

# The Effect of Isotretinoin (Roaccutane) Therapy on Depression and Quality of Life of Patients with Severe Acne

Youssef Fakour, MD<sup>1</sup>  
 Pedram Noormohammadpour,  
 MD<sup>2</sup>  
 Hamed Ameri, MSc<sup>5</sup>  
 Amir Houshang Ehsani, MD<sup>1</sup>  
 Leila Mokhtari, MSc<sup>3</sup>  
 Najmeh Khosrovanmehr, MSc<sup>4</sup>  
 Seyedeh Zahra Hoseini nezhad,  
 MD<sup>6</sup>

**1** Assistant professor, Department of Psychiatry, Tehran University of Medical Sciences, Razi hospital, Tehran, Iran

**2** Assistant professor, Department of Dermatology, Tehran University of Medical Sciences, Razi hospital, Tehran, Iran

**3** Master of Clinical Psychology, Ministry of Education

**4** Master of Clinical Psychology, Shahid Beheshti University of medical sciences, Imam Hussein Hospital

**5** Department of Biomedical engineering, Science and Research branch, Islamic Azad University, Tehran, Iran

**6** Department of Dermatology, Tehran University of Medical Sciences, Razi hospital, Tehran, Iran

## Corresponding author:

Seyedeh Zahra Hoseini nezhad  
 Department of Dermatology, Razi hospital, Immunobullous research center, Tehran University of Medical Sciences, Tehran, Iran  
 Tel: 0098 912 6135028  
 Email:  
 dr.hoseininezhad@yahoo.com

**Objective:** Acne is the most common skin disease and isotretinoin is the most powerful drug among the various drugs used for its treatment, but it has some adverse effects. The aim of this study was to evaluate the effect of isotretinoin on depression and quality of life of a group of patients undergoing isotretinoin therapy before and after the treatment course .

**Methods:** In this prospective study, 98 patients with severe acne were enrolled consecutively and underwent isotretinoin therapy receiving 0.5 mg/kg/d of isotretinoin for 16 weeks. Isotretinoin effects on quality of life and depression were evaluated using Dermatology Life Quality Index (DLQI) and Beck Depression Inventory (BDI) questionnaires, respectively.

**Results:** In this study, 98 patients suffering from severe acne (38 males and 60 females) were enrolled. Treatment of acne was associated with improvement of quality of life scores in both male and female patients ( $p = 0.001$ ). Considering the cutoff value of 13 for mild depressive mood in the BDI score, in total, 48 (49%) of the enrolled patients (21 males and 33 females) had a mild depressive mood before the commencement of the treatment in this study. The analysis of before and after treatment BDI scores showed that the number of patients and also the mean score of BDI were increased in both male and female patients after the treatment ( $p < 0.05$ ).

**Conclusion:** Isotretinoin therapy improved the quality of life of patients suffering from acne, but depression was accentuated in the patients to some extent.

**Keywords:** *Isotretinoin, Depression, Quality of Life*

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**A**cne is the most common skin disease for which people referred to a dermatologist, and it affects about 85% of individuals at any age, particularly adolescents (1-3). There are many treatments for acne including topical agents, topical and oral antibiotics but the most effective is isotretinoin (Roaccutane®). Isotretinoin was first introduced in 1982 and has been used ever since for the treatment of severe acne with nodular and cystic formations and resistant acne not responding to other treatment modalities. (4) Isotretinoin plays its anti-acne effect through four mechanisms: reducing sebum secretion, comedone formation, bacterial load and anti-inflammatory effect, which makes it the most

effective treatment for acne. In addition, isotretinoin has an improving effect on the quality of life of patients with acne (5, 6). Parallel to brilliant anti-acne effect of isotretinoin, which makes it the first choice of treatment for severe acne, it has some side effects and complications including teratogenicity, liver dysfunction and psychological effects (7-11). Mood disorders including depression were reported in patients affected by acne as well as other chronic illnesses (12-14). Considering previous studies, severe acne has greater adverse effect on mood than other chronic cutaneous disorders such as psoriasis or alopecia although the relation between isotretinoin and mood disorders and its aggravating role is still in debate (12-14).

There are many controversies about the effects of isotretinoin on mood. Although there are some studies showing negative effects of isotretinoin such as depression, recent well controlled large prospective studies have failed to find a relationship between isotretinoin and depression (15). The aim of this study was to evaluate the effect of isotretinoin on some psychological characteristics of patients including depression and quality of life of a group of patients undergoing isotretinoin therapy before and after the treatment course.

## Material and Methods

### Participants and Procedure

Between January 2010 and December 2012, patients suffering from acne who were referred to Razi dermatology hospital, affiliated to Tehran University of Medical Sciences, were examined and 98 patients with severe acne were enrolled in this prospective study consecutively and underwent isotretinoin therapy according to international guidelines and treatment protocols. The acne severity was measured according to "Global Acne Grading Scale" (16). Exclusion criteria were: age <12 or >50 years, pregnancy, liver diseases and history of liver diseases, documented history of mood disorders and patients under treatment of psychologic drugs. Demographic data were also obtained. Liver function tests were measured before the treatment and periodically within the therapy period. As mentioned, pregnant patients were excluded from the study.  $\beta$ -HCG test was performed during the study for female patients to exclude the pregnant women. The female patients were also warned to use contraceptive methods during their enrollment in this study. The dosage of isotretinoin therapy was measured according to international therapeutic guidelines and patients received 0.5mg/kg/d of isotretinoin in the study period.

In order to assess the effect of isotretinoin therapy on patients' quality of life, the Dermatology Life Quality Index (DLQI) was filled by each patient twice, once before the treatment and once after the treatment. Depression analysis was also performed using Beck

Depression Inventory (BDI) questionnaire before and after the treatment courses same as the DLQI form. The power of these scales in patients' psychological status assessment has been previously discussed in detail (17, 18). Briefly, higher scores are indicator of greater disability and depression. The scores above 13 in the BDI scoring system indicate mild depression (17). All the psychiatric aspects of the study were performed under the supervision of an expert psychiatrist. Informed consent was obtained from each patient and the study was approved by a local ethics committee.

### Statistical Analysis

The results are expressed as mean  $\pm$  SD. Statistical analysis was performed using SPSS version 16.0.1 (SPSS Inc., Chicago, IL, U.S.A.). The statistical differences between the proportions were determined by  $\chi^2$  analysis. Normality of data was tested using the Kolmogorov-Smirnov test by  $p = 0.05$  threshold for the rejection of normality. Numerical data were evaluated using paired t test and analysis of variance.  $P$  value < 0.05 was considered as significant.

## Results

Between October 2009 and 2011, 98 consecutive patients suffering from severe acne (38 males and 60 females) were enrolled in this prospective study. The mean age of the patients was  $22 \pm 4.4$  years (range 14–38 years). Table 1 demonstrates gender distribution of patients. Patients' characteristics and psychological test scores before and after the treatment including depression and quality of life scores are shown in Table 2. Comparison of the baseline scores (before treatment) in males and females showed that depression and quality of life scores had no significant differences ( $p > 0.05$ ).

Treatment of acne was associated with improvement of quality of life scores in both male and female patients ( $p = 0.001$ ). Considering the cutoff value of 13 for depression in the BDI score, 48 (49%) of the enrolled patients (21 males and 33 females) had a mild depressive mood before the commencement of the study.

**Table 1: Gender Distribution of patients**

Gender	Prevalence	Percent
Male	38	38.8
Female	60	61.2
Total	98	100

**Table 2: Comparison of quality of life, and depression scores at the baseline and after treatment in male and female patients**

Variable	Mean			P Value
	Male (n=38)	Female (n=60)	Total	
<b>Quality of life</b>				<0.05
Before	8.08 $\pm$ 5.01	7.9 $\pm$ 5.3	7.98	
After	2.6 $\pm$ 0.7	2.3 $\pm$ 0.5	2.44	
<b>Depression</b>				<0.05
Before	15.1 $\pm$ 9.7	15.8 $\pm$ 11.2	15.43	
After	17.8 $\pm$ 8.9	18.5 $\pm$ 12.1	16.88	

Comparing the overall mean value of the BDI scores before and after the treatment showed increased depression scores ( $p < 0.05$ ) (Table 2).

## Discussion

In the current prospective study, we tried to evaluate the effect of isotretinoin therapy on depression and quality of life of patients suffering from severe acne. Considering the fact that acne itself has negative effects on quality of life and leads to depression, we tried to exclude its interfering effect by evaluating the depression and quality of life scores in the same patients before and after treatment and we then analyzed the differences.

Previous studies have shown that acne itself has deleterious effects on quality of life which is comparable with other chronic illnesses. The improvement of quality of life after the treatment of acne has been published previously. Our data also revealed that quality of life was improved significantly after acne treatment which is in line with most of previous findings (10, 14, 19).

The relation between isotretinoin therapy and depression is the most debating aspect of isotretinoin side effects on mood. The possible relationship between isotretinoin and depression was primarily reported by cases showing mood disorders including depression with suicidal ideation while under isotretinoin treatment. (22,23) However, in addition to these reports, patients with signs of mania and psychosis were also reported after isotretinoin therapy (24-26). These reports raised attention to isotretinoin side effects on mood and led to more precise evaluation of its psychologic affects. Among these studies, some revealed adverse effects of isotretinoin on mood, and in contrast, some others not only showed no increased risk of depression in acne patients in comparison to normal population but also they showed its improving effect on mood. (27)

Primarily our data showed that about 50% of enrolled patients had depression scores (according to BDI scoring system) confirming the association between depression and acne which has been reported in previous studies.

Additionally, in our study, depression index showed worsening in both male and female patients after isotretinoin therapy and the number of depressive patients increased in spite of improvement in quality of life. As mentioned above, the effect of isotretinoin on mood has been discussed in previous years, but there are still some contradictions. Some studies have shown the negative effect of isotretinoin on mood in animal models. (28) Studies showing the positive effect of isotretinoin on mood explain it by improvements of quality of life in such patients, but in contrast and in line with studies showing deleterious effects of isotretinoin on mood, some studies have introduced possible mechanisms. Several studies have explained the effect of retinoic acid on serotonin and dopamine

secretion and production on molecular levels. They have shown that isotretinoin causes elevation in dopamine production in brain leading to its adverse mood effects; its effect on hippocampus has also been established. There are some other studies which have shown the relation between isotretinoin and depression but have called it an idiosyncratic phenomenon and some others have suggested treating patients for both acne and depression (29,30). However, the most important aspect of studies showing the negative mood effect of isotretinoin is the fact that all of them do agree with this point that isotretinoin mood effects happen gradually and over time. They have explained that retinoic acid mood effects are not an acute event and they suggest a long time follow up studies to explore its precise contribution (30). The present study showed significant improvement in quality of life as well as a decline in depression scores of the participants. Firstly, these two results seem to be discordant but considering this fact that depressive mood is one of the parameters influencing quality of life, their opposite movement is possible. In fact, the negative effect of depression on quality of life could be compensated by other effects of isotretinoin therapy including better self esteem.

## Limitations

We included patients having severe acne and this may be the cause of relative higher depressive mood in patients before the commencement of the study. We had no control group and this was one of our limitations, although it was unfair to leave patients with severe acne untreated. As another limitation, a relatively small sample size of this study limits its power.

## Conclusion

In this study, we found that isotretinoin therapy of acne patients improved their quality of life, but increased depression score. Considering the remaining debates on this topic, we suggest more attention be paid to isotretinoin mood affects. Additionally, conducting more studies which consider the retinoic acid signaling pathways and also its effect on brain function and neurotransmitters is suggested to better understand its effects on mood. In addition, more studies with larger sample size and long time follow-up are also recommended to evaluate the role of time and acute and chronic effects of isotretinoin on mood.

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## References

- Pawin H, Beylot C, Chivot M, Faure M, Poli F, Revuz J, et al. Physiopathology of acne vulgaris: recent data, new understanding of the treatments. *Eur J Dermatol* 2004; 14: 4-12.
- Ng CH, Schweitzer I. The association between depression and isotretinoin use in acne. *Aust N Z J Psychiatry* 2003; 37: 78-84.
- Kellett SC, Gawkrödger DJ. A prospective study of the responsiveness of depression and suicidal ideation in acne patients to different phases of isotretinoin therapy. *Eur J Dermatol* 2005; 15: 484-488.
- King K, Jones DH, Daltrey DC, Cunliffe WJ. A double-blind study of the effect of 13-cis-retinoic acid on acne, sebum excretion rate and microbial population. *Br J Dermatol* 1982; 107: 583-590.
- Beattie PE, Lewis-Jones MS. A comparative study of impairment of quality of life in children with skin disease and children with other chronic childhood diseases. *Br J Dermatol* 2006; 155: 145-151.
- Mallon E, Newton JN, Klassen A, Stewart-Brown SL, Ryan TJ, Finlay AY. The quality of life in acne: a comparison with general medical conditions using generic questionnaires. *Br J Dermatol* 1999; 140: 672-676.
- Cunliffe WJ, Baxter K. The place of oral isotretinoin in the treatment of acne: Benefits and side effects. *CME Bulletin Dermatol* 2000; 2: 56-62.
- Dreno B, Daniel F, Allaert FA, Aube I. Acne; evolution of the clinical practice and therapeutic management of acne between 1996 and 2000. *Eur J Dermatol* 2003; 13:166-170.
- Cordain L, Lindeberg S, Hurtado M, Hill K, Eaton SB, Brand-Miller J. Acne vulgaris: a disease of Western civilization. *Arch Dermatol* 2002; 138: 1584-1590.
- McGrath EJ, Lovell CR, Gillison F, Darvay A, Hickey JR, Skevington SM. A prospective trial of the effects of isotretinoin on quality of life and depressive symptoms. *Br J Dermatol* 2010; 163: 1323-1329.
- Bigby M, Stern RS. Adverse reactions to isotretinoin. *J Am Acad Dermatol* 1988; 18: 543-552.
- Acne, isotretinoin and depression. *Drug Ther Bull* 2003; 41:76-78.
- Wysowski DK, Pitts M, Beitz J. An analysis of reports of depression and suicide in patients treated with isotretinoin. *J Am Acad Dermatol* 2001; 45: 515-519.
- Uhlenhake E, Yentzer BA, Feldman SR. Acne vulgaris and depression: a retrospective examination. *J Cosmetic Dermatol* 2009; 9: 59-63.
- Ng CH, Tam MM, Celi E, Tate B, Schweitzer I. Prospective study of depressive symptoms and quality of life in acne vulgaris patients treated with isotretinoin compared to antibiotic and topical therapy. *Australas J Dermatol* 2002; 43: 262-268.
- Doshi A, Zaheer A, Stiller MJ. A comparison of current acne grading systems and proposal of a novel system. *Int J Dermatol* 1997; 36:416-418.
- 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: 41-46.
- 18-Hahm BJ, Min SU, Yoon MY, Shin YW, Kim JS, Jung JY, et al. Changes of psychiatric parameters and their relationships by oral isotretinoin in acne patients. *J Dermatol* 2009; 36: 255-261.
- Dunn LK, O'Neill JL, Feldman SR. Acne in adolescents: quality of life, self-esteem, mood, and psychological disorders. *Dermatol Online J* 2011; 17: 1.
- Grahame V, Dick DC, Morton CM, Watkins O, Power KG. The psychological correlates of treatment efficacy in acne. *Dermatol Psychosom* 2002; 3:119-125.
- Yazici K, Baz K, Yazici AE, Köktürk A, Tot S, Demirseren D, et al. Disease -specific Quality of life is associated with anxiety and depression in patients with acne. *J Eur Acad Dermatol Venereol* 2004; 18: 435-439.
- Byrne A, Costello M, Greene E, Zibin T. Isotretinoin therapy and depression-evidence for an association. *Irish J Psychosom Med* 1998; 15: 58-60.
- Byrne A , Hnatko G. Depression associated with isotretinoin therapy. *Can J Psychiatry* 1995; 40: 567.
- Cott AD, Wisner KL. Isotretinoin treatment of a woman with bipolar disorder. *J Clin Psychiatry* 1999; 60: 407-408.
- Van Broekhoven F, Verkes RJ, Janzing JG. Psychiatric symptoms during isotretinoin therapy. *Ned Tijdschr Geneesk* 2003; 147: 2341-2343.
- Barak Y, Wohl Y, Greenberg Y, Bar Dayan Y, Friedman T, Shoval G, et al. Affective psychosis following Accutane (isotretinoin) treatment. *Int Clin Psychopharmacol* 2005; 20: 39-41.
- Golchäi J, Khani SH, Heidarzadeh A, Eshkevari SS, Alizade N, Eftekhari H. Comparison of anxiety and depression in patients with acne vulgaris and healthy individuals. *Indian J Dermatol* 2010; 55: 352-354.
- O'Reilly KC, Shumaker J, Gonzalez-Lima F, Lane MA, Bailey SJ. Chronic administration of 13-cisretinoic acid increases depression-related behavior in mice. *Neuropsychopharmacology* 2006; 31: 1919-1927.
- Goodfield MJD, Cox NH, Bowser A, McMillan JC, Millard LG, Simpson NB, et al. Advice on the safe introduction and continued use of isotretinoin in acne in the U.K. 2010. *Br J Dermatol* 2010; 162: 1172-1179.
- Misery L. Consequences of psychological distress in adolescents with acne. *J Invest Dermatol* 2011; 131: 290-292.
- Bremner JD, McCaffery P. The neurobiology of retinoic acid in affective disorders. *Prog Neuropsychopharmacol Biol Psychiatry* 2008; 32:315-331.