Original Article

To assess the efficacy of isotretinoin in acne vulgaris with daily versus pulse therapy

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Abstract

Aim To determine the Efficacy of isotretinoin in acne vulgaris daily versus pulse therapy.

Study design A randomized controlled trial.

Place and duration of study Outpatient Department of Dermatology, Sargodha Medical College, Sargodha, from June 2017 to July 2018.

Methods There were total 150 patients (both male and female) having 75 patients in each group. Group A was given oral isotretinoin capsule 20 mg twice daily for one week after 3 weeks as intermittent/ pulse therapy for 6 months. Group B was given oral isotretinoin capsule 20 mg/daily continuously for 6 months. Group A and B further sub divided into mild, moderate and severe, having 25 patients in each subgroup. The patients were advised to revisit after every 4 weeks for follow-up. Both groups were also advised to apply 1 % clindamycin gel twice a day for 6 months on lesions. The drug is considered efficacious if acne lesion of the patient reduced to 0-5 lesion only.

Results In group A, the oral isotretinoin pulse therapy was efficacious in 22 patients (88%) of mild acne, 23 patients (92%) of moderate acne and 19 patients (76%) of severe acne. In group B, the oral isotretinoin continuous therapy was efficacious in 23 patients (92%) of mild acne, 22 patients (88%) of moderate acne and 21 patients (84%) of severe acne. There was no difference in efficacy of drug in mild moderate or severe acne in group A and B as the p – value calculated by One way Anova is 0.091 and 0.098 respectively, which is not significant. It also revealed that there was no statistical difference in efficacy of drug in group A and B , having p value of >0.05.

Conclusion It is concluded that the efficacy of oral isotretinoin for acne in intermediate/pulse therapy is same. So, we should prefer intermediate/pulse therapy as it is cost effective, there are reduced side effects of drug due to shorter duration and the patient is more compliant.

Key words
Isotretinoin, acne vulgaris.

Introduction

The word acne is taken from Greek origin "acme" meaning "prime of life".[1] Acne vulgaris is a common skin disorder of teenage group with an equal sex ratio. More than 80% population of world face acne during their life.[2] Although in general acne vulgaris is a benign and self-confined condition, it may lead to severe psychological problems due to disfiguring scars. It is caused by chronic inflammation of

pilosebaceous glands leading to different polymorphic emptions.

The lesions may be noninflammatory like open and closed comedones, which later on may become inflamed and form papules and pustules.[3] So, in a patient the characteristic feature include white and black comedones, papules, pustules, cyst, nodules, abscess formation and scaring.[4] It usually occur on face, chest, upper bulk and upper arm.[5]

The pathogenesis of this skin disorder is multifactorial. It comprises of follicular hyper-keratinization, increased production of sebum, presence of *Propionibacterium acnes* (P. acnes), inflammatory mediators, and excess androgens.[5] Acne is more commonly seen in teenagers, as during young adulthood, there is an increase in hormones which include testosterone, dihydrotestosterone (DHT), and dehydroepiandrosterone (DHEA), growth hormone (GH) and insulin-like growth factor 1 (IGF-1). All of these hormones are associated with worsened acne.[6]

Some dermatologists have classified acne according to the lesion on face. If the lesions on half of the face were 0–5 they have mild acne, 6–20 for moderate acne, 21–50 for severe acne, and more than 50 for very severe acne.[7] In our study we have divided acne into three categories: mild, moderate and severe.[8]

There are different treatment modalities available for the treatment of acne. They include topical as well as systemic drugs which are prescribed according to severity of acne.[9] In

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acne vulgaris and isotretinoin have very good therapeutic result. Isotretinoin may be given in conventional dose 0.5 mg/ kg/ day or low dose isotretinoin 0.25 mg/ kg/ day for 6 months.[10] In some studies intermittent fixed dose of 20 mg of isotretinoin is given on alternate day (11) or 0.5–0.75 mg/ kg per day, applied for 1 week every 4 weeks for a period of 4-6 months.[12] It is usually associated high incidence of mucocutaneous and systemic side effect. Most of the patients complaint of persistent dryness of lips. Some have dry eyes, lower back pain, headaches, arthralgia and hair loss.[13] Some reports of behavioral problems like depression, psychosis and mania have also been reported.[14] The other problem with oral isotretinoin is it is quite expensive.[15] So, it is recommended in intermittent pulse therapy to make it more cost effective and reduce its side effects.[16]

Methodology

This prospective study of the comparative efficacy and tolerability was carried out at the Outpatient Department of Dermatology, Sargodha Medical College Sargodha. The patients with acne enrolled in this study were labeled by using non-probability sampling technique. A total 150 patients were included in this study. Females who were pregnant or married, desiring to get pregnant or using temporary methods of contraception, patients having family and/ or personal history of hyperlipidemia or diabetes and those having drug-induced acne were excluded. Informed written consent was taken. Patients' name, age, gender, address and mobile number were noted in a pre-designed proforma. Patients were examined clinically and then categorized as mild, moderate and severe acne according to severity of disease.[17]

- *Mild disease*: Few to several papules/pustules with no nodule.

- *Moderate disease*: Several to many papules/pustules with few to several nodules.
- *Severe disease*: Numerous and/or extensive papules/pustules with many nodules.

Patients were divided into two groups using random number table, containing 75 patients in each group. Group A was given oral isotretinoin capsule 20 mg twice daily for one week after 3 weeks as intermittent/ pulse therapy for 6 months. Group B was given oral isotretinoin capsule 20 mg/ day continuously for 6 months. Group A and B were further sub divided into mild, moderate and severe, having 25 patients in each subgroup. The patients were advised to revisit after every 4 weeks for follow-up. Both groups were also advised to apply 1 % clindamycin gel twice a day for 6 months on lesions. The drug is considered efficacious if acne lesion of the patients were reduced to 0-5 lesion only.

The data collected was processed by using Statistical Package for Social Sciences (SPSS 20). Efficacy of oral isotretinoin intermediate/ pulse therapy versus continuous therapy was shown in tables and figures. One way ANOVA was used to test significance of efficacy of drug in different subgroups of acne (i.e. mild, moderate and severe acne), followed by Post hoc Tukey's test to test significance among groups. One-way ANOVA was also used to test significance of difference between efficacy of drug in group A and B. A *p* value of ≤ 0.05 was considered significant.

Results

There were total 150 patients (both male and female) who were selected for this study. In Group A and group B we had 75 patients each which were subdivided into mild, moderate and severe acne with 25 patients each.

In group A there were 21 (28%) males and 58 (77.33%) females and in group B there were 21 (28%) males and 58 (77.33%) females. Stratification of age is shown in **Table 2** where out of total 150 patients of acne majority of patients presented at age between 21-30 years of age 63 (42%). In group A, the oral isotretinoin pulse therapy was efficacious in 22 patients (88%) of mild acne, 23 patients (92%) of moderate acne and 19 patients (76%) of severe acne. There was no difference in efficacy of the drug in mild moderate or severe acne in group A as the p–value calculated by One way Anova is 0.091, which is not significant.

In group B, the oral isotretinoin continuous therapy was efficacious in 23 patients (92%) of mild acne, 22 patients (88%) of moderate acne and 21 patients (84%) of severe acne. There was no difference in efficacy of drug in mild moderate or severe acne in group B as the p – value calculated by One way Anova is 0.098, which is not significant.

Data was analyzed by using One way Anova to compare the efficacy of oral isotretinoin in intermediate/ pulse therapy versus continuous therapy. It revealed that there was no statistical difference in efficacy of drug in group A and B, having p value of >0.05.

Table 1 Distribution of patients according to gender

Gender	Group A Number (%age)	Group B Number (%age)
Male	21 (28%)	18 (24%)
Female	58 (77.33%	57 (76%)

Table 2 Distribution of patients according to age

Age (years)	Total number of patients with acne (%)
11-20	45 (30%)
21-30	63 (42%)
31-40	27 (18%)
41-50	15 (10%)

Table 3 Number of Patients with reduced lesions 0-5 after treatment with intermediate/ pulse therapy (n=75)

Follow-up	mild acne	moderate acne	severe acne
4 weeks	1	0	0
8 weeks	3	0	0
12 weeks	3	7	1
16 weeks	5	7	7
20 weeks	6	6	5
24 weeks	4	3	6
Total number of patients improved	22	23	19
Standard deviation (SD)	1.75	3.31	3.18
p value	0.091		

Table 4 Number of Patients with reduced lesions 0-5 after treatment with continuous therapy (n=75)

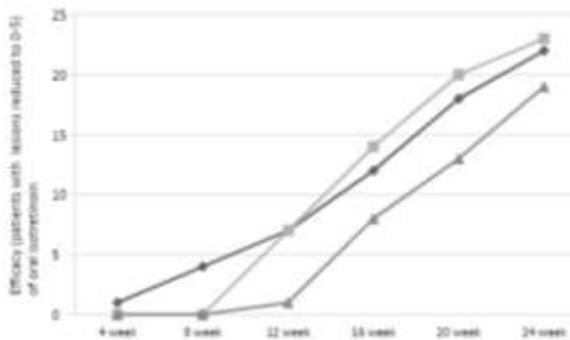| Follow-up	Mild acne	Moderate acne	Severe acne
4 weeks	2	0	0
8 weeks	4	1	0
12 weeks	3	4	2
16 weeks	9	11	10
20 weeks	2	3	2
24 weeks	3	3	7
Total number of patients improved	23	22	21
Standard deviation (SD)	2.63	3.88	4.08
p value		0.098	

Figure 1 Number of Patients with reduced lesions 0-5 after treatment with intermediate/ pulse therapy (n=75)
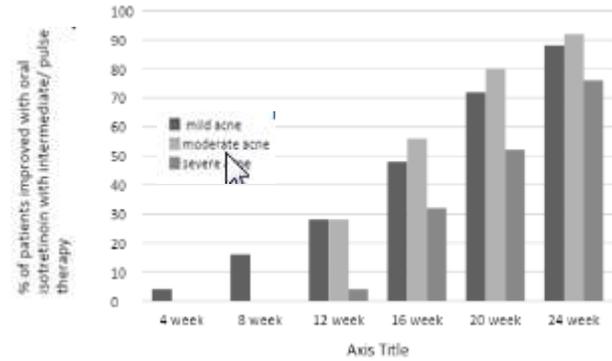

Figure 2 Percentage of patients with reduced lesions 0-5 after treatment with continuous therapy (n=75)
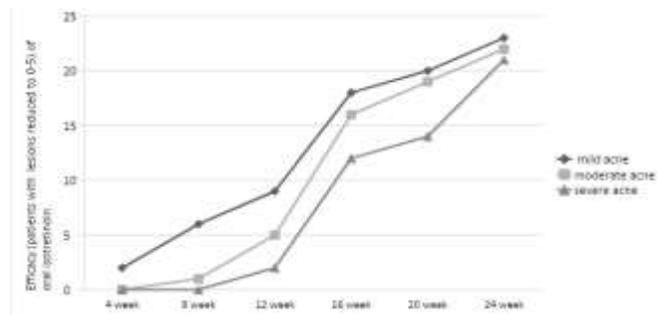

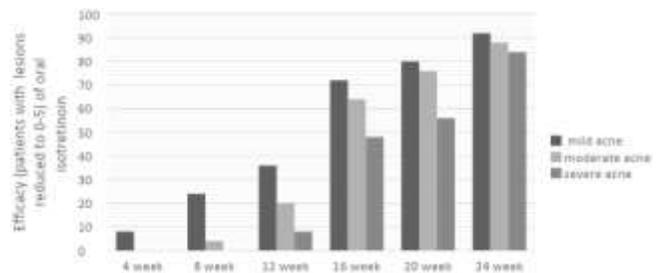**Figure 3** Number of Patients with reduced lesions 0-5 after treatment with continuous therapy (n=75)

Figure 4 Percentage of patients with reduced lesions 0-5 after treatment with intermediate/ pulse therapy (n=75)

Discussion

Acne vulgaris is a very common problem of the modern world as it is eighth most prevalent disease worldwide. The Global Burden of Disease Project has estimated its incidence at 9·4%, ranking it as quite high.[18] Acne is not only widespread but its treatment is quite costly and required for a longer duration. That's why, in USA approximately 50 million people are

treated for acne vulgaris causing yearly burden of $1 billion on health care system in USA.[19] The major cause of this problem include hormonal imbalance for which multiple remedies are devised that include androgen receptor blockers, adrenal androgen production blockers or ovarian androgen production blockers. Androgen receptor blockers include spironolactone, cyproterone acetate, chlormadinone, and flutamide; adrenal androgen production blockers include glucocorticoids; and ovarian production blockers include gonadotropin-releasing agonists and oral contraceptives.[20]

Oral isotretinoin is regarded as the first-line treatment modality for acne vulgaris.[21,22] Isotretinoin is the only therapy available that influences all of the major contributing factors of acne, which include follicular hyper-keratinization, increased production of sebum, inflammation and excess androgens.[23]

In this study we enrolled 150 patients, who were equally divided into group A and group B. Group A was given oral isotretinoin capsule 20 mg twice daily for one week after 3 weeks for 6 months as intermittent/ pulse therapy. Group B was given oral isotretinoin capsule 20 mg/ daily for 6 months continuously. Group A and B were further sub divided into mild, moderate and severe, having 25 patients in each subgroup.

In group A, the oral isotretinoin pulse therapy was efficacious in 88% of mild acne, 92% of moderate acne and 76% of severe acne. There was no difference in efficacy of drug in mild moderate or severe acne in group A as the p–value calculated by One way Anova is 0.091, which is not significant. In group B, the oral isotretinoin continuous therapy was efficacious in 92% of mild acne, 88% of moderate acne and 84% of severe acne. There was no difference in efficacy of drug in mild moderate or severe acne

in group B as the p – value calculated by One way Anova is 0.098, which is not significant. Data was analyzed by using One way Anova to compare the efficacy of oral isotretinoin in intermediate/pulse therapy versus continuous therapy. It revealed that there was no statistical difference in efficacy of drug in group A and B, having p value of >0.05.

Efficacy of oral isotretinoin for acne in intermediate/pulse therapy is statistically same as in continuous therapy. So, we should prefer intermediate/pulse therapy as it is cost effective, less incidence of side effects due to shorter duration and the patient is more compliant.[16]

Conclusion

It is concluded that the efficacy of oral isotretinoin for acne in intermediate/pulse therapy is same. So, we should prefer intermediate/ pulse therapy as it is cost effective, there are reduced side effects of drug due to shorter duration and the patient is more complaint.

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