Original Article

FUTURE JOURNAL OF PHARMACEUTICALS AND HEALTH SCIENCES

Published by Pharma Springs Publication Journal Home Page: https://pharmasprings.com/fjphs

Adapalene gel therapy in patients with moderate to severe *Acne vulgaris*

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Article History:

Received on: 26 Oct 2023
Revised on: 01 Nov 2023
Accepted on: 02 Nov 2023

Keywords:

Acne vulgaris,
Adapalene,
Intermittent,
Serum lipids

Abstract

Acne is a chronic inflammatory disease of pilosebaceous units. Topical Adapalene is the most effective despite the availability of various treatments. Abnormalities in plasma lipids are recognized side effects of Adapalene therapy. Minimal reports compare the lipid changes in intermittent and continuous Adapalene treatment. One hundred patients with moderate to severe acne were randomly assigned to two treatment regimens. Serum levels of lipids were measured at baseline, 4wk, 8wk, 12wk, 16wk, and at the end of the treatment. A significant increase in cholesterol, triglyceride, and LDL concentration and a decrease in HDL levels in a continuous regimen beyond the normal range but not requiring any treatment interruption compared to intermittent therapy. The cholesterol, triglyceride, and LDL concentration increase was within the normal range. Intermittent Adapalene therapy was clinically equally effective, with lesser effects on serum lipid levels and cost than continuous Adapalene therapy.

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eISSN: 2583-116X
DOI: https://doi.org/10.26452/fjphs.v3i4.515

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INTRODUCTION

Acne vulgaris is a long-lasting, inflammatory condition of the pilosebaceous unit that causes comedones, papules, pustules, nodules, and cysts, as well as scars in seborrheic areas like the face, back, and chest. Almost everyone experiences some degree of acne during adolescence, which resolves on its own in early adulthood [1]. Acne is a significant psychological issue for many teenagers and

young adults due to the involvement of the face with cosmetic substantial problems. Acne vulgaris medication does not cure the condition. The goal is to lessen pain from inflammatory lesions, enhance the physical appearance, and avoid scarring. The long-term treatment for acne calls for patience [2]. The patient needs to be told about the problem. Adapalene controls keratinization and has anti-inflammatory effects, according to in vitro tests. The medication specifically impacts only the b and g subtypes of the nuclear retinoic acid receptors (RARs). Contrarily, the first-generation retinoid, tretinoin, binds to the cytosolic retinoic acid binding protein (CRABP) and all RARs. Adapalene's selective binding to RARs helps explain why it is less likely to irritate patients and more well-liked by them. Adapalene is far more stable than tretinoin, even when exposed to light and powerful oxidizers like benzoyl peroxide. After being applied to the skin, Adapalene has been shown to permeate the sebaceous follicle in about five minutes [3]. Adaferin ® gel is a specially formulated medication that is proven to penetrate follicular ducts. It contains micro crystals of Adapalene that are equally disseminated and range in size from 3 to 10 mm.

MATERIALS AND METHODS

Source of data

Subjects who, based on the Indian Acne Grading system, have moderate to severe acne in the Department of Dermatology and Venereal Diseases at Government Medical College, Nellore, were selected.

The subjects were between the ages of 15-45 yrs. A written consent was obtained from them before enrolment, and the study details were thoroughly given to them before enrolment. The study was initiated after thorough scrutiny and processing by the Ethics Committee from the Department of Dermatology and Venereal Diseases at Government Medical College, Nellore.

The selected subjects were interviewed, and a questionnaire about the age, sex, weight, and personal and family history of acne vulgaris was handed over to them before the sample was taken in the patient's native tongue. Subject permission, as well as parental consent, were required for minors.

Study design: the sebaceous trial was performed [4,5].

Sample size: A total of 100 subjects with moderate to severe acne vulgaris are randomly assigned to one of the two treatment regimen groups [6]:

Arm 1: 0.1% Adapalene gel applied once daily for four months (continuous regimen)

Arm 2: 0.1% gel was applied once daily for one week a month, followed by the study duration of 4 months (intermittent therapy).

Sampling method: simple random sampling

Randomization of subjects was done in a 1:1 ratio, containing 50 in each group [7,8]. They are either to receive intermittent therapy or on a continuous regimen.

Baseline data of subjects was obtained by investigating total cholesterol, Triglyceride, HDL, and LDL before starting topical Adapalene therapy (day), and follow-up investigations were carried out at the end of the 4th, 8th, 12th week, and the completion of the treatment. The response to treatment and lipid profile were evaluated at the end of everymonth for four months.

Method of collection of data

Inclusion criteria

a) A male with a clinical diagnosis of acne vulgaris, who is not pregnant or lactating, and who is willing to receive adapalene therapy [9].
b) >25 noninflammatory lesions (open and closed comedones), more than 20 inflammatory lesions (papules and pustules), less than one nodular lesion, and no cystic lesions on the face (Global

Assessment (IGA) of acne severity Grade 2, 3, or 4).

c) Willing to forego using any additional topical antibiotics or acne drugs for the 12-week therapy period.
d) If the subject is a female of childbearing potential, they must start treatment during a regular menstrual cycle, have a negative pregnancy test result within two weeks of starting treatment, and be willing to use an acceptable method of birth control throughout the study.
e) Subjects willing to give permission and consent:

Exclusion criteria

a) Females who refuse to use an appropriate method of birth control during the research, including those who are pregnant, nursing, planning a pregnancy, or who are pregnant [10].
b) The existence of any skin condition that can impede the identification or evaluation of acne.
c) A history of Adapalene, retinoids, or any other component of the test product or RLD hypersensitivity or allergy.
d) Use of estrogens or other forms of contraception within six months of baseline; such therapy must be continued throughout the research.
e) The use of oral contraceptives or estrogens for less than three months before baseline must be continued throughout the study.
f) Use 1) cryodestruction or chemodestruction on the face within one month of baseline or during the trial; 2) Dermal ablation; 3) Photodynamic treatment surgery for acne, 6) Radiation therapy, or 5) intralesional steroids.
g) Using spironolactone, systemic steroids, systemic antibiotics, systemic treatment for acne vulgaris (other than retinoids, which require a washout period of six months), or systemic anti-inflammatory drugs within one month of baseline.
h) Use no later than two weeks before the baseline.
    a. Topically applied steroids,
    b. Topically applied retinoids,
    c. Topically applied acne medications, including over-the-counter options,
    d. Topically applied anti-inflammatory drugs, or
    e. Topically applied antibiotics.
i) Allergy to Adapalene.
j) The patient is not willing to take Adapalene therapy.

Table 1: IGA Scale for Acne Vulgaris

Grade	Description
0	clear skin with no inflammatory lesions or none at all
1	The area is nearly transparent and unusual, with only one little inflammatory lesion.
2	Papules/pastures only; no nodular lesions; mild severity greater than Grade 1; some no inflammatory lesions; no more than a few.
3	More than a tiny modular lesion, moderate severity larger than Grade 2, up to many no-inflammatory lesions, and possibly some inflammatory lesions.
4	Severe; larger than Grade 3 up to several noninflammatory lesions, may have inflammatory lesions, however not more significant than a few nodular lesions

* The Case description Types for acne research allow researchers to describe lesions that get worse with therapy and are worse than Grade 4. It is advised against enrolling subjects with nodulocystic acne as acne vulgaris participants. In the safety evaluation, those who deteriorate past Grade 4 must be described.

Parameters to be studied

Cholesterol estimation using the dynamic extended stability CHOD- POD endpoint method and ERBA XL as a lipid cleaning agent 300 analyzer manufactured by Transasia Bio-medicals Ltd [11].

Estimating triglycerides by GPO-PAP endpoint method by ERBA XL 300 analyzer manufactured by Transasia Bio-medicals Ltd.

Estimation of HDL by immune inhibition method using analyzer ERBA XL 300 analyzer manufactured by AGAPPE Diagnostics.

Estimation of LDL by Friedwald's calculation.

Estimation of Serum Lipid Profile

1) Serum Total Cholesterol

The enzymatic End Point Method (Cholesterol Oxidase Method) was used to quantitatively determine total cholesterol in human serum using the CHOD-POD endpoint method, with a lipid clearing agent by ERBA Manheim analyzer, manufactured by Transasia Biomedicals Ltd.

Principle

The cholesterol is identified in the wake of enzymatic hydrolysis and oxidation. The cholesterol esterase hydrolyzes cholesterol esters to create free cholesterol and fatty acids [12]. The enzyme cholesterol oxidase then transforms cholesterol into cholestene-3-one and hydrogen peroxide. In the presence of peroxidase, hydrogen peroxide oxidatively links with 4-aminoantipyrine and phenol to generate red quinoneimine dye, which has a maximum absorbance range of 510–530 nm. The amount of total cholesterol in the serum is inversely correlated with the intensity of the red color.

Cholesterol esterase

Cholesterol ester + H_20 Cholesterol + Fatty acids

Cholesterol oxidase

Cholesterol + O_2 Cholestene -3-one + H_2O_2

peroxidase

2H2O2 + phenol + 4-AminoantipyrineQuinoneimine + 4H2O 49

Reagent	Composition ContentsConcentrations

R1.Reagent

Goods Buffer 100mmol/L, pH

6.44-Aminoantipyrine

0.3mmol/L Phenol 5mmol/L

Peroxidase ≥ 3000U/L Cholesterol esterase >200U/L Cholesterol Oxidase >100 U/L [13]

Preparation of reagent

R1 Reagent – contents ready for use.

Procedure

Cholesterol was estimated using the ERBA XL300 auto analyzer [14]. The sample used for the assay was 10µl, and the reagent volume used was R1- 1000µl.

Typical Values in serum plasma

Risk levels

Value Interpretation < 200 mg/dl Desirable blood cholesterol 200- 239 mg/dl Border line- high blood cholesterol ≥ 240mg/dl High blood cholesterol 50.

2. Serum triglycerides:

Enzymatic Method (GPO- PAP Method) was used to quantitatively determine triglycerides in human serum using the Erbaauto analyzer [15].

Principle

Following enzymatic hydrolysis utilizing lipoprotein lipase, the triglyceride is identified.

The hydrogen peroxide in the presence of peroxidase oxidizes 4-aminophenazone and 4- 4-chlorophenol to create the 510–530 nm absorbent red quinoneimine dye.

The intensity of the red color is proportional to the amount of triglyceride present in the serum [86]. Triglycerides + H20 Lipoprotein lipase Glycerol + fatty acids combined with ATP Globule kinase ADP plus glycerol-3-phosphate

Glycerol + ATP Glycerol kinase Glycerol-3-phosphate + ADP

Glycerol-3-phosphate + O2 Glycerol phosphate oxidase dihydroxy acetone phosphate +H2O2.

2H2O2 + 4-aminophenazone + 4-chlorophenol peroxidase Quinoneimine +HCl+ 4H2O 51

Reagent Composition Contents Concentrations

Buffer pipes 40mmol/L, pH 7.0

4-Aminoantipyrine 0.4mmol/L Magnesium-ions 2.5mmol/L Enzyme Reagent

ATP 2.0mmol/L

Lipoprotein Lipase 4000U/L Glycerol-kinase 1500U/L

Glycerol-3-phosphate oxidase 4000 U/L Peroxidase 2200U/L

DHBS 0.2mmol/L [16]

Preparation of Reagent

Buffer/ Enzyme Reagent – Reagents R1 and R2 are prepared for usage. The working reagent is created by carefully combining four parts of R1 and 1 part of R2 [17].

Procedure

Triglyceride was estimated using an ERBA auto analyzer. The sample volume used for the assay was two µl, and the reagent volume used was R1-180 µµl

Values in serum: Intended cut-off points

Normal < 150mg/ dl High 150 – 199 mg/dl

Hypertriglyceridemia 200-499 mg/dl 52

Very high > 499 mg/ dl [18]

3) Serum HDL- cholesterol

The direct method was used to determine HDL-cholesterol using quiche HDL quantitatively. Cholesterol with calibrator in an auto analyzer [19].

Principle

The electrostatic interaction between polyanions and cationic compounds inhibits the response between cholesterol other than HDL and the enzyme for cholesterol testing. The free cholesterol in HDL is converted to hydrogen peroxide by cholesterol oxidase. In the presence of peroxidase, hydrogen peroxide causes the oxidative condensation of EMSE and 4-AA, and the absorbance of the resultant red-purple quinine is measured to determine the HDL cholesterol value [70]. HDL polyanions are not the only lipoproteins that inhibit enzyme reactions.

Cationic substances

HDL (cholesterol esters) +H2O cholesterol esterase HDL (free cholesterol) + FFA HDL (free cholesterol) + O2 + H cholesterol oxidase cholestenone +H2O2

2H2O2 +4-AA+EMSE+H3 + O peroxidase red-purple quinine +5H2O

Reagent composition

HDL –C Direct R1 N-ethyl-N-(3-methylphenyl)-Nsuccinylethyenediame(EMSE) HDL-C Direct R2 Cholesterol oxidase 4-Aminoantipyrine HDL –C Direct calibrator

Preparation of reagents

The R1 enzyme reagent's usable contents are Ready-to-use and the R2 enzyme reagent.

Procedure

HDL cholesterol was estimated using an Erba XL 300 auto analyzer. The sample volume used for the assay was 5µL, and the reagent volume used was R1 450µL and R2 150µL.

Normal range: Male: 35-80mg/dl

Female: 42-88mg/d

4. Serum LDL Cholesterol

LDL cholesterol in human serum was quantitatively determined using the Friedewald equation.

Friedewald Equation

[LDL-cholesterol] = [Total cholesterol] – [HDL- cholesterol] – [Triglyceride/5] Limitations for Friedewald Equation:

There are two main limitations where the Friedewald Equation cannot be applied:

1. If the triglyceride concentration is above 400mg/dl.

2. VLDL is present in people with type III hyperlipoproteinemia who have this condition. -VLDL is a kind of VLDL that has a higher cholesterol content than VLDL. The calculation of LDL for the current study has considered the restrictions above.

Risk Levels:

Optimal <100mg/dl

Near or above optimal 100 -129 mg/dl

Borderline High 130-159 mg/dl

High 160- 189mg/dl

Very high >189mg/dl

Statistical analysis using GraphPad Prism version 8.03: Using GraphPad Prism version 8.03, statistical data analysis was performed.

Results and Discussion

100 patients diagnosed to have moderate to severe acne vulgaris attending the Dermatology & Venereal Diseases OPD at Government Medical College, Nellore, who fulfilled the inclusion and exclusion criteria, were studied from October 2019- February 2020. The study aimed to assess the lipid profile changes in intermittent and continuous Adapalene topical therapy in moderate to severe acne vulgaris cases.

Table 2: Distribution of 100 acne cases based on age of the patient

Age	Number of Cases
15-24	84
25-34	20
35-45	4

Most of the patients, i.e., 84 patients, were in the age group of 15-24 years, 20 patients were in the age group of 25-34years, and four patients were in the age group of 35-45 yrs.

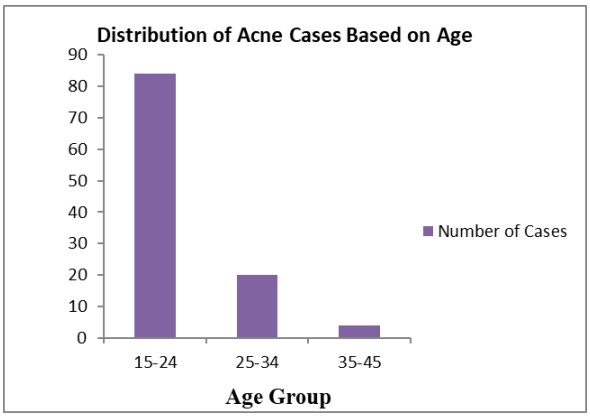

Figure 1: Age-based distribution of acne cases

Table 3: Cases are distributed according to sex

GENDER	NUMBER OF CASES
Male	60
Female	45

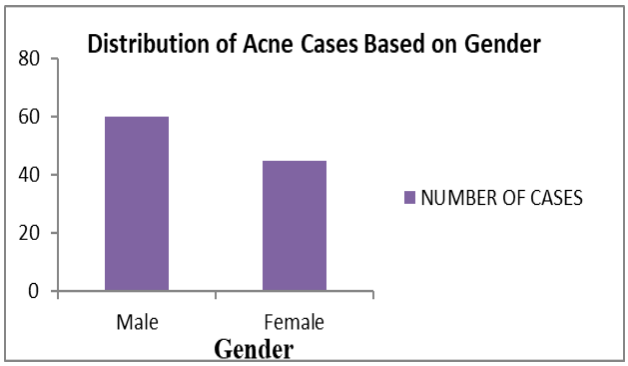

Figure 2: Sex distribution

Of the 100 patients, 60 (58%) were males and 45 (42%) were females. There was an overall male preponderance, with a male-to-female ratio of 1.38:1.

Table 4: Site of acne

Anatomical site of acne	Number of cases
Facial acne	85
Truncal	6
Both	15

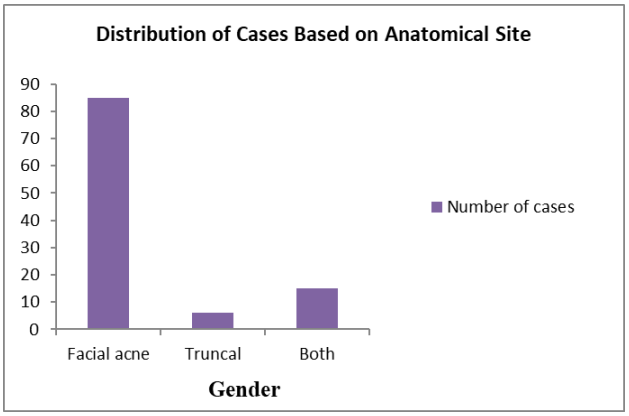

Figure 3: Site of Acne

Eighty-five patients had facial acne, which was the most prevalent type. Six patients had Truncal, and 15 had face and Truncal acne. (Table 7, figure 3).

Table 5: Previous treatment

Previous treatment	Number of patients
Antibiotics+Topical	42
Antibiotics	34
Topical therapy	15
Isotretinoin	6
Adapalene	2
No treatment	20

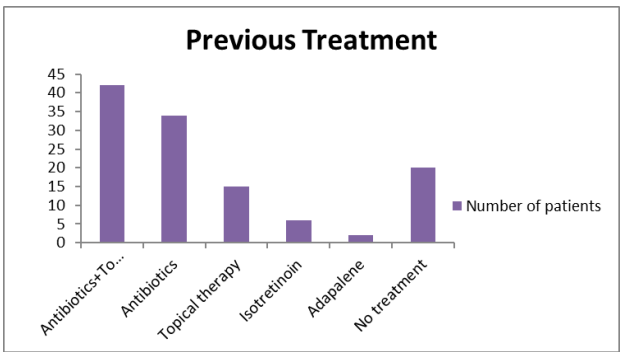

Figure 4: Previous treatment

Regarding the previous treatment taken by the patients, the majority of the patients, i.e., 42 patients, had taken treatment with both antibiotics and topical therapy, 34 patients had taken treatment with antibiotics alone, and 15 patients had taken topical treatment. With topical therapy alone, six patients had taken treatment with isotretinoin; two patients had Adapalene, and 20 patients had not taken any treatment before.

Table 6: Grade of acne

Grade of Acne	Week 0	Week 4	Week 12	After four months
0	--	--	10%	10%
I	--	15%	85%	96%
II	65%	69%	16%	4%
III	45%	30%	--	--

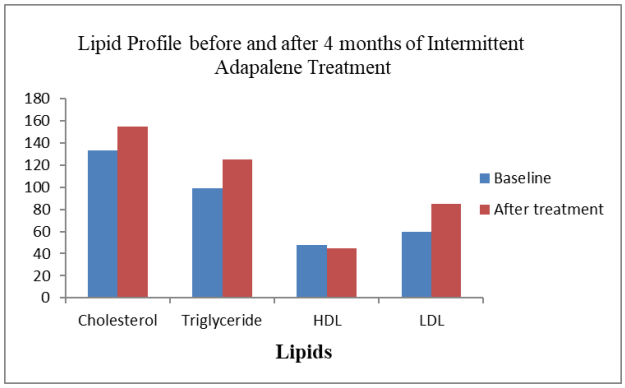

Figure 5: Lipid profile before and after four months of intermittent Adapalene treatment

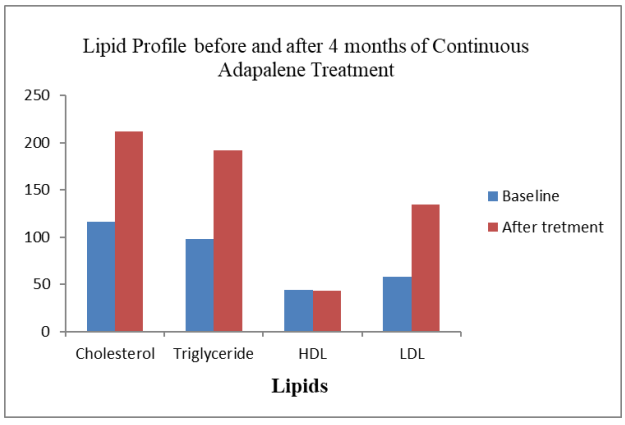

Figure 6: Lipid profile before and after four months of continuous adapalene treatment

On cutaneous assessment, it was found that at week 0, 60 % of patients had grade II acne, and 40% had grade III acne. At week 4, 10% had grade I, 64% had grade II acne, and 26% had grade III acne. At 12 weeks, 5% of patients had

Table 7: Lipid profile before and after four months of intermittent Adapalene treatment

Lipid	Baseline	After treatment	p-value
Cholesterol	133.35± 34.12	155.56±22.68	<0.0001
Triglyceride	99.59±45.08	125.88±41.27	<0.0001
HDL	48.28±15.40	45.46±13.08	<0.0001
LDL	60.65±30.45	85.82±26.12	<0.0001

Table 8: Lipid profile before and after four months of continuous Adapalene treatment

Lipid	Baseline	After treatment	p-value
Cholesterol	116.54± 25.09	212.56±15.55	<0.0001
Triglyceride	98.56±24.05	192.87±16.23	<0.0001
HDL	44.67±11.34	43.99±8.92	<0.0001
LDL	58.62±26.33	134.65±25.04	<0.0001

Table 9: Comparison of Total cholesterol between Intermittent and Continuous Treatment

Period	Intermittent therapy	Continuous therapy	P value
Baseline	126.35±35.09	115.55±25.09	<0.450
After four weeks	128.75±35.46	136.85±28.53	<0.142
After eight weeks	132.79±32.95	157.85±26.22	<0.0001
After 12 weeks	138.87±34.46	178.15±27.78	<0.0001
After 16 weeks	145.62±30.72	195.25±28.78	<0.0001
After 20 weeks	156.58±25.70	210.56±16.57	<0.0001

Table 10: Comparison of Triglycerides between Intermittent and Continuous Treatment triglycerides

Period	Intermittent therapy	Continuous therapy	P value
Baseline	98.59±45.02	98.57±24.01	<0.785
After 4 weeks	98.49±45.95	115.50±24.65	<0.0440
After 8 weeks	105.48±45.08	132.09±22.91	<0.0002
After 12 weeks	108.50±43.79	150.52±20.20	<0.0001
After 16 weeks	115.26±45.99	165.25±18.82	<0.0001
After 20 weeks	126.90±42.25	188.90±16.25	<0.0001

grade 0 acne, 82% had grade I acne, and 13% had grade II acne. After completing treatment, at 16 weeks, it was found that 5% had grade 0, 93% had grade I, and 2% had grade II. (Table 9) 61.

Serum cholesterol, triglycerides, and HDL significantly changed on continuous Adapalene therapy. Values were elevated when compared with baseline but were above average levels. (Table 11, figure 6).

Cholesterol

The measured baseline cholesterol in the intermittent therapy group was 126.3535.09, and the values at four weeks, eight weeks, 12 weeks, and 16 weeks later, as well as after the treatment, were 128.75±35.46, 132.79±32.95, 138.87±34.46, 145.62±30.72 and 156.58±25.70 respectively. Compared to baseline, there was a rise in cholesterol at every interval, but it stayed within normal

limits. A fundamental value that was measured of cholesterol in the continuous therapy group was 115.55±25.09, then after at 4, 8, 12wk, 16, and the end of the treatment were 136.85±28.53, 157.85±26.22, 178.15±27.78, 195.25±28.78 and 210.56±16.57 respectively. There was a significant increase in cholesterol compared to baseline and above the upper limit at all intervals. (Table 12, figure 7).

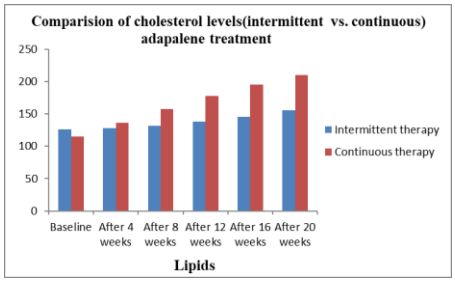

Figure 7: Comparison of Cholesterol levels in adapalene treatment

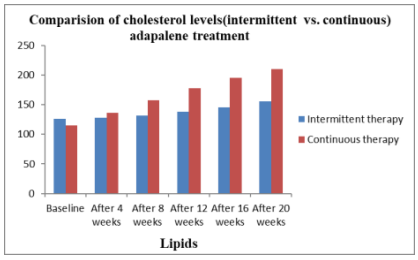

Figure 8: Comparison of triglyceride levels in adapalene treatment

Cholesterol levels compared between intermittent and continuous therapy at four weeks of treatment were 128.75±35.46 and 136.85±28.53. The difference was statistically insignificant, with a value of 0.142. When reached at 8, the values were 132.79±32.95 and 157.85±26.22, and the difference was statistically significant with a p-value (0.0001). At 12, the values were 138.87±34.46 and 178.15±27.78, and the difference was statistically significant with a p-value(0.0001). At 16, the values were 145.62±30.72 and 195.25±28.78, and the difference was statistically significant with a p-value(0.0001). At 20wk, the values were 156.58±25.70 and 210.56±16.57, and with a p-value of (0.0001), the difference was statistically significant. (Table 12).

Triglyceride

Triglycerides' baseline values in the group receiving intermittent treatment were 98.59±45.02, then after at 4, 8wk, 12wk, 16wk, and at the end of the treatment were 98.49±45.95, 105.48±45.08, 108.50±43.79, 115.26±45.99 and 126.90±42.25 accordingly. Compared to the baseline, triglycerides increased at every interval but within normal limits.

Table 11: Comparison of HDL between Intermittent and Continuous Treatment

Period	Intermittent therapy	Continuous therapy	P value
Baseline	50.26±11.38	44.64±10.32	<0.0865
After four weeks	50.48±12.69	43.86±9.20	<0.0176
After eight weeks	49.63±13.95	45.00±11.28	<0.0662
After 12 weeks	51.08±12.60	41.80±9.59	<0.0054
After 16 weeks	49.62±12.99	41.42±8.56	<0.0029
After 20 weeks	48.45±10.09	40.98±7.91	<0.0085

Table 12: Comparison of LDL between Intermittent and Continuous Treatment

Period	Intermittent therapy	Continuous therapy	P value
Baseline	59.62 ±32.45	60.62 ±26.34	<0.853
After four weeks	65.95±34.28	75.06 ±28.90	<0.102
After eight weeks	66.69±30.20	91.55 ±28.76	<0.0003
After 12 weeks	72.45±28.80	106.99 ±27.61	<0.0001
After 16 weeks	75.30±27.99	122.26 ±28.95	<0.0001
After 20 weeks	86.80±28.12	134.65 ±27.20	<0.0001

The measured baseline values of Triglycerides in the continuous therapy group were 98.57±24.01 then after 4 4, 8wk, 12wk, 16wk, and at the end of the treatment were 115.50±24.65, 132.09±22.91, 150.52±20.20, 165.25±18.82 and 188.90±16.25 respectively. There was a significant increase in triglycerides at all the intervals compared with baseline and above the standard limit. (Table 13, Figure 8).

Triglyceride levels compared between intermittent and continuous therapy at four weeks of treatment were 98.49±45.95 and 115.50±24.65. The difference has been statistically insignificant, with a value of 0.0440. When compared at 8, the values were 105.48±45.08 and 132.09±22.91, and the difference was statistically significant with a p-value (0.0002). At 12, the values were 108.50±43.79 and 150.52±20.20, and the difference was statistically significant with a p-value (0.0001). At 16, the values were 115.26±45.99 and 165.25±18.82, and the difference was statistically significant with a p-value(0.0001). At 20wk, the values were 126.90±42.25 and 188.90±16.25, and the difference was statistically significant with a p-value(0.0001).

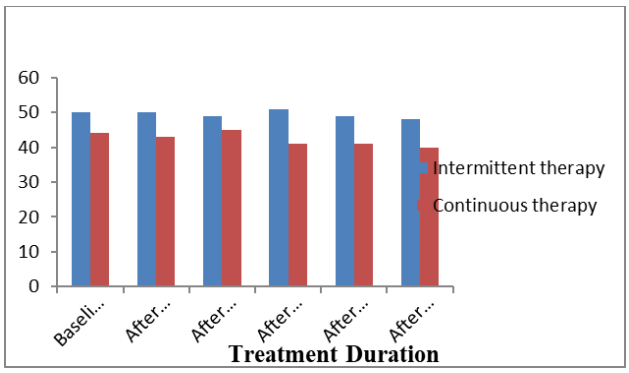

Figure 9: Comparison of HDL levels of adapalene treatment

HDL levels in the intermittent therapy group were measured at baseline at 50.26 11.38 and again at 4 wk, 8, 12, 16, and at the end of the treatment were 50.48±12.69, 49.63±13.95, 51.08±12.60, 49.62±12.99 and 48.45±10.09 accordingly. Compared to baseline, HDL decreased at every interval but stayed within normal limits. The measured baseline values of HDL in the continuous therapy group were, 44.64±10.32 then after at 4, 8wk, 12wk, 16wk, and at the end of the treatment were 43.86±9.20, 45.00±11.28, 41.80±9.59, 41.42±8.56, 40.98±7.91 respectively. There was a significant reduction in HDL relative to baseline at each period. (Table 14, Figure 9).

HDL levels compared between intermittent and continuous therapy at four weeks of treatment were 50.26±11.38 and 44.64±10.32. The difference has been statistically insignificant with a p-value (0.0174). When compared at 8, the values were 49.63±13.95 and 45.00±11.28, and the difference was statistically slight with p-value(0.0660). At 12, the values were 51.08±12.60 and 41.80±9.59, and the difference was statistically insignificant with a p-value(0.0052). At 16, the values were 49.62±12.99 and 41.42±8.56, and the difference was statistically significant with a p-value(0.0028). At 20wk, the values were 48.45±10.09 and 40.98±7.91, and the difference was statistically significant with a p-value(0.0084).

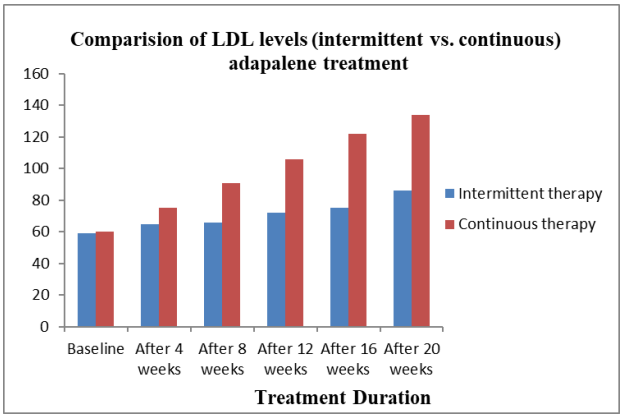

Figure 10: Comparison of DL levels of adapalene treatment

LDL baseline values in the group receiving intermittent treatment were 59.62 ±32.45, then after at 4, 8, 12wk, 16wk, and the end of the treatment were 65.95±34.28, 66.69±30.20, 72.45±28.80, 75.30±27.99, 86.80±28.12 respectively. Compared to baseline, there was

an increase in LDL at every interval, but it was within normal limits. HDL baseline value measured in the continuous therapy group was 59.62 ±32.45, then after at 4wks, 8wk , 12wk, 16wk and following the course of treatment were 65.95±34.28, 66.69±30.20, 72.45±28.80, 75.30±27.99, 86.80±28.12 respectively. There was significant every interval saw a rise in LDL compared to baseline. (Table 14, figure 10).

LDL levels compared between intermittent and continuous therapy at four weeks of treatment were 65.95±34.28 and 75.06 ±28.90. The difference has been statistically insignificant with a p-value (0.101). When compared at 8, the values were 66.69±30.20 and 91.55 ±28.76, and the difference was statistically significant with a p-value (0.0001). At 12, the values were 72.45±28.80 and 106.99 ±27.61, and the difference was statistically significant with a p-value(0.0001). At 16, the values were 75.30±27.99 and 122.26 ±28.95, and the contrast was statistically significant with a p-value(0.0001). At 20wk, the values were 86.80±28.12 and 134.65 ±27.20, and the difference has been statistically significant with a p-value (0.0001).

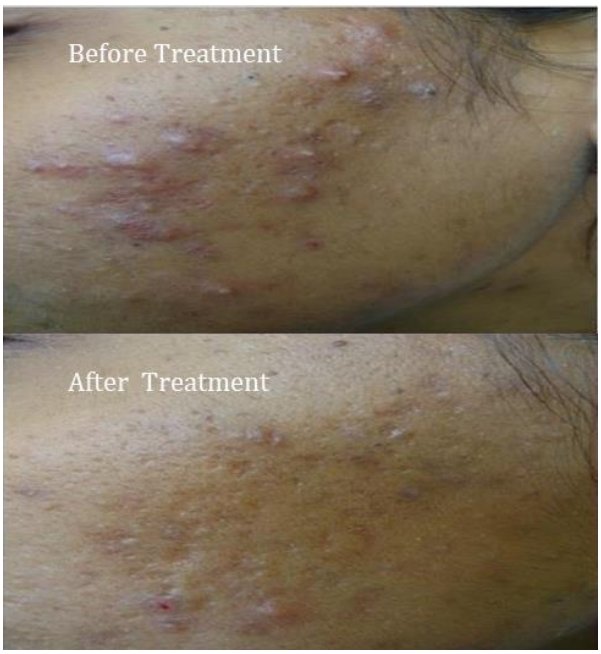

Figure 11: Moderate acne

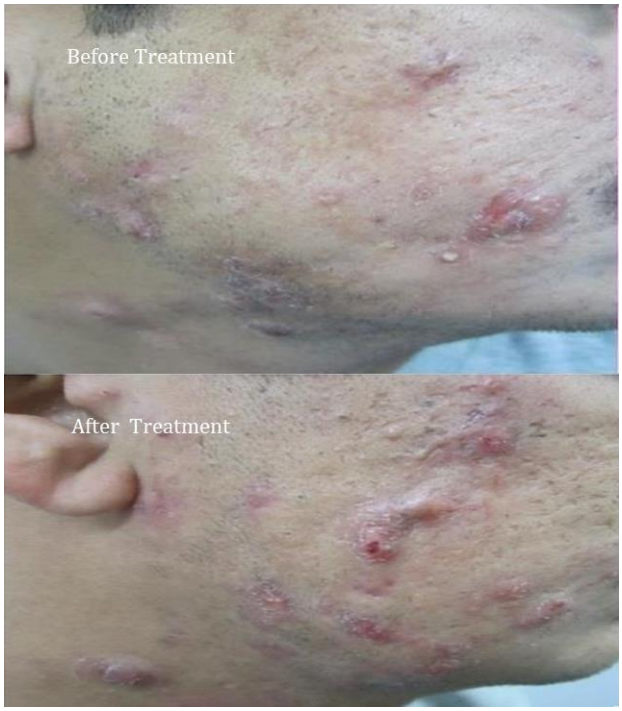

Figure 12: Severe Acne

DISCUSSION

Acne vulgaris is a multifactorial disease characterized clinically by inflammatory and noninflammatory lesions. Successful acne therapy dramatically improves acne and minimizes its effects. Adapalene is a drug that acts on all pathogenic factors and is associated with side effects. The study aimed to assess the lipid profile changes in intermittent and continuous Adapalene topical therapy in acne vulgaris.

A study done by Stern et al. showed the prevalence of acne was virtually 100% by mid-teens in both the sex. Another survey by Smithard et al. showed that the majority of acne was 56% in boys and 45%. Girls between 14-16 yrs, with moderate to severe acne in 11%.10.

Similar to the study done by Smithard et al., in our research, out % of 100 patients, 56% were males, and 44% were female. There was an overall preponderance of males. In a study by Goulden et al., 25% of acne patients had a mean age of 24 years, and 8% had late onset (over 25 years) acne. In our study, the mean

age was found to be 21.8 years. Our study showed intermittent regimen with less effects on lipid profile. Our study reported that on periodic Adapalene medication, blood triglycerides, HDL, and LDL exhibited no discernible changes. Compared to the baseline, values were higher at all intervals but were within the average level. Our result was similar to an RCT conducted by Akman et al., which compared intermittent. Adapalene treatment with conventional treatment reported that an intermittent regimen represented an effective alternative treatment with fewer side effects. There are studies done independently to evaluate the lipid profile changes in traditional medicine, showing a significant increase in cholesterol, triglycerides, and LDL.

An RCT of 90 patients with severe acne showed that patients using Adapalene daily for three months developed a significant increase in cholesterol and triglyceride levels. Another study indicates stopping the therapy when triglyceride levels are above 800mg/dl because of the risk of pancreatitis.

Our study found that Continuous Adapalene medication resulted in significant changes in serum cholesterol, triglycerides, and HDL. Values were higher than baseline, but they were above average level. As reflected in our present study, it showed statistically significant changes compared with the baseline at all intervals. The effect of Adapalene is dose-dependent because usage of the drug daily could have been probable reason for influencing the increase in the lipids in continuous therapy compared with intermittent treatment.

Our study proved that a lipid profile change in intermittent therapy was less than in continuous treatment. Intermittent therapy is better than constant therapy. Further, we can standardize the treatment by extending the study to a large group of patients.

Some studies have shown the effects of lipid profiles in continuous therapy. Another multicenter randomized controlled trial showed that low-dose Adapalene had significantly elevated serum triglycerides.

Previous studies have examined serum lipid abnormalities associated with conventional Adapalene use and have estimated the incidence of lipid abnormalities.

The present study demonstrated that intermittent Adapalene therapy has little effect on plasma cholesterol, triglyceride, LDL, and HDL, and the results or changes were within the standard acceptable level. Lipid changes were more frequent in continuous therapy when compared with intermittent regimens. Other side effects were less in an intermittent regimen. Because the side effects of Adapalene are dose-dependent, it could be one reason why the lipid profile was significant in continuous therapy. The changes are reversible on stopping the treatment. Patients with acne who develop a considerable increase in triglyceride levels during Adapalene therapy are at increased risk for future hyperlipidemia and metabolic syndrome. In his study, Kannelet et al. commented on the potential cardiovascular risk of this lipid change.

CONCLUSION

The present study demonstrated that intermittent Adapalene therapy has little effect on plasma cholesterol, triglyceride, LDL, and HDL, and the results or changes were within the standard acceptable level. At the same time, continuous Adapalene therapy caused an increase in cholesterol, triglycerides, LDL, and HDL above the normal range with a grade 1 increase. Lipid changes were more frequent in continuous therapy when compared with intermittent regimens. Other side effects were less in the intermittent regimen. Our study found that intermittent Adapalene regimens are clinically effective, cost-effective, less impacting plasma lipid levels, and considered a better alternative.

Acknowledgment

The authors are thankful to the Principal (Dr. Y. Prapurna Chandra) & HOD (Dr. Yerikala Ramesh) from Ratnam Institute of Pharmacy, Pidathapolur, SPSR Nellore, for providing the necessary facilities to carry out this research work.

Conflict of Interest

The authors declare no conflict of interest, financial or otherwise.

Funding Support

The authors declare that they have no funding for this study.

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