Psychological Impact of Isotretinoin Treatment in Patients with Moderate and Severe Acne

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A B S T R A C T

Acne patients are subject to different degree of psychosocial distress. The emotional impact of acne vulgaris *due to disfigurement caused by the disease is undisputed. Most common reactions to the acne are depression and anxiety. The use of isotretinoin, one of the most effective options in acne treatment, increases depression symptoms. The aim of this study was to investigate the psychological status of the patients with moderate to severe acne and to compare patients treated with isotretinoin with patients treated with vitamin C. A total of 85 patients suffering from* acne vulgaris *were included in the study. The results of this study do not find a significant correlation between the use of isotretinoin and the psychological effects of the drug.*

Key words: acne vulgaris*, isotretinoin, depression, anxiety*

Introduction

Acne vulgaris is based on follicular keratosis of sebaceous glands that occurs mainly during puberty, but also during adolescence. The origin of the acne is complex and not completely understood. At least 4 pathophysiologic events take place: androgen-mediated stimulation of sebaceous gland activity, abnormal keratinization leading to follicular plugging (comedonic formation), proliferation of the bacterium *Propionibacterium acnes* within the follicle, and inflammation[1]. It belongs to the most frequent clinical pictures in dermatology and can be a painful and disfiguring disease. Acne is equally observed in people of both sexes, severer courses occurring primarily in young males[2].

Isotretinoin, a naturally occurring metabolite of vitamin A, inhibits sebaceous gland differentiation and proliferation, reduces sebaceous gland size, suppresses sebum production and normalizes follicular epithelial desquamation. Isotretinoin is the most effective treatment indicated in severe and acne unresponsive to other therapies. It is used over a 4 to 6 month treatment period.

Some reviews examined the issue of reported cases of depression and anxiety with isotretinoin. Epidemiological evidence for an association between isotretinoin and depression is currently lacking[3]. While the role of psychosomatic components in the pathogenesis of acne is differently assessed, secondary emotional impairment due to disfigurement by the disease is almost undisputed[4]. Although the knowledge concerning the psychoemotional implications of acne has been constrained by poor methodological design[5] few studies have assessed the impact of effective physical intervention upon the psychoemotional functioning of patients[6].

The aim of the present investigation was to determine the emotional impact of acne and the effect of the treatment with isotretinoin.

Patients and Methods

The prospective study was conducted at the Department for Dermatology and Venerology University Clinical Hospital Mostar and included 85 patients. The participants were outpatients suffering from moderate acne, aged from 13 to 25 years, average 17.4, and others suffering from severe acne aged from 14 to 24, average 18.2. Acne patients were treated with isotretinoin 1 mg/kg *per*

day, and control group with vitamin C 500 mg *per* day. There were 46 moderate acne patients (20 treated with isotretinoin and 26 patients were control group) and 39 severe acne patients (21 treated with isotretinoin, and 18 were control group). All participants provided written informed consent. Exclusion criteria included prior use of or allergy to isotretinoin, and pregnancy in female participants. In the isotretinoin group, all female participants subjected of childbearing potential used 2 forms of birth control. The clinical classification of acne was done according to Plewig and Kligman[7]. All patients underwent an assessment before the treatment, during the 8 week treatment and at the end of the 4 week after finished treatment. Consenting participants completed the same psychometric instruments, standardized with optimal psychometric characteristics. None had any other severe dermatological or psychiatric diseases. The psychologist, as a member of the team, conducted psychological testing and interview.

Following questionnaires were used in the research to assess psychological state of our patients:

»Assessments of the Psychological and Social Effects« of Acne (APSEA): specific questionnaire consisted of 15 answers. Sensitive scale ranging from 10 to 117 assessment the psychosocial effects of acne. The test is important for monitoring disorder on psychological status during therapy.

»Beck Depression Inventory« (BDI): is a widely used clinical and research instrument to determine the severity of depressive symptoms[8]. It is a 21 item self-report rating inventory measuring characteristic in patients older than 13 years. The scores range from 0 to 63, over 30 indicates a clinical depressive disorder[9].

»State Trait Anxiety Inventory« (STAI): is an original questionnaire for measuring state (STAIs) and trait (STAIt) anxiety. It consists of two questionnaires with 20 statements. State anxiety estimates tension, anxiety and stress. Trait anxiety measures the degree of anxiety as a relatively stabile personal characteristics and long lasting anxiety which is not related to the specific situations. The score on each of questionnaire are given on a 5-point Libert scale. Minimum result is 0, and maximum is 80. The questionnaire is often use in clinical trials and practice.

»Measure of Psychological Stress« (MPS): is questionnaire which measure level of experienced stress regardless of the specific experience that has caused the stress. It consists of 48 questions. The total result is a sum of estimations given for all 48 statements which is then presented on a scale range from 0 to 20. It shows the level of experienced everyday stress related to the disease.

Statistical analysis of the result was done using SPSS, version 12. Descriptive statistics were calculated for all variables. Student t-test was calculated to determine the differences between groups.

Results

A total of 85 patients were enrolled in the study. Overall 65.8% (n=56) were male and 34.2% (n=29) were female. Patients were 13 to 25 years old, with the average age being 19 years. 46 were moderate and 39 severe acne patients. From 46 moderate acne patients, 20 were treated with isotretinoin 1 mg/kg *per* day, and 26 were control group treated with vitamin C 500 mg *per* day. From 39 severe acne patients 21 were treated isotretinoin 1 mg/kg *per* day and 18 were control group treated with vitamin C 500 mg *per* day.

To investigate the possible influence of isotretinoin on psychological status of our patients, we compared patients on isotretinoin with the control group taking vitamin C, and we did the comparison separately for moderate and severe acne patients. The comparison was made during the 8th week of therapy and 4 weeks after the completion of therapy.

We compared patients during the therapy to detect possible changes in psychological status on time, in order to stop the treatment with isotertionoin if needed. Patients with moderate acne show low level of depressive symptoms, low anxiety and low reactive anxiety to acne (Table 1). In moderate acne patients there was no significant difference between the patients taking isotretinoin

TABLE 1
RESULTS ON DIFFERENT MEASURES OF PSYCHOLOGICAL STATUS IN ISOTRETINOIN GROUP AND CONTROL GROUP AMONG MODERATE ACNE PATIENTS DURING THE 8TH WEEK OF TREATMENT

TEST	GROUP	N	$\overline{X}$	SD
BDI	Isotretinoin	19	4.00	4.910
	Control	26	4.15	4.986
MPS	Isotretinoin	20	41.40	27.021
	Control	26	30.35	32.325
STAI – s	Isotretinoin	20	33.35	7.686
	Control	26	35.96	11.746
STAI – t	Isotretinoin	19	37.42	8.474
	Control	26	35.77	12.028
APSEA	Isotretinoin	19	42.16	16.122
	Control	26	36.65	12.393

TABLE 2
THE COMPARISON OF ISOTRETINOIN GROUP AND CONTROL GROUP AMONG MODERATE ACNE PATIENTS ON DIFFERENT MEASURES OF PSYCHOLOGICAL STATUS DURING THE 8TH WEEK OF TREATMENT, T-TEST FOR INDEPENDENT GROUPS

	t	df	p
BDI	0.103	43	0.919
MPS	1.233	44	0.224
STAI – s	0.861	44	0.394
STAI – t	0.512	43	0.611
APSEA	1.296	43	0.202

TABLE 3
RESULTS ON DIFFERENT MEASURES OF PSYCHOLOGICAL STATUS IN ISOTRETINOIN GROUP AND CONTROL GROUP AMONG SEVERE ACNE PATIENTS DURING THE 8TH WEEK OF TREATMENT

TEST	GROUP	N	$\overline{X}$	SD
BDI	Isotretinoin	21	5.43	5.464
	Control	18	8.17	6.888
MPS	Isotretinoin	21	39.05	26.009
	Control	17	50.18	38.767
STAI – S	Isotretinoin	21	37.71	10.598
	Control	18	37.61	12.035
STAI – T	Isotretinoin	21	38.33	11.804
	Control	17	39.29	12.593
APSEA	Isotretinoin	21	47.38	20.084
	Control	18	46.89	18.464

TABLE 5
RESULTS ON DIFFERENT MEASURES OF PSYCHOLOGICAL STATUS IN ISOTRETINOIN GROUP AND CONTROL GROUP AMONG MODERATE ACNE PATIENTS 4 WEEKS AFTER THE END OF THE TREATMENT

TEST	TREATMENT	N	$\overline{X}$	SD
BDI	Isotretinoin	20	3.65	5.354
	Control	26	3.27	5.583
MPS	Isotretinoin	20	33.80	26.971
	Control	26	30.27	34.741
STAI – S	Isotretinoin	20	32.40	9.605
	Control	26	33.35	11.384
STAI – T	Isotretinoin	19	37.05	10.113
	Control	26	34.96	11.626
APSEA	Isotretinoin	18	41.17	14.569
	Control	26	34.73	14.847

and the control group on any of the psychological tests during the treatment (Table 2).

Patients with severe acne also showed good psychological status with low level of depression and anxiety (Table 3). There was no difference between patients on isotretinoin and control group in severe acne patients on any of the measures of psychological status (Table 4). None of the patients in isotretinoin group (both among moderate and severe acne patients) showed significant symptoms of depression or anxiety during the 8th week and all of them were able to continue with therapy. Four weeks after the treatment patients who used isotretinoin were compared with control group once again to check for the possible cumulative influence of isotretinoin on psychological status. After the end of the treatment, all patients showed improvement on psychological status, low level of both depression and anxiety (Table 5 and 7). In moderate acne patients there was no difference between patients on isotretinoin and control group on any of the measures of psychological status (Table 6). There was no difference between patients on isotretinoin and control group in severe acne patients either (Table 7).

To double check the possible influence of isotretinoin on psychological status we compared results on psychological tests for all patients taking isotretinoin before

and after the therapy. Among the patients taking isotretinoin, before the treatment, the mean score on BDI was 7.36, on STAI 37.36, on MPS 42.05 and on APSEA 46.45. All results mentioned indicate good psychological functioning with minimal number of depressive symptoms, low anxiety and mild reactive anxiety as a reaction to acne. Even though mean results on all tests show improvement after the therapy (BDI=4.18; STAI=34.74; MPS=32.87; APSEA=41.03), there was no statistically significant difference between the results before and after the therapy on any of the measures of psychological status. The present research illustrated that the isotretinoin treatment does not cause psychological disorder in acne patients (Table 8).

Discussion

The aim of this study was to investigate depression and anxiety in facial acne patients. The adverse effect of acne upon the patient's psychological state has been observed by many authors. However, most studies have considered the patients with severe, generally cystic acne[10]. Despite the broad range of available therapies for acne, relatively few studies have assessed the impact of treatment upon the psychological functioning[11]. From a

TABLE 4
THE COMPARISON OF ISOTRETINOIN GROUP AND CONTROL GROUP AMONG SEVERE ACNE PATIENTS ON DIFFERENT MEASURES OF PSYCHOLOGICAL STATUS DURING THE 8TH WEEK OF TREATMENT, T-TEST FOR INDEPENDENT GROUPS

	t	df	p
BDI	1.384	37	0.175
MPS	1.056	36	0.298
STAI – S	0.028	37	0.977
STAI – T	0.242	36	0.810
APSEA	0.079	37	0.937

TABLE 6
THE COMPARISON OF ISOTRETINOIN GROUP AND CONTROL GROUP AMONG MODERATE ACNE PATIENTS ON DIFFERENT MEASURES OF PSYCHOLOGICAL STATUS 4 WEEKS AFTER THE END OF THE TREATMENT, T-TEST FOR INDEPENDENT GROUPS

	t	df	p
BDI	0.233	44	0.817
MPS	0.375	44	0.709
STAI – S	0.299	44	0.767
STAI – T	0.629	43	0.533
APSEA	1.424	42	0.162

TABLE 7
RESULTS ON DIFFERENT MEASURES OF PSYCHOLOGICAL
STATUS IN ISOTRETINOIN GROUP AND CONTROL GROUP
AMONG SEVERE ACNE PATIENTS 4 WEEKS AFTER THE END
OF THE TREATMENT

TEST	TREATMENT	N	$\overline{\text{X}}$	SD
BDI	Isotretinoin	21	5.86	5.918
	Control	18	8.94	8.881
MPS	Isotretinoin	21	38.71	29.311
	Control	18	52.72	40.287
STAI – S	Isotretinoin	21	36.24	10.549
	Control	18	38.56	12.133
STAI – T	Isotretinoin	21	36.81	10.524
	Control	18	41.44	12.775
APSEA	Isotretinoin	21	47.86	18.402
	Control	18	47.56	18.478

clinical perspective, the majority of acne patients have moderate disease. The acne patients are mainly adolescents and young adults who are more vulnerable to the cosmetic impact of their illness and can provoke significant emotional burden for the patient. In this study we evaluated psychological factors, depression and anxiety, among the groups of patients with moderate to severe facial acne and prospectively examined their relation to treatment with isotretinoin. In the past, isotretinoin was traditionally reserved for severe acne only, but today it is indicated in acne unresponsive to other therapy.

Each patient was tested with psychological questionnaires before the beginning of the treatment, during the 8th week of treatment, and at the end of 4th week after the completion of treatment. The psychological questionnaires included the MPS, BDI, STAI and APSEA tests. These tests measure common reaction to acne, depression and anxiety.

The greatest variations were observed before and after the treatment finished. Among our patients, the average result on BDI before treatment was 7.35. Most of the patients had the results indicating minimal number of depressive symptoms. At the end of treatment isotretinoin the same test was 4.17, which is lower, but the difference was not statistically significant. It was demon-

TABLE 8
THE COMPARISON OF ISOTRETINOIN GROUP AND CONTROL
GROUP AMONG SEVERE ACNE PATIENTS ON DIFFERENT MEA-
SURES OF PSYCHOLOGICAL STATUS 4 WEEKS AFTER THE END
OF THE TREATMENT, T-TEST FOR INDEPENDENT GROUPS

	t	df	p
BDI	1.294	37	0.204
MPS	1.254	37	0.218
STAI – S	0.638	37	0.527
STAI – T	1.243	37	0.222
APSEA	0.051	37	0.960

strated in the literature demonstrate that patients with acne suffer from emotional distress and psychological problems caused by their disease when compared to people with healthy skin; however impairment is not correlated with the objective severity of acne[2]. On the other hand, Kellet and Gawkrodger[6] in their study reported that acne patients reported relatively poor psychological disorders in comparison with other medical patients groups. This result is in line with our findings, since we didn't find a strong emotional reaction to acne among our patients.

Some authors have described depressive symptoms during the treatment with isotretinoin[3]. This is the reason why we used BDI test, which was very important for monitoring depressive symptoms during the treatment. *Acne vulgaris* is disease which occurs primarily in young people, at a time when they are undergoing a great psychological change – during puberty. Therefore it was very important to stop the therapy with isotretinoin on time if any depressive or anxiety symptoms should occur. The results in this study obtained in moderate and severe acne patients on the different psychological tests during the treatment did not indicate the existence of psychological symptoms, so that all our patients were able to complete the treatment with isotretinoin. Our results correlated with the findings from literature which suggested a positive effect of isotretinoin on the manner the acne patients personally viewed themselves shortly after commencement of treatment. Isotretinoin treatment reduced the level of depressive symptoms what may be explained by the fact that the patients had fewer skin lesions[12].

At the last follow-up, at the end of the treatment, the tests scores showed only improvement in depression, not an increase in the number of depressive symptoms both in the isotretinoin group and in the control group. The isotretinoin group had a decreased level of symptoms after treatment. Our study indicated that there are no more depressive symptoms in the isotretinoin treatment group when compared to the control group at the end of the treatment. In his study, Cooper described that patients after the treatment with isotretinoin were in remission from acne and had non-significant reduction in anxiety[13]. In this study, we showed that acne had a relatively small impact on depression and anxiety, especially in patients treated with isotretinoin. The use of isotretinoin in the treatment of moderate to severe acne did not increase depressive symptoms. On the contrary, our study showed that isotretinoin treatment of acne does not lead to occurrence of depressive symptoms. Our participants were recruited from clinic outpatients seeking medical treatment for their moderate to severe acne and most of them were male. The gender difference may suggest the final result of the study, because women are more likely to experience greater psychological difficulties than male. However, our results suggest that the isotretinoin treatment has a general positive effect upon the manner in which the acne patients perceived themselves. Welp and Gieler[14] and Medanski[15] did not find a significant correlation between objective clinical findings

and significant psychometric variables which complies with our results. Patients with severe acne may feel less disfigured if they are accepted by their environment and are given a steadfast self-image because of other abilities and a special personality[16,17].

Conclusion

We examined the depressive symptoms and anxiety among moderate and severe acne patients. Our data obtained through clinical psychiatric interviews and standard questionnaires demonstrates that patients with moderate to severe acne did not suffer from significant psychological problems (depression and anxiety). This is contrary to previous observation that patients with disfiguring acne experience depression and other psychological problems. The use of isotretinoin in the treatment of moderate to severe acne did not increase the symptoms of depression and anxiety. Treatment of acne with isotretinoin had better results and improves depressive symptoms. The reason for that may lay in good effects isotretinoin has on the illness and correlations to the patient's emotional reaction.

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PSIHOLOŠKI UTJECAJ LIJEČENJA ISOTRETINOINOM U BOLESNIKA S UMJERENO TEŠKIM I TEŠKIM OBLIKOM *ACNE VULGARIS*

SAŽETAK

Bolesnici s *acne vulgaris* pokazuju različit stupanj psiholoških poremećaja. Emocionalni utjecaj akni narušavanjem vanjskog izgleda je upitan. Najčešće reakcije na pojavu akni su depresija i anksioznost, a i izotretinoin, kao najbolji izbor u liječenju akni, može dovesti do pojave simptoma depresije. Cilj našeg istraživanja bio je ispitati psihološki status u bolesnika s umjereno teškim i teškim oblikom *acni vulgaris* i usporediti bolesnike liječene izotretinoinom s onima koji su uzimali vitamin C. U istraživanju je bilo uključeno 85 bolesnika s *acne vulgaris*. Rezultati istraživanja ne upućuju na signifikantnu povezanost upotrebe izotretinoina i psihološkog efekta lijeka.