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Original Research Article

Study to Determine the Association of Depression with Isotretinoin Therapy in Acne Vulgaris

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ABSTRACT

Aims and objectives: Studies on the association of depression with acne or its drugs are mostly case reports or series. The present study was done to study the association of depression with isotretinoin therapy.
Materials and methods: this questionnaire based study was conducted in Department of dermatology in 2014. The sample consisted of 33 patients clinically diagnosed as grade III and IV acne vulgaris. Proper history about mental illness and previous isotretinoin intake was taken. Beck depression inventory questionnaire was given and scores calculated. Patients were treated with isotretinoin 0.5mg/kg and followed up every 30 days for 4 months.
Result: mean BDI score decreased with treatment of the patient and no patient showed any signs of worsening of mental condition.
Conclusion: Though there have been reports of suicides and depression with variable doses of isotretinoin, we could not find any such correlation.

Key words: acne, isotretinoin, depression, correlation.

INTRODUCTION

Acne vulgaris is a chronic disease of adolescence and is associated with lot of mental, hormonal and physical changes in the patient. The appearance of acne takes a heavy toll on the psychological status of the patient especially if it is of severe variety which is characterized by nodules and abscesses leading to lot of scarring. A study showed that 22.4% of school-going girls and 12.8% of school-going boys had depression of various grades using BDI with a cut-off score of 16. [1]

The retinoic acid derivative isotretinoin was developed in 1982 by Hoffmann-La Roche. Isotretinoin is synthetic derivative of Vitamin A known as 13-cis-retinoic acid. Oral isotretinoin revolutionized the treatment of acne when it was introduced in the UK in 1983. Two decades later, it remains the most clinically effective anti acne therapy.

Isotretinoin is the only treatment that has an effect on all the major etiological factors involved in acne. lt significantly reduces elevated sebum production, comedogenesis and ductal colonization with P. acnes. [2,3] Isotretinoin therapy is always accompanied by side effects that mimic those seen in the chronic hypervitaminosis a syndrome. [4]

BDI has been developed and used in various studies as a validated method of assess of medicines and study of depression in patients. [5] It's a questionnaire of 21 questions with score from 0-63 varying from mild to severe. A score of 0-16 is considered as normal, 17-20 borderline

clinical depression, 21-30 moderate depression, 31-40 severe depression and over 40 is extreme depression.

Many case reports and series have stated the association of depression and suicides with isotretinoin therapy. Between 1982 and 2000, the FDA has received reports of 394 cases of depression, and 37 suicides occurring in patients exposed to isotretinoin. It is the fifth most common drug reported to the US Adverse Event Reporting System (AERS) in association with depression, and the tenth most common (and the only non psychotropic drug) in suicide reports. [6]

In a prospective study, 124 courses of treatment with isotretinoin at a dose of 1 mg/kg/day for 4 months for severe acne were followed. Depression occurred in 4% of patients and tended to persist throughout the treatment. [7] Rate of depression among isotretinoin users ranged from 1% to 11% across studies with similar rates in oral antibiotics control groups. Overall studies comparing depression before and after treatment did not show a statistically significant increase in depression diagnosis or symptoms. Most of such studies are of foreign patients and this study was conducted to study the same in Indian scenario.

Aims

1. To study the association of depression in acne vulgaris patients treated with isotretinoin.

MATERIALS AND METHODS

After approval from institutional ethics committee, this cross sectional study was undertaken by the Department of Dermatology in a tertiary teaching hospital with an attached medical college in 2012. 33 patients who fulfilled the below mentioned criteria were given isotretinoin 0.5mg/kg (rounded off to nearest available preparation). Clindamycin topical gel was prescribed to each patient.

They were followed at 30, 60, 90 and 120 days with their psychological assessment (BDI score) and routine investigations each time. Patients were advised to report to us during the intervening periods also, if they experience any mood changes or any other medical problem. They were advised to avoid sun exposure. Patients were counselled about the side effects of isotretinoin therapy like cheilitis (for which they were asked to apply emollients) constipation, dry eye, alopecia, photosensitivity, teratogenicity.

Inclusion Criteria for Prescribing Isotretinoin

1) Acne of grade 3 and above.
2) Females of child bearing age with pregnancy test negative and who were ready to use contraceptives if need be.

Exclusion Criteria for Prescribing Isotretinoin

1) Pre-treatment BDI score more than 10.
2) Pregnancy or lactation.
3) Previous personal or family history (first degree relatives only) of depression or suicidal ideation or attempted suicide or psychiatric disorder.
4) Patients with systemic disease.
5) Not given consent for the study.
6) Patients who are known allergic to isotretinoin

End Of Treatment Criteria (whichever is earlier);

i. 120 days of treatment.
ii. Any indication of deterioration in psychological functioning by BDI score.

Data was analysed statistically at the end of the study

RESULTS

Total number of patients registered in the study was 33 but the dropouts were 7, over a period of 4 months. If the BDI score was more than 10 at any point of time, such patients were excluded from further study. Out of 33 patients, none of the patients' treatment was discontinued due to increase in their BDI score to more.

Table 1: Variations of bdi at various follow UPS

GROUPS	BDI (MEAN ± SD)
Pre-treatment(N=33)	8.58±1.15
At 30 days of treatment (n=32)	8.28 ± 1.04
At 60 days of treatment(n=30)	8.07 ± 1.97
At 90 days of treatment (n=30)	7.51 ± 2.31
At 120 days of treatment (n=26)	6.94± 2.84

The baseline BDI score of 33 patients was 8.58± 1.15. At 30 days, 32 patients came with mean BDI score of 8.28± 1.04. At 60 days the mean score decreased to 8.47 ± 1.97 (of 30 patients) and then to 7.51± 2.31 at 90 days of follow up. At 120 days, 26 patients had mean BDI score of 6.94 ± 2.84. This chart shows the decrease in BDI score at successive follow ups with improving mental status of the patients.

Table 2: comparison of bdi scores at pre-treatment, at 30 days, at 60 days, at 90 days and 120 days of follow up of patients (n=26)

Time Points	MEAN ± SD
Pre-treatment	8.46 ± 1.15
At 30 days	8.15 ± 0.95
At 60 days	7.96 ± 1.09
At 90 days	7.58 ± 1.21
At 120 days	7.11 ± 1.65

The mean BDI score of 26 patients (who came till the last follow up of 120 days) decreased at 3 follow ups at 30, 60, 90 and 120 days. The pre treatment BDI mean score was 8.46 which came down to 7.11 over 4 months of treatment with isotretinoin.

Table no 3: Significance of differences (p value) of the bdi scores at pretreatment, at 30 days, at 60 days, at 90 days and at 120 days of follow up (n=26)

Time Points	Pre-Treatment	At 30 Days	At 60 Days	At 90 Days	At 120 Days
Pre-treatment	*	0.294	0.114	**0.010**	**0.001**
At 30 days	0.294	*	0.506	0.065	**0.008**
At 60 days	0.114	0.506	*	0.240	**0.033**
At 90 days	**0.010**	0.065	0.240	*	0.247
At 120 days	**0.001**	**0.008**	**0.033**	0.247	*

This data was calculated by applying student t test.

None of the patients complained of any increase in mental distress. Their BDI score improved overtime. The differences between the means of BDI scores at various intervals which were statistically significant (representing significant improvement) are pre-treatment and 90 days- 0.010, pre-treatment and 120 days-0.001, 30days and 120 days- 0.008, 60 days and 120 days- 0.033. Rest of the differences was not significant.

DISCUSSION

There are a number of foreign studies describing in detail the association between isotretinoin therapy with depression. They prescribe higher doses of the molecule up to 1mg/kg. In India, a lower dose of drug is usually prescribed keeping in mind the side effect profile and patients' compliance to the therapy. Out of 33 patients who were prescribed oral isotretinoin 0.5mg/kg and were followed-up at 30, 60, 90, 120 days, a total of 7 patients dropped out at the end of study. None of the patients had BDI score of more than 10 at any point of the study. That is their psychological status was normal. The mean BDI scores decreased over time with treatment of isotretinoin. The mean BDI scores of 32 patients (who came at 30 day follow-up) were less than their pre-treatment mean BDI score, although the difference was not significant.

Similarly, mean BDI scores decreased over time with oral isotretinoin treatment in 30 patients who came for follow-up at 60 days. Their differences were not significant. On comparing the mean BDI scores of 30 patients who came for 3rd follow-up (90 days) with their pre-treatment scores, 1st and 2nd follow-up scores, there was statistically significant reduction between pre-treatment and 3rd follow-up (90 days) but not between the other two (Table 3).

On comparing the mean BDI scores of 26 patients who came for 4th follow-up (120 days) with their pre-treatment scores, 1st, 2nd and 3rd follow-up scores, there was an overall decrease in the score with statistically significant reduction between

pre-treatment and 3rd follow-up (90 days), pre-treatment and 4th follow-up (120 days), 1st and 4th and 2nd and 4th. But there was no significant difference between the rests (Table 3).

In view of the foregoing discussion, the results of the present study showed that the mental status of patients with severe acne improved when they were treated with oral isotretinoin. Thus, the exaggerated concerns, which were expressed in some reports [6,8] that treatment with isotretinoin may give rise to depression in acne, appears to be incorrect. The results which show no association between treatments with isotretinoin of patients with acne and onset of depression, have been reported by some studies. [9,10] A few studies have, using different methods, demonstrated that the level of depression may decrease in patients with severe acne receiving isotretinoin. [11] However, in these studies, statistically significant decrease in depression scores was not seen. The present study appears to provide the data that psychological status may indeed significantly improve when patients with severe acne are treated with oral isotretinoin.

Limitations

Even after conducting the present study using sound methodology and strict inclusion criteria, there seems to be certain limitations. A small sample size with lack of a healthy control group is the limiting factor of the study.

CONCLUSION

The present study was conducted in the background of several reports suggesting that patients with severe acne, when treated with oral isotretinoin may develop depression and some studies contradicting these suggestions.

Out of the 33 patients who were given oral isotretinoin 0.5 mg/kg, none reported any depressive psyche or any suicidal ideation. Comparison of BDI scores at pre-treatment and subsequent follow-ups showed that there was a general significant decline in the BDI score of the patients.

The results of the study include (a) statistically significant decline in BDI scores of patients with severe acne when they were treated with oral isotretinoin; (b) no deterioration of mental status / BDI score / depression was seen with oral isotretinoin treatment suggesting that is there is no association between the two.

Abbreviations

BDI- Beck's depression inventory

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