https://doi.org/10.31925/farmacia.2023.1.21 **ORIGINAL ARTICLE**

PREVALENCE OF PSYCHIATRIC COMORBIDITIES IN PATIENTS WITH PSORIASIS AND THEIR EVOLUTION UNDER TREATMENT

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Abstract

Psoriasis is a chronic, immune-mediated inflammatory dermatosis that associates a number of conditions such as cardiovascular disease, metabolic syndrome, inflammatory bowel disease, neoplasia or psychiatric disorders, amongst the most frequent being depression and anxiety. This article aims to highlight the common pathogenetic pathway between psoriasis and psychiatric comorbidities, depression and anxiety, their prevalence among psoriasis patients, as well as the evolution of these conditions under psoriasis-specific systemic therapy (biological therapy and conventional systemic therapy) using specific scales to quantify depression severity and anxiety (HAM-D, HAM-A), determined at a certain time interval after the initiation of therapies. We conducted an observational study in the Dermatology Department of the Slatina Emergency County Hospital on a group of 51 patients clinically diagnosed with psoriasis. Thus, we found that the degree of mental impairment in the studied group was significant, 49% of patients showed mild depression, 15.7% moderate depressive episodes and 5.9% severe depression. Only 29.4% were not affected by depression. In terms of anxiety, 21.6% had moderate anxiety. Psoriasis is a chronic condition associated with the secretion of numerous pro-inflammatory cytokines. Increased levels of pro-inflammatory cytokines are also found in major depressive disorders. Thus, the common pathogenic pathway between psoriasis and depression may be the overexpression of proinflammatory cytokines such as IL-6, IL-17 or TNF-α. In the last two decades, with the advent of biological therapies, the treatment of psoriasis has evolved dramatically, and they have also had a positive impact on comorbidities, particularly psychiatric ones.

Rezumat

Psoriazisul este o dermatoză inflamatorie cronică, imun-mediată, care asociază o serie de afecțiuni precum cele cardio-vasculare, sindrom metabolic, boli inflamatorii intestinale, neoplazii sau tulburări psihiatrice, mai frecvent întâlnite fiind depresia și anxietatea. În acest articol ne propunem să evidențiem calea patogenică comună între psoriazis și comorbiditățile psihiatrice, depresie și anxietate, prevalența acestora în rândul pacienților cu psoriazis, dar și evoluția acestor afecțiuni sub terapie sistemică specifică pentru psoriazis (terapie biologică și terapie sistemică convențională) prin utilizarea unor scale specifice pentru cuantificarea gradului de depresie și anxietate (HAM-D, HAM-A), determinate la un anumit interval de timp de la inițierea terapiilor. Am efectuat un studiu observațional în cadrul Secției de Dermatologie a Spitalului Județean de Urgență Slatina, pe un lot format din 51 de pacienți diagnosticați clinic cu psoriazis. Astfel, am descoperit faptul că gradul de afectare psihică la lotul studiat a fost unul semnificativ, 49% dintre pacienți au prezentat depresie ușoară, 15,7% episoade depresive moderate, iar 5,9% depresie severă. Doar un procent de 29,4% nu era afectat de depresie. În ceea ce privește anxietatea, 21,6% prezentau anxietate moderată. Psoriazisul este o afecțiune cronică asociată cu eliberarea de numeroase citokine proinflamatorii. Un nivel crescut de citokine proinflamatorii întâlnim și în cazul tulburărilor depresive majore. Astfel, calea patogenică comună între psoriazis şi depresie poate fi reprezentată de supraexpresia unor citokine proinflamatorii precum IL-6, IL-17 sau TNF-α. În ultimele două decenii, odată cu aparitia terapiilor biologice, tratamentul psoriazisului a cunoscut o evoluție spectaculoasă, acestea având un impact pozitiv și asupra comorbidităților, îndeosebi a celor psihiatrice.

Keywords: psoriasis, depression, anxiety, treatment

Introduction

Psoriasis is a chronic inflammatory dermatosis, with a strong genetic background, immune-mediated, characterized by the appearance of erythematous-scaly plaques and plaques, well delimited, located mainly on the extension areas of the body. It has a global prevalence ranging between 0.09 and 11.4%,

and the B:F ratio is 2:1. It can occur at any age, but the higher prevalence is around the age of 50 - 69. The emotional and social impact of psoriasis on patients is very important, they face stigma, social isolation, anxiety, depression and even suicidal tendencies [1, 2].

Depression, a real public health problem, has an increasing prevalence and a negative impact on the individual and society. Adults with depression frequently face clinical underdiagnosis, difficulties in establishing treatment, or unnecessary or inappropriate treatments, which makes integrative condition management even more difficult [3].

Depressive episodes, according to the ICD-10 (International Statistical Classification of Diseases and related health problems) classification, include [3]: depressed mood, loss of interest and enjoyment, and a reduction in energy leading to increased fatigue and decreased activity, with a minimum duration of the entire episode of about 2 weeks.

According to studies the association between psoriasis and depression is bidirectional. Stressful events in an individual's life have a clearly proven risk in the onset of the disease or in triggering flares. The bi-directionality between the two conditions is supported by the fact that depression is associated with an increased risk of developing psoriasis and the skin condition (psoriasis) is associated with a high risk of developing psychiatric disorders (mainly depression). Literature shows that 9 to 55% of psoriasis patients have associated depressive symptoms of varying intensity [4]. A recent study shows that the incidence of moderately-severe depressive episodes in patients with psoriasis vulgaris was present in 13.9% of cases [5].

Psoriasis is a chronic condition associated with the secretion of pro-inflammatory cytokines such as IL-12, IL-23, TNF-α, IL-22, IL-17, IL-2, IFN-γ. In regard to psychiatric disorders, the link between major depressive disorder and inflammation is well documented in the literature [6]. In patients with major depressive disorder increases of the proinflammatory cytokines: prostaglandin E2 (PGE2), C-reactive protein (CRP), TNF-α, IL-1β, IL-2 and IL-6, IL-8, IL-17, IL-21, IL-23, TGF-β have been reported [7-10].

Anxiety is one of the most common mental disorders with significant social and economic consequences. Mood anxiety is a risk factor for the development of anxiety and emotional disorders, which are not caused by any particular object or situation. Irrational fear of an illness or an accident may be present, as well as other fears and doubts [11, 12] with numerous acute disease flares and eventually chronicity [13]. Anxiety is associated with the activation of the sympathetic nervous system and mainly with the inhibition of parasympathetic nervous system activity.

Biological therapies available in psoriasis target a number of proinflammatory cytokines involved in both the etiopathogenesis of psoriasis and other associated diseases, thus explaining the beneficial effects of these molecules on other associated pathologies by reducing systemic inflammation. Four classes of biological agents are currently available in Romania for the treatment of moderate-severe psoriasis: anti-TNF-α agents (etanercept, adalimumab, infliximab, certolizumab pegol), anti-IL-12/23 agents (ustekinumab), anti-IL-17 agents (secukinumab, ixekizumab, brodalumab), anti-IL-23 agents (risankizumab, guselkumab, tildrakizumab).

The current study aimed to determine the prevalence of depression and anxiety in patients with psoriasis regardless of its clinical form and severity and how specific therapy for psoriasis influences psychiatric comorbidities (depression and anxiety), by using the Hamilton depression and anxiety scales.

Materials and Methods

Study design

We conducted an observational study on a group of 51 patients with psoriasis presenting to the Dermatology Department of Emergency County Hospital Slatina during 2018 and 2022.

Clinical characteristics of these patients (age > 18 years, sex, weight, height, clinical form of psoriasis, PASI (psoriasis area and severity index) and DLQI (dermatology life quality index) scores), education, marital status, comorbidities, as well as data on alcohol consumption and smoking were collected. An important factor in the selection of patients was the treatment, as only patients who had undergone local or conventional systemic treatment and were candidates for biological therapy were included in this study. The degree of mental impairment was quantified using the HAM-D (Hamilton depression rating scale) and HAM-A (Hamilton anxiety rating scale) scales.

The study was conducted in accordance with international (Declaration of Helsinki revised in 2013) and national (Patients' Rights Act, No 46/2003) standards. Access to patient information was carried out under the protection of data confidentiality.

To assess psoriasis severity and therapeutic efficacy we used the PASI score, which ranges from 0 to 72 [14, 15].

As for the impact on quality of life, we measured it by using DLQI score and HAM-A and HAM-D scales [16, 17].

Measuring quality of life using DLQI score involves the patient completing a questionnaire that includes 10 items, which relate to the last 7 days.

For the presence of psychiatric comorbidities (depression, anxiety) in patients with psoriasis, we used the Hamilton scale for the assessment of depression

(HAM-D), which includes 17 items and it is the gold standard for depression scales in psychiatry. HAM-D values range from 0 - 52. Depending on the score, the classification is as follows: HAM-D: 0 - 7 = normal; 8 - 13 mild depression; 14 - 18 moderate depression; 19 - 22 severe depression; > 22 very severe depression.

To assess the severity of anxiety we used the HAM-A scale, which includes 14 items with values ranging from 0 to 56. The HAM-A has the following classification: HAM-A < 17 mild anxiety; 18 - 24 moderate anxiety; 25 - 30 moderately severe anxiety; > 30 severe anxiety.

Statistical analysis

IBM SPSS Statistics for Windows, Version 26.0 software (Armonk, NY: IBM Corp.) was used for the statistical processing of the study data. A value of the coefficient $p<0.05$ was considered significant.

Results and Discussion

The study group included subjects of both sexes, with 56.9% male representatives and 43.1% female representatives. We found that the mean age of patients in the study group was 50.35 years. The minimum age was 22 years, while the maximum age was 74 years. Regarding marital status, 84.3% of the patients were married, 11.8% were unmarried and 2% were divorced or widowed. Analysing the distribution of the group according to education, most of the patients have secondary education (58.8%), 31.4% have higher education, and 9.8% have only elementary education. The majority of the people studied were from urban areas (60.8%), while 39.2% were from rural areas. The vast majority of patients (88.2%) are diagnosed with psoriasis vulgaris type. Smaller percentages also include forms such as psoriatic arthritis (9.8%) and pustular psoriasis (2%). The average disease course was 9.94 years. The minimum period was 2 years, while the maximum period was 30 years (Table I).

Regarding the treatment, out of the 51 patients included in the study, 48 of them presented moderate-severe forms of the disease (PASI > 10) and were initiated on biological (adalimumab, etanercept, ixekizumab, secukinumab and risankizumab) or conventional systemic (methotrexate, cyclosporine, acitretin) treatment and 3 patients remained on topical treatment (Table II).

Table I

General data of psoriasis patients

Parameter	Value (numeric/media)/ (Percentage (%))
Number of patients (N)	51
Sex F (N/%)	22 (43.13%)
Sex M (N/%)	29 (56.86%)
Age (years)	50.35
Evolution (years)	9.94
Type of psoriasis (N/%)	45 (88.23%) 5 (9.80%) 1 (1.96%)
Vulgar	21.34
Arthropathic	20.10
Pustular	28.03
PASI	3 (5.88%) 8 (15.68%) 40 (78.43%)
DLQI	38 (74.51%)
BMI (kg/m2)	14 (27.45%)
Current medication	21 (41.17%)
Local therapy (N/%)	4 (7.84%)
Conventional systemic therapy (N/%)	38 (74.50%)

Table II

Distribution of psoriasis therapies at baseline

		Percentage (%)	Frequency
Validated data	Adalimumab	4	7.8
	Ciclosporine	1	2.0
	Etanercept	3	5.9
	Ixekizumab	14	27.5
	Local	3	5.9
	Metotraxat	6	11.8
	Acitretin	1	2.0
	Risankizumab	3	5.9
	Secukinumab	15	29.4
	Ixekizumab + MTX	1	2.0
	Total	51	100.0

To assess the psychiatric comorbidities in the study group we determined the values of psychometric scales (HAM-D, HAM-A) that psoriasis patients completed prior to the initiation of any conventional biological/ systemic therapy. Thus, we found that the mean HAM-D value at baseline was 10.22. HAM-D values deviate from the mean by plus or minus 3.93. The mode (modal value) has a value of 7, being the most common in the group. The minimum HAM-D value was 7, while the maximum value was 19.

Analysing the study group according to HAM-A level at baseline, the mean value was 13.94. The

minimum value was 7, while the maximum was 24. The HAM-A values deviate from the mean value of plus or minus 4.38.

Almost half of the patients (49%) have mild depression, and 29.4% are not depressed. 15.7% have moderate depression and 5.9% have severe depression.

Just over three-quarters (78.4%) of patients had mild anxiety, with the remaining 21.6% having moderate anxiety (Tables III).

Table III

Baseline HAM-D and HAM-A scores

Parameter			Frequency	Percentage (%)
HAM-D score	Validated data	Normal	15	29.4
		Mild depression	25	49.0
		Moderate depression	8	15.7
		Severe depression	3	5.9
		Total	51	100.0
HAM-A	Validated data	Mild anxiety	40	78.4
		Moderate anxiety	11	21.6
		Total	51	100.0

To quantify the effectiveness and impact of biological *vs.* conventional therapies in psoriasis on patients' mental state, we divided the group in two, and scales were determined at baseline (T0), 6 months (T6), and respectively, 12 months (T12) after initiation of therapy.

Biological therapy group

Differences in PASI score values measured over the 3-time points were statistically significant according to the Friedman test result ($p < 0.001$). PASI score values differed statistically significantly between each of the measurements taken two by two. PASI scores over the 3 measurements were decreasing, as can be seen in Table IV.

Table IV

PASI, DLQI, HAM-D, and HAM-A scores evolution in biological and conventional therapy groups

Parameter	Biological therapy group (N = 40) (mean ±standard deviation)	Conventional therapy group (N = 8) (mean ±standard deviation)
PASI-T0	23.06 ± 8.4	16.57 ± 7.54[a]
PASI-T6	7.79 ±2.57*	7.17 ± 3.84
PASI-T12	0.9 ± 0.92*[#]	4.86 ± 4.01[a]
DLQI-T0	21.15 ± 3.78	16.5 ± 7.44[a]
DLQI-T6	11.83 ± 3.17*	12.38 ± 4.72
DLQI-T12	3.33 ± 1.98*[#]	9.13 ± 6.53 *[a]
HAM-D-T0	10.5 ± 3.94	9.63 ± 4.53
HAM-D-T6	8.85 ± 2.43	9.13 ± 3.44
HAM-D-T12	7.28 ± 0.55*	8.25 ± 2.86
HAM-A-T0	14.13 ± 4.13	13.5 ± 6.02
HAM-A-T6	11.45 ±2.91*	12.25 ± 5.12
HAM-A-T12	8.9 ±1.39*[#]	11.38 ± 4.89*

Note: *$p < 0.05$ compared with the T0 value of the parameter calculated by the Wilcoxon test; [#]$p < 0.05$ compared with the T6 value of the parameter calculated by the Wilcoxon test; [a]$p < 0.05$ compared with the biological therapy group calculated by Mann- Whitney test

Regarding the evolution of the mean values of DLQI score, in the 3 measurement moments (at baseline, at 6 months, and at respectively 12 months after the initiation of therapy) it is observed a decrease in DLQI score from a mean value of 21.15 measured at baseline to a value of 3.33 measured after 12 months of therapy. The Friedman test result ($p < 0.001$) showed significant differences between the 3 measurements in terms of DLQI score values. The Wilcoxon test result indicates important differences between the values measured at all 3-time points, taken two by two (Table IV). The DLQI score improves significantly following biological therapy (Table IV).

It can be seen that the HAM-D score decreased from a mean value of 10.50 measured at baseline to a value of 8.85 after 6 months, respectively 7.28 after 12 months of treatment.

The Friedman test result ($p < 0.001$) shows significant differences between the 3 measurements.

HAM-D score also improved significantly following biological therapy (Table IV).

The Friedman test result ($p < 0.001$) showed significant differences between the 3 measurements in terms of HAM-A score. We also used the Wilcoxon test to compare the HAM-A values at the three-time points, also taken two by two. As the significance threshold p-value was less than 0.001 in

all cases, it follows that there are notable differences between all three measurements taken in pairs. We can conclude that the HAM-A score decreased significantly from one measurement to another (Table IV).

Conventional therapy group

Differences in PASI score values measured over the 3-time points in patients on conventional systemic therapy were statistically significant according to the Friedman test result ($p < 0.001$). PASI score values were significantly different between each of the measurements taken two by two. PASI scores over the 3 measurements were decreasing in time (Table IV).

In patients who received conventional therapy, DLQI score decreased from an average of 16.50 at baseline to a value of 12.38 after 6 months, respectively to 9.13 after 12 months after initiation of therapy (Table IV).

The Friedman test result ($p < 0.001$) shows that there are significant differences between the 3 measurements.

The table with descriptive statistics (Table IV) shows the evolution of the mean values of the HAM-D score in the 3 measurement moments (at baseline, after 6 months, and respectively after 12 months of therapy). Although there is a decrease in the score from a mean value of 9.63 measured at baseline to a value of 8.25 measured after 12 months of therapy, the Friedman test result ($p = 0.097$) showed no significant difference in the HAM-D score between the 3 measurements.

It can be seen that HAM-A score also decreased from a mean value of 13.50 measured at baseline to a value of 12.25 after 6 months, and then to 11.38 after 12 months of treatment (Table IV). The Friedman test result ($p < 0.001$) showed significant differences between the 3 measurements. Wilcoxon test results showed notable differences only between time T0 and time T12.

In order to assess the efficacy of systemic therapies in psoriasis as accurately as possible, we compared the mental state of the patients from the two groups (biological therapy group and conventional therapy group) at three-time points (at baseline, after 6 months and respectively after 12 months of therapy).

Timepoint T0 (baseline)

We compared the mental state scores of patients from the two groups (biological therapy group and conventional therapy group) at baseline.

We observed that the HAM-D and HAM-A scores did not differ significantly, showing that the two groups were homogeneous in this respect at baseline.

In terms of PASI and DLQI scores, the two groups differed significantly, with the group of patients who subsequently received biological therapy being in a deficit at the start of therapy (higher values of psoriasis severity scores) compared to the group who received conventional therapy (Table IV).

Time T6 (6 months after initiation of therapy)

After 6 months of therapy, it is observed that the mean level of the analysed scores is similar in the two groups.

In relation to PASI and DLQI scores, it should be taken into account that at the initial moment, in the biological therapy group, they were significantly higher than in patients with conventional therapies, and after 6 months they reached levels similar to those of patients with conventional therapies, demonstrating also in this way the efficacy of these biological therapies (Table IV).

Time T12 (12 months after initiation of therapy)

After 12 months of treatment, PASI and DLQI scores were significantly better in the biologic therapy group compared to patients in the conventional therapy group. In this regard, and taking into account the analysis of these scores, we can conclude that biological therapies had significantly higher efficacy than conventional therapies.

The depression and anxiety scores after 12 months of treatment did not differ significantly between the two groups, but the trend of these indicators shows that biological therapies were more effective than conventional therapies, especially for depression (Table IV).

However, all these conclusions should be reinforced by a study in which the group of those who received conventional therapies is larger, in the case of this study, it had only 8 subjects.

Since the early 1970s, studies on the association between psoriasis and anxiety, depression and suicidal ideation have been conducted [18].

A meta-analysis of studies published between 1990-2015 showed a clear association of psoriasis with anxiety and depression. Other psychiatric conditions found with increased frequency in patients with psoriasis are: psychotic disorders, personality disorders, sexual dysfunction, sleep disorders, and substance abuse [19].

The influence of psychological stress, as well as the maintenance of the stress factor, causes a series of inflammatory reactions in the skin that induce secretion of cytokines such as IL-6, IL-1, INFγ, activation of corticotropin-releasing hormone (CRH), proopiomelanocortin (POMC), adenocorticotropic hormone (ACTH), melanocytostimulating hormone (MSH) [20].

According to studies, 9 to 55% of patients with psoriasis associate depressive symptoms of varying intensity [4]. Tian Z *et al*., in a recent study, found the incidence of moderate-severe depressive episodes in psoriasis vulgaris patients in 13.9% of cases, while 10.6% had anxiety symptoms [5]. In our study, moderate depressive episodes were present in 15.7% and severe depressive episodes in 5.9% of cases, results similar to the literature. Patients with moderate-severe

forms of depression received specific psychiatric treatment.

A large meta-analysis showed that psychological stress increases inflammatory markers, CRP, TNF-α, IL-1 and IL-6, and in psoriasis, a marked increase in proinflammatory potential could cause exacerbation of the disease. In fact, 40 - 80% of psoriasis onset or exacerbation is attributed to psychosocial factors, with mood playing a significant role in modulating psoriasis [21].

Inflammatory cytokines are not the only biomarkers that provide the link between depression and psoriasis. Depression is associated with disruptions in melatonin secretion, a secretion that physiologically follows the circadian rhythm with high levels during the night with a maximum peak in the morning between 2 and 4 a.m. [22]. By reducing levels of TNF-α, IL-6 and IL-8, melatonin can theoretically alleviate the severity of inflammatory disorders [23, 24]. Deregulation of melatonin secretion has also been seen in other inflammatory diseases, including sarcoidosis and psoriasis vulgaris. In those with depression, decreased melatonin levels and altered circadian rhythms may result in the release of melanocytostimulatory hormone (MSH) [25, 26]. Thus, MSH may be increased in depression, both due to low melatonin levels and hypersecretion of corticotropin-releasing hormone (CRH), which could contribute to the exacerbation of psoriasis lesions [27, 28]. However, further research is needed to determine the exact role that cyclic changes in melatonin secretion play in both depression and psoriasis and the mechanism by which this role is achieved.

The overlapping inflammatory cascades in both conditions may also play an important role, as the approach may have a synergistic effect on psoriasis improvement by alleviating both the basal inflammatory state and the depression and anxiety that cause exacerbations, hence the growing interest in biological therapy. In addition, it is interesting to note the potential that melatonin offers in modulating chronic inflammatory processes among the various associations of psoriasis with mood disorders, including HPA axis abnormalities, altered epidermal barrier function, diabetes and cardiovascular comorbidities.

The psycho-emotional status of psoriasis patients in the present study clearly shows by the psychometric tests used, namely, HAM-A and HAM-D, that these patients showed significant psychological impairment compared to the general population. There is thus a concordance between the results of our study and the data in the literature. Bulat V *et al*., in another recent study, point out that psoriasis has a strong negative impact on the psychological state of patients, particularly among females [29].

According to the present study, the therapies used in psoriasis led to a significant improvement in the psycho-emotional state, clinically and paraclinically, obtaining a good outcome in the experimental group. In a recently published meta-analysis, Gonzalez-Cantero A *et al*. evaluated the impact of biological agents on cardiovascular biomarkers. The results of the study showed that anti-TNF-α agents, specifically Adalimumab, significantly reduced CRP, TNF-α, IL-6 and blood glucose levels. Phototherapy has been shown to be helpful by lowering CRP and IL-6 and increasing HDL. Both CRP and IL-6 are cardio-vascular risk factors that show significantly increased levels in patients with psoriasis [30].

Biological therapy has been a game changer in psoriasis treatment over the last two decades. This was also possible due to a better understanding of the pathogenic mechanisms. A major role in the pathogenesis of psoriasis is played by tumour necrosis factor α (TNF-α) and the IL-23/IL-17A axis, as evidenced by the excellent response to biological therapy targeting TNF-α, IL-23, and IL-17. Given that in psoriasis there is a better therapeutic response to anti-IL-23 and anti-IL-17 molecules compared to anti-TNF-α, it has been hypothesized that the IL-23/Il-17A axis plays a crucial pathogenic role in the development of the disease [31-33].

With the advent of biological molecules, numerous studies have been done to demonstrate their benefits not only on psoriasis but also on numerous associated diseases [34-36]. All four classes of biological agents have been studied for their possible beneficial effects on patients with psoriasis and psychiatric disorders.

Anti-TNF-α agents etanercept and adalimumab have proven their efficacy in numerous clinical trials, significantly lowering depression scores in psoriasis patients compared to conventional systemic therapies [37-39]. Also, anti-IL12/23 inhibitors (ustekinumab) have been shown to significantly improve HAM-D in patients with psoriasis and depression.

As for the anti-IL-17 agents, ixekizumab and secukinumab, a number of studies demonstrate their beneficial role with the disappearance of depressive symptoms by assessing HAM-A and HAM-D scales [40]. However, Komori *et al*. also reported a case in which anti-IL-17 therapy, secukinumab, caused exacerbation of depressive symptoms in a patient with psoriatic arthritis [41].

According to studies, anti-IL-23 agents induced the best outcomes in patients with psoriasis and depression. Gordon *et al.* [42] in a study that included 989 patients with psoriasis, determined the beneficial effects of guselkumab on anxiety and depression compared to placebo and adalimumab. Thus, HAM-A and HAM-D scales were determined before treatment, after 16 weeks for guselkumab vs placebo group and after 24 weeks of treatment for guselkumab *vs*. adalimumab group. Thus, at week 16, the ratio of patients who had HAM-A and HAM-D > 8 at baseline to those who had HAM-A < 8 (guselkumab *vs*. placebo) was 51.4% *vs*. 25.9%; ($p < 0.001$) and for HAM-D < 8

was 59.2% *vs*. 27.0%; ($p < 0.001$). At week 24, guselkumab *vs*. adalimumab group, showed the following results: the rate of those with HAM-A < 8 was 58.4% *vs*. 42.9%; ($p = 0.028$) and HAM-D < 8, 59.8% *vs*. 46.4%; ($p = 0.079$). Improvement in PASI score was correlated with decreases of HAM-A and HAM-D scores. Also, Augustin *et al.* [43] demonstrated in a recent study that Risankizumab treatment has markedly superior effects to ustekinumab on both psoriasis and psychiatric comorbidities achieving a reduction in anxiety by 69.1% *vs*. 57.1% ($p = 0.004$) and 71.1% *vs*. 60.4% ($p = 0.01$) for depression.

According to the most recent study by Jiang Y *et al*. the first therapeutic option in patients with moderate-severe psoriasis and depression should be anti-IL-23 agents (risankizumab, guselkumab, tildrakizumab), followed by IL-17 inhibitors (secukinumab and ixekizumab) and anti-IL-12/23, and finally, the third therapeutic option can be anti-TNF-α agents [34].

Conclusions

Psychiatric disorders (depression, anxiety) are common in psoriasis patients. In our research group, we encountered different degrees of depression in 70.6% of patients, and anxiety was present in 78.4% of cases. Their importance in the onset, relapse or progression of psoriasis is an ongoing researched topic.

Identifying the underlying common biological mechanisms of this relationship may optimize the treatment of psoriasis patients with psychiatric co-morbidities.

Our research showed that biologic therapies (Adalimumab, Etanercept, Ixekizumab, Secukinumab, Risankizumab) are more effective than conventional therapies (Methotrexate, Cyclosporine, Acitretin), especially for depression.

The patient with psoriasis, in terms of comorbidities and associated diseases, requires a holistic approach, with emphasis on the collaboration of dermatologists and psychiatrists for early initiation of optimal treatment.

Conflict of interest

The authors declare no conflict of interest.

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