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Original Research Article

Open label multi-centre trial on efficacy and tolerability of microionized isotretinion therapy in treatment of moderate to severe acne vulgaris

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ABSTRACT

Background: Isotretinion was approved by United States Food and Drug Administration (US FDA) in 1982 for the treatment of severe recalcitrant nodulocystic acne. Its conventional recommended dose has been 0.5-1.0 mg/kg body weight per day for 16-32 weeks, with a maximum cumulative dose of 120 mg/kg. Objective of the study was to assess the efficacy and tolerability of 24 week of once daily micronized isotretinoin therapy in the treatment of moderate to severe acne vulgaris was conducted.
Methods: Total n=580 of patients were included with 249 (43%) male and 331 (57%) females. Patients were assessed at baseline 6, 12 and 24 weeks and 12 weeks post treatment follow-up based on the assessment of severity of acne vulgaris using global acne grading system (GAGS), assessment of improvement in lesion counts, global assessment of overall efficacy by doctor (based on overall assessment) and by patients (based on overall relief in symptoms) and overall assessment of drug tolerability.
Results: In terms of improvement in lesions, excellent results from 4% (22) in week 6th has move to 34% (193) in week 24th. In terms of global efficacy examined by doctors, very effective results i.e. 40% (234) in 12th week has moved to 70% (403) in 24th week. In terms of drug tolerability, excellent results have moved from 119 patients to 190 patients by end of the study.
Conclusions: Hence the micronized isotretinoin therapy had overall satisfactory outcome in the treatment of patients with moderate to severe acne vulgaris (grade 2, 3 and 4).

Keywords: Low-dose isotretinoin, Acne vulgaris, Efficacy

INTRODUCTION

Acne vulgaris is a common chronic skin disease involving blockage and/or inflammation of pilosebaceous units (hair follicles and their accompanying sebaceous gland). Isotretinoin is widely used in the treatment of acne.[1,2] Treatment of acne is based on the type and grades of severity. Once daily isotretinoin therapy 0.5-1.0 mg/kg body weight per day is the standard treatment in patients of moderate to severe acne vulgaris. While standard isotretinion therapy is well effective; a better understanding of micronized isotretinion may lead to development of new treatment that are more directed and effective against moderate to severe acne vulgaris.[3-6] All the patients enrolled were of Indian origin. As the skin type of Indians varies from Europeans and Americans, it is important to demonstrate the tolerability and efficacy of micronized isotretinion in Indian patients suffering from acne vulgaris. Therefore the aim of this phase 4, post-marketing surveillance (PMS) study was to assess the efficacy and tolerability of 24 week of once daily micronized isotretinion.

METHODS

It is a hospital based study among patients attending dermatovenereology outpatient department (OPD) consultancy done from August 2019 to January 2020 in B. J. Medical College and Civil Hospital, Ahmedabad, India.

65 Dermatologists were involved. Out of 1000 patients, total 580 patients diagnosed as a case of acne vulgaris in a 6 months period, which gave consent, were chosen at random from the patients attending the OPD consultancy. Patients' name, age, sex, occupation, weight, address, diagnosis, treatment given, was recorded in a proforma. Assessment parameters were also included such as assessment of severity, improvement in lesion count, global assessment by efficacy of doctor, global assessment of efficacy by patients, and drug tolerability. Global assessment of efficacy by treating physician as well as by the patient was done at 6, 12, 24 weeks and 12 weeks post treatment. Side-effects were recorded at each visit which included incidence and severity of cheilitis, dry skin, mouth, nose and eyes, epistaxis, facial redness, hair loss, photosensitivity, nail changes and systemic side-effects like fatigue, bone/joint pains and muscular cramps and its tolerability was assessed.

All patients between ages 18-45 years were included after written informed consent. After recording detailed demographic data, the patients were examined under good illumination and were graded into mild, moderate, severe and very severe on the basis of severity as assessed by GAGS: mild disease 1-18, moderate disease 19-30, severe disease 31-38, very severe disease >38.

Patients diagnosed with moderate to severe acne were given micronized isotretinoin soft gel capsule (0.4 mg/kg/day). Patients were followed up at two-weekly intervals for 24 weeks. Improvements in lesions were recorded by measuring reduction in the lesion counts at each visit.

Inclusion criteria

Patients with written informed consent, subjects of both sexes of age group between 18 years and 45 years (both inclusive), and patients with moderate to severe acne were included in the study. The severity of acne was evaluated using GAGS of Doshi, Zaheer and Stiller. Patients with absence of hormonal disorders were also included.

Exclusion criteria

Patients with hypersensitivity to isotretinoin/other retinoid or any of the ingredients; patients with a personal/family history of hyperlipidaemia and/or diabetes; patients with hypervitaminosis A; patients with drug induced acne; pregnant women, women desiring pregnancy, and women using temporary methods of contraception; patients with hepatic/renal insufficiency; and patients receiving drugs with known drug-drug interactions with isotretinoin were excluded from the study.

All statistical data were analysed in statistical package for the social sciences (SPSS-20 IBM, Armonk, NY, USA).

RESULTS

It included a total of 580 patients, 43% (249) males and 57% (331) females. Majority of the patients i.e. 67% (388) belonged to the age group of 20-30 years. 34% (197) patients had acne face grade 2 which was followed closely by acne face grade 3 in 32% (186) patients.

To start with, 44% patients had severe grade of acne based on GAGS which included 127 males and 128 females respectively which decreased to 11% patients (14 males and 50 females respectively) at the end of 24 weeks. 8% patients had very severe acne (which included 26 males and 22 females) which decreased to 0.4% (1 male and 1 female respectively) at the end of 24 weeks. In terms of improvement in lesions, excellent results were noted in 4% (23) patients at 6th week which increased to 16% (93) patients at 12th week which further increased to 34% (197) patients at the end of 24th week.

On assessment of global efficacy by treating physician, very effective results at 12th week was noticed in 40% (234) patients which moved to 70% (403) patients at the end of 24 weeks. Overall 170 males and 233 females had very effective results at the end of 24 weeks. In terms of global assessment by patients, 43% (251) patients found the drug to be very effective at the end of 12 weeks which increased to 65% (377) patients at the end of 24 weeks. Overall 159 males and 218 females experienced very effective results by the end of 24 weeks.

Assessing on drug tolerability, excellent results were seen in 21% (119) patients at the end of 12th week which increased to 33% (191 comprising 77 males and 114 females) at the end of the study i.e. at week 24 hence the drug was tolerated well.

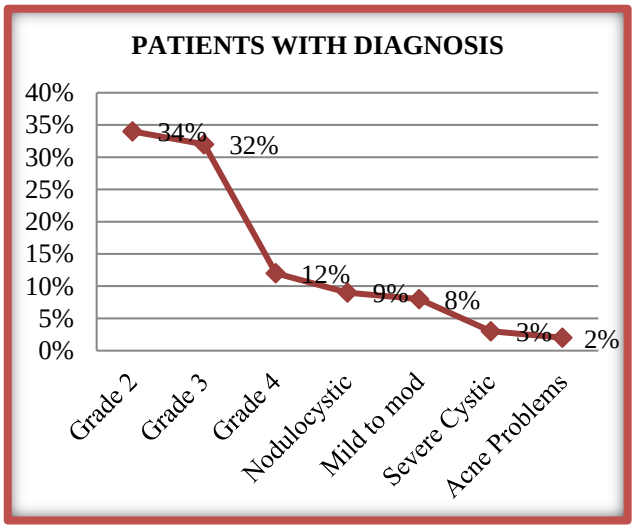

Figure 1: This figure indicates the percentage of patients diagnosed with different grades and severity of acne included in the study.

Table 1: Severity of acne.

Acne type	Week 0 (%)	Week 24
Severe	44	11
Very severe	11	0.8

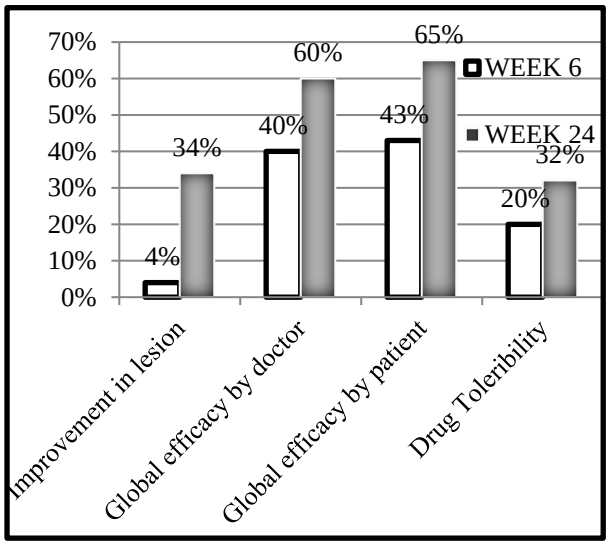

Figure 2: This figure indicates the results at week 6 and week 24.

DISCUSSION

Isotretinoin has been in use for treatment of acne for more than thirty years.[2] Traditionally it was used for severe nodulo-cystic acne in dose of 1=-2 mg/kg/day.[7]

In the recent years however a number of investigators have found it to be useful even in relatively low doses ranging from 0.3 to 0.5 mg/kg/day.[8-10]

It has been seen that there is dose dependent decrease in sebum production with oral isotretinoin. Though isotretinoin is effective in acne even in low doses but there are significantly higher chances of relapses and need of retreatment. The advocates of low doses state that decreasing the dose also decreases the side effects.[10-13]

There are limited studies available on the use of microionizsed isotretinion in treatment of acne vulgaris. Two trials conducted by Strauss et al and Webster et al assessed the primary and secondary on standard oral isotretinion versus other formulations of oral isotretinion.

The study stated that main outcome of the other formulations of oral isotretinoin was that they were not food-dependent, there was decrease in total inflammatory lesions and severity of acne after 20 weeks use and fewer side effects were also noted.[13-15]

In our study, we have presented that once daily dosage of micrionized isotretinion was found to effective during the treatment period with low incidence and severity of side effects. The treatment was tolerated by all the patients and reported significant decrease in the acne lesion. This study also had 12 week post follow up period and promising results were reported at the end of the treatment. There is no doubt that taking proper duration of treatment course, patient compliance and lower dose of isotretinion is major therapeutic advantage.

CONCLUSION

Acne vulgaris is a common skin disease affecting approximately 9.4% of the world's population. Isotretinoin is an important therapy for managing severe, recalcitrant nodular acne. Micronized isotretinoin therapy had overall satisfactory outcome in the treatment of patients with moderate to severe acne vulgaris (grade 2, 3 and 4). Hence, microionized isotretinion can be used as standard therapy in acne vulgaris grade (2, 3 and 4).

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