DOI: https://doi.org/10.53350/pjmhs20221612554

ORIGINAL ARTICLE

Analyzing the Effects of Low-Dose Isotretinoin on Acne Vulgaris Against the Standard Treatment Protocol

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ABSTRACT

Objective: The study's objective was to evaluate the effectiveness and safety of low-dose isotretinoin vs the standard-dose regimen for the treatment of acne vulgaris.
Study Design: Randomized controlled trial
Place and Duration: This study was conducted at Department of Dermatology, Bannu Medical College and Federal Government Polyclinic Hospital Islamabad in the period from March, 2022 to August, 2022.
Methods: Randomization was used to split the total of 190 patients with acne vulgaris who participated in the study into two groups of 95 sample size each. Patients of both sexes were affected with acne vulgaris. Isotretinoin was administered orally to patients in group I at a dose of 20 milligrammes per day for 12 weeks, whereas patients in group II received conventional dosing regimen 80 milligrammes per day. After a total of 12 weeks of therapy, both groups had a final assessment of their effectiveness. SPSS 23.0 was used to analyze all data.
Results: In all 190 cases, majority of the cases 110 (57.9%) were females and 80 (42.1%) were male patients. Mena age of the patients in group I was 24.16±10.52 years and in group II mean age was 25.8±9.87 years. We found that efficacy of conventional dosing regimen was higher in 73 (76.8%) as compared to low doze isotretinoin in 50 (52.6%) with p value <0.005. Post-treatment frequency of complication were higher in group II 46 (48.4%) as compared to group I 28 (29.5%). Dry eyes and headache were the common complications in all cases.
Conclusion: As a result of this research, we came to the conclusion that the typical dosing regimen for the treatment of acne vulgaris is more effective but poses a greater risk of side effects than the low dose of isotretinoin.
Keywords: Efficacy, Safety, Acne vulgaris, low dose isotretinoin

INTRODUCTION

Acne vulgaris, also known simply as acne, is the most common kind of skin disease in the world. Acne vulgaris is a chronic inflammatory illness that affects the pilosebaceous units.[1] In the event that it is ignored, it may result in catastrophic psychological and physiological implications. The illness is more common in younger age groups, having estimates ranging from 70%[2] to 90%[3] in the prevalence of the condition in teens. [3] Acne is typically treated with antibiotics and retinoids, which can be applied topically or taken orally. Isotretinoin, also known as 13-cis retinoic acid, was one of the most important pharmacological advancements made in the field of acne treatment when it was first introduced. The typical dose is between 0.5 and 1 mg/kg per day, and it can be administered all at once or in divided doses throughout the day. The current gold standard for treating severe acne is to give a cumulative oral dose of isotretinoin ranging from 120–150 mg/kg of body weight over the course of 16–24 weeks. This treatment is given in combination with other anti-acne medications. Despite this, researchers have been compelled to look for alternative methods as a result of the frequent adverse effects that have a tendency to become worse as the dose is increased. 4 Other research, on the other hand, have not been able to uncover any alternatives that are noteworthy, and some more recent studies have pushed for a safer and virtually as successful treatment plan that utilises lower dosages of oral isotretinoin. When treating moderate to severe acne, retinoid compounds are essential [4,5]. This is true regardless of the therapeutic approach that is taken. In the early 1980s, there was a limitation placed on the administration of oral isotretinoin for the treatment of nodulocystic acne [6]. In any event, as a result of increased clinical experience, the range of conditions that can be treated with oral isotretinoin broadened. This medicine was also prescribed to patients with less severe forms of acne who did not experience any improvement while receiving more conventional treatments such as topical retinoids and oral antibiotics. Isotretinoin taken orally may be beneficial for patients suffering from acne with moderate severity who also have scarring. Acne is most usually associated to both threats to one's health and concerns with one's appearance. Acne can result in a wide range of mental health problems, including feelings of depression and anxiety, as well as challenges in one's professional life and personal relationships. Isotretinoin treatment has been shown to lead to significant improvements in a patient's social functioning as well as their level of self-confidence, according to research that utilised quality of life questionnaires. [7] It may take anything from a few weeks to a few months before the treatment begins to show any noticeable effects. The discontinuation of medication is frequently accompanied by ongoing progress in health. Because of this, it is not necessary to keep up the treatment until all of the lesions have disappeared completely. [8]

Isotretinoin is an effective medication for the treatment of acne; nevertheless, the drug does have a number of negative effects, and selecting patients to take it requires great care. For a period of between four and six months, the recommended dose is between 0.5 and 1 mg/kg per day. According to the findings of a study that was carried out in India in 2014 involving fifty people who suffered from moderate to severe pimples, low-dose isotretinoin was shown to be beneficial, with fewer adverse effects and a more cost-effective treatment option. Isotretinoin was administered once daily at a dosage of 0.3-0.4 mg/kg to the patients in this clinical research. [9] In addition, a research conducted in 2012 indicated that severe acne might be efficiently treated with low doses of isotretinoin (0.1-0.3 mg/kg/day). Government of low-dose isotretinoin (0.25 mg/kg/day) for six months seems logical able to give that adverse effects are dose-dependent; however, there is currently no relevant, detailed survey with follow-up period in Iran; and although compliance is dependent on side effects and the cost of the drug, the cost of the drug combined with economic status of patients has turned it into a severe issue. [10]

In addition to the studies of the standard therapeutic dose that led to the US Regulatory approval in 1982 and the international agreement guidelines in 1997, we analysed all of the trials of low-dose roaccutane in acne vulgaris. Our goal was to

compare the efficacy and relapse rate of the standard therapy to that of the low-dose therapy and determine which was more effective. [11,12] Objectives Patients with severe acne vulgaris who come to our tertiary care hospital will have their efficacy and safety of both high and low doses of oral isotretinoin evaluated. The patients will be given the drug in pill form.

MATERIAL AND METHODS

This prospective study was conducted at Department of Dermatology, Bannu Medical College and Federal Government Polyclinic Hospital Islamabad in the period from March, 2022 to August, 2022 and comprised of 190 patients. Following the collection of written consent, participants' age, BMI, weight, place of residence, and level of education were recorded in detail. Excluded patients were those who needed many courses of systemic antibiotics, had acne brought on by medication, were taking oestrogens or a birth control pill, tested positive for pregnancy, or were lost to follow-up.

Male and female patients aged 16-45 with a clinical diagnosis of acne vulgaris were included. The total sample size was split in half. There were 95 participants in the low-dose isotretinoin group I and 95 in the control group II. Patients assigned to Group I were given oral isotretinoin 20 mg/day for a total of 12 weeks. Patients in Group II were prescribed 80 milligrammes of oral isotretinoin twice daily for 12 weeks. During the course of the trial, participants were not permitted to use any additional medications or cosmetics. From the beginning of the study through the end, 12 weeks of treatment were given. Safety checks were performed by calling patients every 15 days. After 12 weeks of treatment, the effectiveness of both groups was assessed. SPSS 23.0 was used to analyze all data. Categorical variables were represented using frequency and percentages, and continuous variables were represented using means and standard deviations.

RESULTS

In all 190 cases, majority of the cases 110 (57.9%) were females and 80 (42.1%) were male patients.(figure 1)

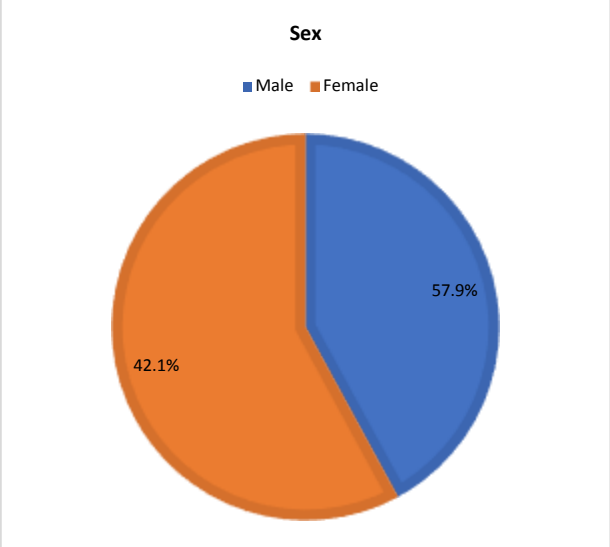

Figure-1: Association of gender among all cases

Mena age of the patients in group I was 24.16±10.52 years and in group II mean age was 25.8±9.87 years. Mean weight of the patients in group I was 67.8±32.80 kg and in group II mean weight was 68.3±13.67 kg. Mean GAGS score in group I was 25.9±5.25 and in group II 25.3±5.36 was GAGA score. Mean duration of complaint in group I was 1.0±3.7 years and in group II mean duration was 1.6±0.44 years.(table 1)

Table-1: Case-in-point data from the enrolled population

Variables	Group I	Group II
Mean age (years)	24.16±10.52	25.8±9.87
Mean Weight (kg)	67.8±32.80	68.3±13.67
Mean GAGS score	25.9±5.25	25.3±5.36
Mean Duration of disease (years)	1.0±3.7	1.6±0.44

We found that efficacy of conventional dosing regimen was higher in 73 (76.8%) as compared to low doze isotretinoin in 50 (52.6%) with p value <0.005.(figure 2)

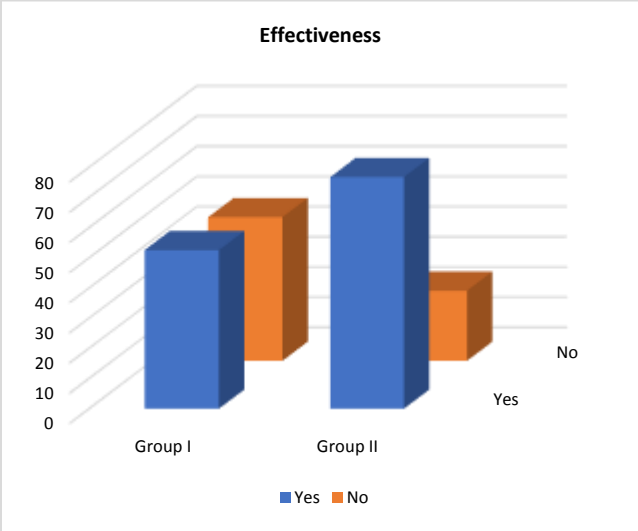

Figure-2: The relative efficacy of the two groups is compared

Post-treatment frequency of complication were higher in group II 46 (48.4%) as compared to group I 28 (29.5%).(table 2)

Table-2: Post-treatment association of complications3

Variables	Group I	Group II
Complications		
Yes	28 (29.5%)	46 (48.4%)
No	67 (70.5%)	49 (51.6%)

Among 46 cases of adverse events in group I, 30 cases had dry eyes and 16 cases had headache while in group II 17 cases had dry eyes and 11 cases had headache among 28 cases.(table 3)

Table-3: types of complications among both groups

Variables	Group I	Group II
Types Complications		
Dry eyes	17 (17.9%)	30 (31.6%)
Headache	11 (11.6%)	16 (16.8%)

DISCUSSION

Comedones, erythematous papules and pustules, and less commonly nodules and pseudocysts, are the primary lesions seen in acne, a chronic inflammatory disease of the pilosebaceous units. Scarring may occur in conjunction with this condition. Although it lacks antibacterial capabilities, isotretinoin significantly lowers the population of Propionibacterium acnes by suppressing sebum production, showing comedolytic activity, having direct and indirect anti-inflammatory effect. The matrix is degraded thanks to the isotretinoin impact on metalloproteinases (MMP) and tissue inhibitors of MMPs (TIMP). [13] Isotretinoin medication is quite effective, but it also has some unwanted side effects, so researchers are still trying to figure out what those side effects are.

In current study 190 patients of acne vulgaris were presented. In all 190 cases, majority of the cases 110 (57.9%) were females and 80 (42.1%) were male patients. Patients were

split in two groups. Mena age of the patients in group I was 24.16±10.52 years and in group II mean age was 25.8±9.87 years. Mean weight of the patients in group I was 67.8±32.80 kg and in group II mean weight was 68.3±13.67 kg. Results were comparable to the previous studies.[14,15] In our research, we found that the conventional dosing schedule was more effective (76.8%) than the low dose regime (56.2%). Patients getting low dose therapy were less likely to experience adverse effects, with just 17.9% reporting dry eyes and 11.6% reporting headaches, compared to 31.6% and 16.8%, respectively, for patients receiving standard dose therapy. In treating acne vulgaris, a research by Blasiak RC, et al. found that low-dose isotretinoin was 57.7% effective, while the normal dosing regimen was 71.9% effective, dry eyes occurred in 31.6% of patients, and headache occurred in 13.2% of patients. [16]

Contrary to our findings, a prior study by Rao et al. shown the safety and efficacy of low-dose isotretinoin for the treatment of moderate to severe acne vulgaris. In this study, 50 people with moderate to severe acne vulgaris were recruited over the course of 2 years and followed for 3 months to determine the safety and efficacy of low-dose isotretinoin for the treatment of moderate to severe acne vulgaris. Acne leaves scars not only on the face, but also on the mind and the heart, which is why they advocated for the cautious use of low-dose isotretinoin in patients with moderate to severe acne. [17] Similarly, Agerwal et al. found that, across all forms of acne, smaller doses of oral isotretinoin were both more effective (69%) and safer (89%) than higher doses (100%).[18]

There is no unambiguous victor in a head-to-head matchup between the treatment of severe acne vulgaris with the conventional high-dose regimen and the alternative treatment of low-dose oral isotretinoin administered over a period of 12 weeks. On the other hand, its safety profile is statistically superior to that of the latter, with fewer mucocutaneous adverse events. It is important for future research to prospectively examine not only the superiority and noninferiority of nonstandard treatment plans in comparison to the conventional high-dose treatment plan, but also the overall cost-effectiveness of these nonstandard treatment plans.

CONCLUSION

As a result of this research, we came to the conclusion that the typical dosing regimen for the treatment of acne vulgaris is more effective but poses a greater risk of side effects than the low dose of isotretinoin.

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