

STUDY OF EFFICACY, SAFETY & TOLERABILITY OF ORAL ISOTRETINOIN IN PATIENTS OF MODERATE TO SEVERE ACNE VULGARIESChetan D. Rajput¹, D. G. Saphale²**HOW TO CITE THIS ARTICLE:**

Chetan D. Rajput, D. G. Saphale. "Study of Efficacy, Safety & Tolerability of Oral Isotretinoin in patients of moderate to severe Acne Vulgaris". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 55, October 23; Page: 12622-12626, DOI: 10.14260/jemds/2014/3671

ABSTRACT: BACKGROUND: Acne vulgaris is an almost universal problem of adolescence characterized by inflammation in and around sebaceous gland. Effective treatment is essential to prevent physical and psychological scarring. Antibiotic requires frequent administration and associated with side effects contributing to reduced compliance. Isotretinoin was a major therapeutic advanced which revolutionized the treatment of acne. Thus it is important to analyze its risk-benefit ratio at lower dosages. Hence the present study carried out with the objective of oral Isotretinoin in patients of moderate to severe grade acne vulgaris. **METHODOLOGY:** The present prospective study carried out among the acne vulgaris cases attending the out-patient department of dermatology at a tertiary care Centre during January 2007 to December 2007. Oral isotretinoin was started at a dose of 0.5 mg/kg/day for a total duration of 20 weeks. Patients were scheduled for 3 visits i.e. at the end of 1st, 2nd & 5th month after start of treatment. All collected data entered and analyzed using SPSS for efficacy of drug on different lesions. **RESULTS:** 38 (95%) patients completed the study and same were evaluated for efficacy and safety. 50% decrease in comedons at the end of 2 month from the initiation of treatment. The efficacy of oral isotretinoin on inflammatory lesions shows decreased from baseline 36.13 to 4.87 at the time of last visit at 5 month. This was statistically significant (0.0001). Side effects observed an 11% case includes dryness, palmoplantar peeling, exfoliative dermatitis, photosensitivity, facial dermatitis. **CONCLUSION:** The oral isotretinoin is effective and safe as well as showing early response especially for inflammatory lesions.

KEYWORDS: Acne Vulgaris, Oral Isotretinoin, Efficacy.

INTRODUCTION: Acne vulgaris is an almost universal problem of adolescence characterized by inflammation in and around sebaceous gland. Acne usually appears at adolescence, a period of uncertainty of life when a person is making a physical transition from childhood to adulthood. Therefore effective treatment is essential to prevent physical and psychological scarring.¹ So it's essential to target the inflammatory lesions. Antibiotics continue to play an integral role in the management of acne.² Systemic treatment is required in patients with moderate to severe acne, especially when acne scars start to occur.³

For the last 2-3 decades, systemic antibiotics mainly tetracycline and erythromycin, have assumed the main role in the management of acne patients with inflammatory lesions. They require frequent administration and are sometimes associated with side effects, contributing to reduced compliance.⁴ Isotretinoin (13 cis retinoic acid) is an isomer of transretinoic acid.

The introduction of isotretinoin was a major therapeutic advanced which revolutionized the treatment of acne. Isotretinoin is the only treatment that has an effect on all the major etiological

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factors involved in acne i.e. decrease sebum production, comedogenesis, surface and ductal colonization of *P. acne*, anti-inflammatory.

Isotretinoin is the only systemic therapy, which has advantage of cure, but has significant side effects at higher dosages. Thus it is important to analyze its risk- benefit ratio at lower dosages. Hence the present study carried out with the objective of oral Isotretinoin in patients of moderate to severe grade (grade II to grade IV) acne vulgaris.

METHODOLGY: The present prospective study carried out among the acne vulgaris cases attending the outpatient department of dermatology at a tertiary care Centre in Maharashtra during January 2007 to December 2007. The study includes all patients with grade II to grade IV acne vulgaris as per Pillsbury's scale, within the age group of 14-25 yrs. Less severely affected patients who have responded unsatisfactorily to conventional treatment including long term antibiotics and/or appropriate topical anti-microbial or retinoid like therapies.

Moderate acne that has failed to respond to treatment that includes two courses of oral antibiotics each lasting three months each. Patients with abnormal baseline investigation, positive pregnancy test, lactating female, known hypersensitivity to isotretinoin, questionable compliance to therapy, history of depression, psychosis or suicidal tendencies & concomitant use of other antibiotics such as tetracycline were excluded from study. Institutional ethical committee approval was taken prior to the study. Written informed valid consent of the Patients fitting into the criteria was taken.

Pre-treatment laboratory investigations carried out which included Complete Blood Count, Fasting blood sugars, LFT, Lipid profile. A wash out period of 1 week for those using topical application and 2 weeks for those using systemic drugs for acne is given. The study includes variables like age of onset of acne, duration of lesions, previous therapy & history of allergy to any product. In all these cases a general and cutaneous examination was carried out and type and distribution and count of acne lesions comedons, inflammatory lesions as well as total lesions were recorded.

The lesions were counted by using Leeds technique of Burke and Cunliffe. Oral isotretinoin was started at a dose of 0.5 mg/kg/day for a total duration of 20 weeks. Patients were scheduled for 3 visits i.e. at the end of 1st, 2nd & 5th month after start of treatment. Efficacy was determined by evaluating inflammatory lesions count at baseline and at every visit. A safety evaluation was carried out for cutaneous and mucosal, hair and nail changes and any systemic side effects at each schedule visit. All collected data entered and analyzed using SPSS for efficacy of drug on different lesions.

RESULTS: The numbers of patients enrolled during study period were 40. There were 2 dropouts in the study. The 38 (95%) patients completed the study and same were evaluated for efficacy and safety. Table 1 shows the efficacy of isotretinoin on comedons, the mean of comedons decreases from baseline 40.08 to 13.9 at the time of last visit i.e. on 5th day. 50% decrease in comedons at the end of 2 month from the initiation of treatment.

This was statistically significant (0.0001). Table 2 shows the inflammatory lesions decreased on subsequent visit i.e. from baseline 36.13 to 4.87 at the time of last visit at 5 month. 50% decreased in inflammatory lesion was observed at the end of 1 month after initiation of treatment. This was statistically significant (0.0001). Graph 1 shows the efficacy of oral isotretinoin on total lesions at monthly interval.

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Number of total lesions decreased from 76.2 to 19.37 at the time of last visit i.e. 5th month. 60% decreased in the total lesions was after at the end of 2 month from initiation of treatment. This was statistically significant (0.0001).

Safety evaluation of the drug was observed with the side effect of the drug during or at the end of the treatment. Dryness, palmo-plantar peeling, exfoliative dermatitis, photosensitivity, facial dermatitis, skin infections, pyogenic granuloma like lesions (11%) & Cheilitis (5%) were observed. Systematic side effects like Nausea, diarrhea, abdominal pain (5%) was observed. No other major even of side effect observed.

DISCUSSION: Traditionally the role of isotretinoin in acne has been limited to nodular cystic forms of acne. However in more recent times the drug is being increasingly prescribed in moderate cases of acne that are unresponsive to conventional therapy and even in mild acne patients who have significant psychosocial impairment. Oral isotretinoin if used in correct dose, it is very seldom fails to clear acne completely and it effects a permanent cure in large number of cases.⁵ Pandey⁶ in his study observed prevalence rate of acne vulgaris to be 50% for boys and 38% for girls.

In the present study, out of 38 patients 27 were males (67.5%) and 13 were females (33.5%) and there was no statistical significance in both the groups and thus were comparable. In our study oral isotretinoin was started at a dose of 0.5 mg/kg/day for a total duration of 20 weeks, in 40 patients irrespective of severity of acne and no topical therapy was offered for the same. Out of which 38 (95%) completed the study and 2 (5%) were lost to follow up. We included moderate to severe cases of acne, we did not follow the criteria of total accumulated dose schedule of 120 mg/kg as followed in other studies carried for the more severe forms of acne.

Even patient not followed up after clinical cure. Mandekou –Lefai et al⁷ in their study “low – dose schema of isotretinoin in acne vulgaris” treated a group of 32 patients of different types and grades of acne vulgaris with oral isotretinoin in dose from 0.15 – 4 mg/kg/day. The mean success rate was only 69%. Hermes B et al⁸ in their study “medium dose isotretinoin for the treatment of acne” treated 94 patients of moderate to severe acne vulgaris with stepwise incremental dose, for a mean duration of 8.3months, at a mean dose of 34.4mg. In their study oral isotretinoin is administered in a initial dose of 10 mg/day with a variable increase according to tolerability, reaching a mean dose 0.43 mg/kg and reported very good results in 62.8% and good results in 31.9% of patients.

The improvement in inflammatory lesion was 86.12%.the 100%-80% improvement which was considered excellent was seen in 39.47% patients, 79%-50% improvement which was considered good response was seen in 55.27%.it was seen that the results were comparable with few of the above mentioned studies. The total number of patients with side effects in isotretinoin group was 6(16%) suggesting that drug is safe. 6 (16%) out of 38 patients showed muco cutaneous side effects which include redness, dryness.

4 (11%) scaling of face,2 (5%) patients presented with chelitis. 2 (5%) patients developed mild gastrointestinal side effects including nausea and vomiting. However this did not require discontinuing of treatment and the symptoms were controlled by symptomatic treatment. According to Leyden et al study less than one third patients developed xerosis and is more common with patients having history of atopy.⁹The study concludes that isotretinoin was effective in reducing the inflammatory lesions. Also the efficacy of isotretinoin in reducing total lesions was high.

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The side effects were limited to mild mucocutaneous and mild gastrointestinal intolerance. Hence the oral isotretinoin is effective and safe as well as showing early response especially for inflammatory lesions.

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Monthly interval	Comedons Mean	SD	SE	Z score	P value
Baseline	40.08	19.62	3.18		
1 month	28.89	17.99	2.92	- 5.36	0.0001
1 month	28.89	17.99	2.92		
2 month	21.34	14.08	2.29	- 4.70	0.0001
2 month	21.34	14.08	2.29		
5 month	13.97	9.81	1.59	- 5.04	0.0001
Baseline	40.08	19.62	3.18		
5 month	13.97	9.81	1.59	- 5.38	0.0001

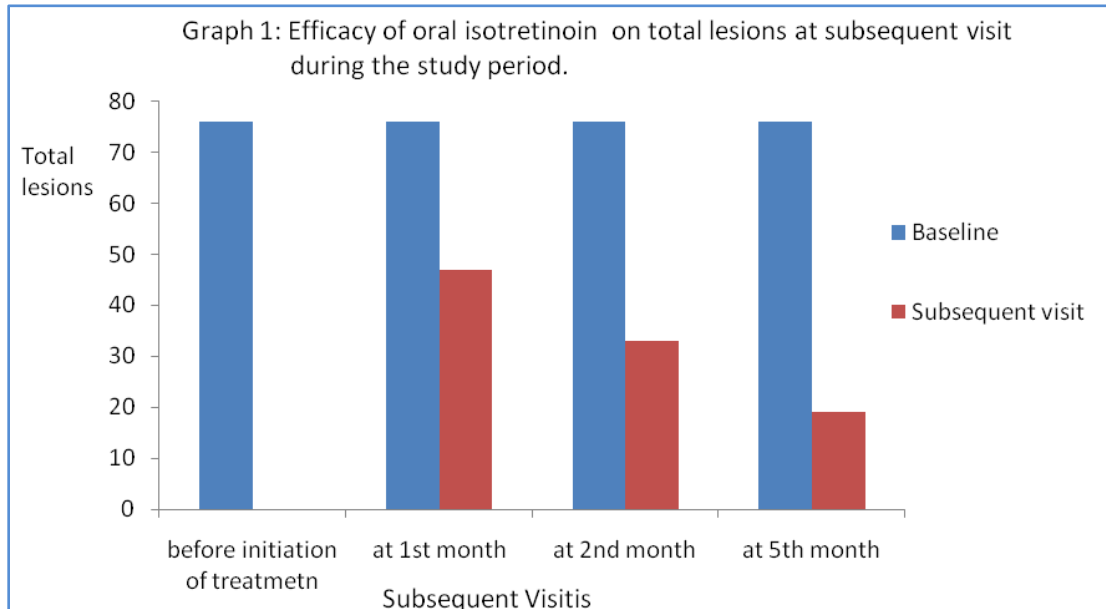
Table 1: Efficacy of oral Isotretinoin on number of comedons at monthly interval during the study period

Monthly interval	Inflammatory Lesion Mean	SD	SE	Z score	P value
Baseline	36.13	18.04	2.92		
1 month	17.97	11.94	1.95	- 5.37	0.0001
1 month	17.97	11.94	1.95		
2 month	11.24	7.98	1.30	- 5.05	0.0001
2 month	11.24	7.98	1.30		
5 month	4.87	4.65	0.75	- 5.31	0.0001
Baseline	36.13	18.04	2.92	- 5.38	0.0001

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5 month	4.87	4.65	0.75		
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Table 2: Efficacy of oral Isotretinoin on inflammatory lesions at monthly interval during the study period

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Date of Submission: 22/09/2014.

Date of Peer Review: 23/09/2014.

Date of Acceptance: 18/10/2014.

Date of Publishing: 22/10/2014.