IJD ORIGINAL ARTICLE

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

Nasim Niknezhad, MD [1]
Behnaz Hamedani, MD [1*]
Abbas Zamanian, MD [2]
Reza Mahmoud Robati, MD [1,3]
Elnaz Hamedani, MD [4]

1. Skin Research Center, Shohada-e-Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Department of Dermatology, Iran University of Medical Sciences, Tehran, Iran
3. Department of Dermatology, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
4. Department of Nursing, Islamic Azad University, Tehran, Iran

*Corresponding author:
Behnaz Hamedani, MD
Skin Research Center, Shohada-e-Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Tel: (+9821)22744393-5
Fax: (+9821)22744392
Email: hamedanibehnaz@gmail.com

Received: 16 February 2020
Accepted: 6 June 2020

Introduction: Acne vulgaris affects individuals of all ages, and isotretinoin is the most effective treatment available for this disease. However, serious adverse effects, including the possibility of depression and suicide, could limit its use.This study aimed to investigate the frequency of depression in patients with acne vulgaris treated with oral isotretinoin.

Materials and Methods: Forty acne vulgaris patients treated with oral isotretinoin and 40 age- and sex-matched controls treated with a systemic antibiotic (doxycycline 100-200 mg/day) and a topical retinoid were enrolled in this study. The depression score was measured based on Beck's Depression Inventory (BDI) in both groups before and after two months of treatment.

Result: The BDI score and the rate of depression were not significantly different between the two groups after the two-month treatment period. Moreover, we did not find any significant change in BDI score in each group after treatment ($P > 0.05$).

Conclusion: Our study showed that short-course oral isotretinoin therapy does not increase the depression rate among acne vulgaris patients. It should be noted that oral isotretinoin causes a significant clinical improvement in patients with moderate to severe acne vulgaris, which could be associated with a decrease in depression scores.

Keywords: depression, acne vulgaris, isotretinoin

Iran J Dermatol 2020; 23: 150-154

DOI: 10.22034/ijd.2020.120834

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

population [8], while others assert that isotretinoin is not associated with depression or anxiety [9].

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

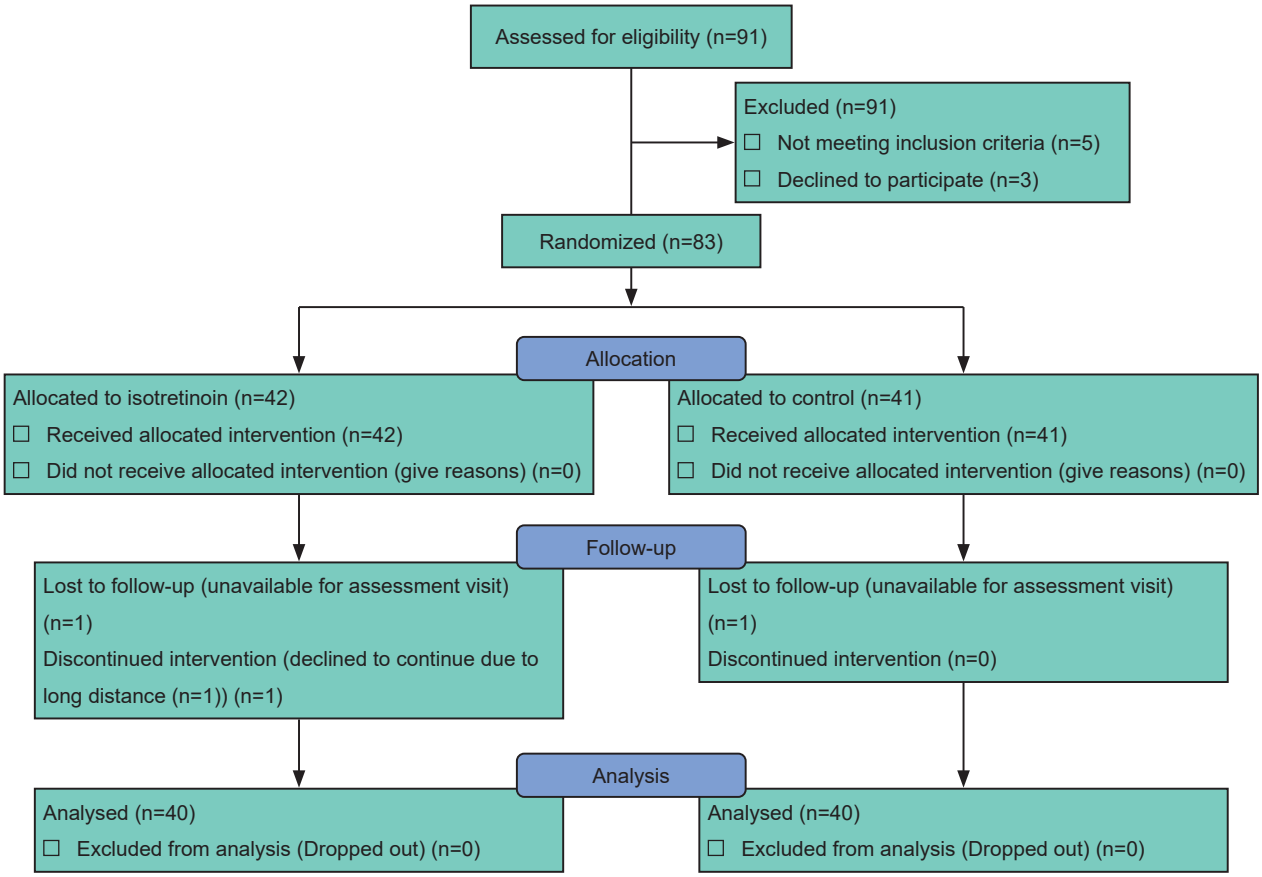

Figure 1. Study flowchart.

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].

Data analysis

Data were analyzed and reported only for patients with complete information. Statistical analysis was performed using SPSS version24 software (SPSS Inc., Chicago, IL, USA). The Chi-squared test was used to compare qualitative variables between the groups. The Kolmogorov-Smirnov test was used to evaluate the normal distribution of the quantitative parameters. The independent t-test was used to assess variables with normal distribution, while the Mann-Whitney test was used for variables without normal distribution. Two-tailed p-values less than 0.05 were considered significant.

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, Gnanaraj *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.

Variables	Groups		*P*-value
	Isotretinoin (n=40)	Control (n=40)	
Age (year)	23.5 ± 6.4	24.4 ± 5.7	0.51
Gender (female)	27 (67.5 %)	29 (72.5 %)	0.62
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.

with an increased incidence of suicidal tendencies related to depression [14]. 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 [15]. 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 [16] or among those with a personal or family history of psychological/mental disorders [12]. Other studies suggest that only individuals with bipolar disorder should not be treated with isotretinoin due to worsening signs and symptoms during treatment [16,17]. Considering the high rate of migraine in bipolar disorder, especially in the predominantly depressive type [18], and given that some signs such as panic attacks and obsessive doubting seem to worsen during isotretinoin treatment [19-22], 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 [23]. Moreover, Bremner *et al.* reported that depression resolved after isotretinoin discontinuation and, in some cases, returned with its reintroduction [24]. Sundström *et al.* showed that isotretinoin increased the risk of attempted suicide for up to six months after the end of treatment [25]. 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

1. Gollnick HP, Finlay AY, Shear N. Can we define acne as a chronic disease? If so, how and when? Am J Clin Dermatol. 2008;9(5):279-284.
2. Bhate K, Williams HC. Epidemiology of acne vulgaris. Br J Dermatol. 2013;168(3):474-485.
3. Kontochristopoulos G, Platsidaki E. Chemical peels in active acne and acne scars. Clin Dermatol. 2017;35(2):179-182.
4. Williams HC, Dellavalle RP, Garner S. Acne vulgaris. Lancet. 2012;379(9813):361-372.
5. Suh DH, Kwon HH. What's new in the physiopathology of acne? Br J Dermatol. 2015;172 (Suppl 1):13-19.
6. Chen X, Wang S, Yang M, et al. Chemical peels for acne vulgaris: a systematic review of randomised controlled trials. BMJ open. 2018;8(4):e019607.
7. Sathish D, Shayeda, Rao YM. Acne and its treatment options: a review. Curr Drug Deliv. 2011;8(6):634-639.
8. Truitt JM, Reichenberg JS, Sharghi KG, et al. Isotretinoin: the ups are just as troubling as the downs. G Ital Dermatol Venereol. 2018;153(4):535-539.
9. Suarez B, Serrano A, Cova Y, et al. Isotretinoin was not associated with depression or anxiety: A twelve-week study. World J Psychiatry. 2016;6(1):136-142.
10. Kaymak Y, Taner E, Taner Y. Comparison of depression, anxiety and life quality in acne vulgaris patients who were treated with either isotretinoin or topical agents. Int J Dermatol. 2009;48(1):41-46.
11. Hahm BJ, Min SU, Yoon MY, et al. Changes of psychiatric parameters and their relationships by oral isotretinoin in acne patients. J Dermatol. 2009;36(5):255-261.
12. Oliveira JM, Sobreira G, Velosa J, et al. Association of Isotretinoin With Depression and Suicide: A Review of Current Literature. J Cutan Med Surg. 2018;22(1):58-64.
13. Huang YC, Cheng YC. Isotretinoin treatment for acne and risk of depression: A systematic review and meta-analysis. J Am Acad Dermatol. 2017;76(6):1068-1076.e9.
14. Gnanaraj P, Karthikeyan S, Narasimhan M, et al. Decrease in "Hamilton Rating Scale for Depression" following isotretinoin therapy in acne: an open-label prospective study. Indian J Dermatol. 2015;60(5):461-464.
15. Rubio-Garcia L, Pulido-Diaz N, Jimenez-Lopez JL. [Isotretinoin and depressive symptoms in patiens with

severe and recurrent acne]. Rev Med Inst Mex Seguro Soc. 2015;53 Suppl 1:S54-59.

16. Schaffer LC, Schaffer CB, Hunter S, et al. Psychiatric reactions to isotretinoin in patients with bipolar disorder. J Affect Disord. 2010;122(3):306-308.
17. Barak Y, Wohl Y, Greenberg Y, et al. Affective psychosis following Accutane (isotretinoin) treatment. Int Clin Psychopharmacol. 2005;20(1):39-41.
18. Baptista T, Uzcategui E, Arape Y, et al. Migraine life-time prevalence in mental disorders: concurrent comparisons with first-degree relatives and the general population. Investigacion clinica. 2012;53(1):38-51.
19. Yesilova Y, Bez Y, Ari M, et al. Effects of isotretinoin on obsessive compulsive symptoms, depression, and anxiety in patients with acne vulgaris. J Dermatolog Treat. 2012;23(4):268-271.
20. Segmiller FM, Ruther T, Linhardt A, et al. Psychosis during treatment with isotretinoin. Ther Adv Psychopharmacol. 2013;3(4):244-245.
21. Rajagopal S. Acute psychosis induced by isotretinoin. Indian J Psychiatry. 2014;56(3):295-297.
22. Poblete AC, Herskovic MV, Eva CP. Panic attacks in a patient treated with isotretinoin for acne. Report of one case. Rev Med Chil. 2006;134(12):1565-1567.
23. Ludot M, Mouchabac S, Ferreri F. Inter-relationships between isotretinoin treatment and psychiatric disorders: Depression, bipolar disorder, anxiety, psychosis and suicide risks. World J Psychiatry. 2015;5(2):222-227.
24. Bremner JD, Shearer KD, McCaffery PJ. Retinoic acid and affective disorders: the evidence for an association. J Clin Psychiatry. 2012;73(1):37-50.
25. Sundstrom A, Alfredsson L, Sjolin-Forsberg G, et al. Association of suicide attempts with acne and treatment with isotretinoin: retrospective Swedish cohort study. BMJ (Clinical research ed). 2010;341:c5812.