Frequency of depression in patients with acne vulgaris treated with short-course low dose oral isotretinoin

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INTRODUCTION

Acne vulgaris is a chronic, self-limiting, and common skin disorder 1. It usually begins in the adolescent ages (85%–90% of adolescents) and can last for over 10 years 2,3. Acne vulgaris is characterized by inflamed skin lesions (papules, pustules, nodules, and cysts) and non-inflamed comedones with oily skin 4. Exacerbation of acne may occur in association with menstruation, sweating, diet, stress, and occupational conditions 4,5. Acne treatments include systemic therapies (such as oral antibiotics and isotretinoin), topical therapies (such as benzoyl peroxide and topical retinoids), and physical modalities (such as laser therapy and chemical peeling) 6. Acne vulgaris can adversely affect the patients’ appearance, consequently reducing their self-esteem. Thereby, it could cause or deteriorate several psychological conditions like anxiety and depression and can reduce the quality of life, even leading to suicidal thoughts in severe types 2,7. To further complicate this issue, some recent studies indicate isotretinoin may cause mood instability (depression and mania) in a predisposed
population⁸, while others assert that isotretinoin is not associated with depression or anxiety⁹.

To the best of our knowledge, there are not enough prospective studies about the correlation between depression and systemic isotretinoin treatment in acne patients. Therefore, this study was designed to evaluate and compare the depression rate in acne vulgaris patients with and without systemic isotretinoin treatment.

MATERIALS AND METHODS

Study design and target group

This prospective, case-control study was conducted at the Department of Dermatology of Rasul Akram Hospital, Tehran, Iran from January 2014 to May 2015. Based on Beck’s Depression Inventory (BDI), the depression score in acne vulgaris patients receiving systemic isotretinoin (case group) was compared against acne patients receiving a systemic antibiotic (doxycycline 100-200 mg/day) and a topical retinoid (adapalene 0.1%) (control group). Inclusion criteria consisted of subjects referred to our dermatology clinic with the diagnosis of moderate to severe acne vulgaris and aged between 12 and 50 years. Acne severity was determined by the physician via clinical assessment. Exclusion criteria included subjects with acne fulminans, acne conglobata, current or past liver diseases, hormonal disorders, history of mood disorders or psychiatric drug consumption, pregnancy or intention to become pregnant, breastfeeding, allergy to retinoids, use of systemic retinoids in the past six months, consuming other supplementary therapies during the study, dissatisfaction to participate in or to continue the study, and irregular visits or loss to follow up. We also excluded patients with incomplete data.

Participants

The study flowchart is shown in Figure 1. Ninety-one patients with a diagnosis of acne vulgaris...
diagnosed by a dermatologist were included based on the mentioned inclusion and exclusion criteria. The study received ethics approval from the Ethics Committee of Tehran University of Medical Sciences, and all participants provided written informed consent.

Eighty patients completed the study; 40 in the case group and 40 in the control group. Random assignment was performed using the block randomization method matched for age, sex, and acne vulgaris severity. Case subjects were treated with oral isotretinoin (brand of HEXAL, Germany) at a dose of 0.5 mg/kg/day for two months, and control subjects received a systemic antibiotic (doxycycline 100-200 mg/day) and a topical retinoid (adapalene 0.1%) for two months. Before and after the treatment period, the severity of depression was measured using the BDI, which is a 21-question, multiple-choice, self-reported questionnaire. The power of this scale in the assessment of patients’ psychological status has been elaborately assessed in past studies, confirming its high power and reliability 10,11. Based on the BDI, higher scores are indicative of a higher depression rate and scores above 16 signify depression 11.

**RESULTS**

Demographic features including age (p = 0.51) and gender (p = 0.62) were not significantly different between the isotretinoin and control groups. Moreover, the BDI score (10.2 ± 4 for the isotretinoin group vs. 10.3 ± 3.7 for the control group; P = 0.88) and the rate of depression (10 % for the isotretinoin group vs. 5 % for the control group; P = 0.33) were not significantly different between the two groups before treatment (Table 1).

Two months after treatment, the BDI score (9.8 ± 3.2 for the isotretinoin group vs. 10.6 ± 2.6 for the control group; P = 0.27) and the rate of depression (7.5 % for the isotretinoin group vs. 5 % for the control group; P = 0.5) showed no significant difference between the two groups (Table 1). We also found no significant change in BDI score in each group after treatment (P > 0.05).

**DISCUSSION**

According to our results, isotretinoin at a dose of 0.5 mg/kg/day for a period of two months does not increase the rate of depression in acne vulgaris patients. The systematic review performed by Oliveira et al. showed that people receiving isotretinoin might be at risk of depression and suicide, particularly those with a personal or family history of psychological and mental disorders 12. This is while another systematic review performed by Huang et al. showed that isotretinoin treatment for different kinds of acne does not appear to be correlated with an increased risk of depression. Furthermore, they reported that the treatment of moderate to severe acne appears to ameliorate depressive symptoms 13. Moreover, Gnararaj et al. showed that oral isotretinoin caused significant improvement of acne lesions and significantly reduced depression scores and was not correlated

| Table 1. Comparison of studied variables between the isotretinoin and control groups. |
|-----------------|-----------------|------------------|
| Age (year)      | Isotretinoin (n=40) | Control (n=40)   | P-value |
| Gender (female) | 23.5 ± 6.4 (67.5 %) | 24.4 ± 5.7 (72.5 %) | 0.51     |
| BDI score before intervention | 10.2 ± 4 | 10.3 ± 3.7 | 0.88     |
| Depression rate before intervention | 4 (10 %) | 2 (5 %) | 0.33     |
| BDI score after intervention | 9.8 ± 3.2 | 10.6 ± 2.6 | 0.27     |
| Depression rate after intervention | 3 (7.5 %) | 2 (5 %) | 0.5      |

BDI: Beck’s Depression Inventory.
Depression and oral isotretinoin in acne vulgaris

with an increased incidence of suicidal tendencies related to depression. In addition, Rubio-García et al. reported that isotretinoin treatment in patients with severe and recurrent acne did not increase depressive symptoms, but rather gave rise to improvement due to boosting the self-perception of patients. However, we found no significant reduction or rise in the depression score among acne vulgaris patients treated with isotretinoin.

Some studies concluded that the deleterious effects of isotretinoin related to depression occurred in patients with neural side effects of isotretinoin such as headache or among those with a personal or family history of psychological/mental disorders. Other studies suggest that only individuals with bipolar disorder should not be treated with isotretinoin due to worsening signs and symptoms during treatment. Considering the high rate of migraine in bipolar disorder, especially in the predominantly depressive type, and given that some signs such as panic attacks and obsessive doubting seem to worsen during isotretinoin treatment, isotretinoin-induced depression could be related to multiple factors in patients with a history of psychological/mental disorders. Since we excluded the patients with psychological and mental disorders from this study, we did not observe depression deterioration after two months of treatment. Ludot et al. demonstrated that the risk of depression, attempted suicide, and successful suicide increased significantly following isotretinoin treatment. Moreover, Bremner et al. reported that depression resolved after isotretinoin discontinuation and, in some cases, returned with its reintroduction. Sundström et al. showed that isotretinoin increased the risk of attempted suicide for up to six months after the end of treatment. All these results are in contrast to our results, which may due to different sample sizes, different inclusion and exclusion criteria, and different methods of controlling confounding variables.

Conclusion

Our results demonstrated that short-term oral isotretinoin treatment did not increase the depression rate in acne vulgaris patients. On the other hand, oral isotretinoin gives rise to significant clinical improvements in patients with moderate to severe acne vulgaris, which could be associated with a decrease in depression scores. Further structured randomized prospective studies with larger sample sizes and longer durations of oral isotretinoin treatment could be more beneficial to elucidate the risk of depression during and after treatment with oral isotretinoin among acne vulgaris patients.

Conflicts of interest: None declared.

REFERENCES


