In the study done by Shalita and Weiss, Adapalene produced numerically greater lesion reduction than Tretinoin gel for all lesion types.<sup>12</sup> In another study by Grosshans and Marks, the efficacy of Adapalene gel was found to be superior to Tretinoin gel after one week of treatment with respect to reduction in inflammatory lesion counts.<sup>13</sup> These findings were in accordance with the results of our study.

In our study, side effects were more commonly seen in patients who applied Tretinoin than in patients who applied Adapalene. More patients in Group A- 68% were free of symptoms compared to only 28% in Group B. Dryness and Photosensitivity was seen more with tretinoin (36% and 16% respectively). Mild Burning, minimal itching and photosensitivity was seen with Adapalene (8%).

In the study done by Dunlap and Mills, Adapalene 0.1% gel showed significantly less irritation in terms of dryness, erythema, desquamation and burning or stinging.<sup>14</sup> This was in concurrence with the findings of our study.

### Conclusion

Adapalene was found to be a better topical retinoid in the treatment of Grade I and II acne with respect to faster clinical clearance, mean reduction in number of lesions and reduction in Grade of Acne. Patient tolerance was also better to Adapalene as it was less irritant.

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