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Treatment of Vulgar Psoriasis with Netakimab

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Introduction

Psoriasis is a genetically determined, autoinflammatory/autoimmune skin disease, a relapsing disease characterized by impaired differentiation and hyperproliferation of keratinocytes, inflammatory reaction in the dermis and immune disorders, prevalence of about 0.33%-0.6% in different races. [1,2]

Relevance

The relevance of this topic is due to the high prevalence and poor study of the disease. About 90% of psoriasis cases are psoriasis vulgaris, the clinical manifestations of which are clearly defined erythematous, itchy plaques covered with silvery scales. Plaques can merge and cover large areas of the skin. [3]

The study of this disease is becoming even more relevant due to the decrease in the quality of life of patients, so the disease is also socially significant. [4]

Currently, pharmacological approaches are insufficient due to the poor understanding of the pathogenesis of the disease. Over the past 15 years, breakthroughs in understanding the pathogenesis of psoriasis have been translated into targeted and highly effective treatments, providing fundamental insights into the pathogenesis of chronic inflammatory diseases with a dominant IL-23/Th17 axis. [3]

Some biological drugs have demonstrated tremendous success in the treatment of psoriasis. However, side effects, safety, loss of efficacy, and relapses after discontinuation of these biologics encourage the exploration of new therapeutic strategies. [4]

The condition of patients and the effectiveness of the therapy can be assessed by a number of different tests. PASI assessment is widely used in clinical trials, especially those related to the development of biological drugs. [5]

Previously, it was believed that Th-17 cells are the main source of IL-17 and the subsequent occurrence of psoriatic inflammation. However, recently the role of neutrophils, cells of the innate immune system, in the development and further progression of psoriasis has been discussed, forming adaptive immunity through interaction with antigen-presenting cells and lymphocytes at the sites of inflammation. [4] In one study, Keijsers et al. demonstrated immunohistochemistry that neutrophils and other cells of the innate immune system are the main source of IL-17A secretion in psoriasis. In one of the studies, Lin et al29 showed the presence of neutrophils' mechanisms of IL-17A secretion, due to the ability to form extracellular traps from nuclear material. [3] In turn, IL-17A affects keratinocytes to increase the expression of the CCL20 chemokine receptor CCR6, which recruits CLA+ T cells expressing CCR6 into the epidermis and promotes their maturation under the influence of IL-23 and IL-1β and further secretion of IL-17A and the formation of psoriatic inflammation. It should be noted that IL-23 and IL-1β stimulate IL-17A in keratinocytes. Therefore, immunobiological drugs blocking IL-17A are the mainstay of treatment, reducing the number of infiltrating neutrophils through apoptosis or

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mobilization from the bone marrow through the induction of G-CSF deficiency.[3]

Objective

Study of the parameters of patients with vulgar psoriasis, characterizing the physical and mental state under the influence of the drug netakimab.

Materials and methods

A prospective study is being conducted at the Department of Skin and Venereal Diseases of the I.M. Sechenov First Moscow State Medical University and the Department of Pathophysiology and Clinical Pathophysiology of the N.I. Pirogov Russian National Research Medical University.

The study included 12 patients with moderate to severe vulgar psoriasis who had not previously received therapy with netakimab. The amount and morphological structure of extracellular traps of neutrophils and monocytes in the peripheral blood were studied before treatment, after 2 weeks and 2 months from the first injection of the month with a parallel assessment of the physical and mental state of patients using the PASI index and PASI, MFI-20, DLQI, mPEST, sPGA, NAPSI (hands, feet) questionnaires. The work used neutrophil cell fractions isolated on a double Ficoll density gradient. Sterilely isolated neutrophils were transferred to RPMI-1640 medium and used in the experiments. The viability of the isolated neutrophils was at least 90%, which was determined in a test with 0.1% trypan blue solution. Fluorescence microscopy was also used to identify and count neutrophil extracellular traps. Neutrophil extracellular traps were stained with the fluorescent dye SYBR Green (Evrogen). The number of neutrophil extracellular traps was counted among 100 neutrophils. The results were expressed as a percentage - as the ratio of the number of neutrophil extracellular traps to the total number of neutrophils and were presented as the mean ± error of the mean.

Results

The results of the study demonstrate a decrease in clinical tests (PASI, MFI-20, DLQI, mPEST, sPGA, NAPSI (hands, feet)) against the background of treatment with netakimab. The numerical indicators for the tests are clearly shown in Table 1.

The study also observed the formation of mixed forms of extracellular traps. Therapy with netakimab showed the formation of mixed forms of NEL and an increase in their number in the peripheral blood. The number of neutrophil extracellular traps in patients was 5.87 ± 1.43%. Under the influence of the drug netakimab, the number of neutrophil extracellular traps 2 weeks after injection of the drug was 7.75±2.18%, and after 2 months it increased to 11.60±2.57%.

Before treatment (point 1), Spearman correlations were

Table 1: *Indicators of clinical assessment of the condition of patients and neutrophil and monocyte extracellular traps (NEL and MEL) in patients with psoriasis in dynamics - before treatment and during treatment with netakimab*

Indicators (M±m)	Before treatment - point 1 (n=12)		2 weeks after the start of treatment - point 2 (n=11)		2 months after the start of treatment - point 3 (n=11)	
PASI (psoriasis severity and extent index), points	45,11±5,35		**20,43±3,95** [1]		**2,93±1,34** [1, 2]	
MFI-20 (subjective assessment of asthenia), points	13,55±0,92		**11,36±1,02** [1]		**9,45±1,15** [1, 2]	
DLQI (Life Quality Impact Index), points	13,55±2,67		**5,27±1,84** [1]		**1,45±1,26** [1, 2]	
mPEST (psoriatic arthritis screening), scores	4,91±2,01		4,73±1,99		3,73±1,45	
sPGA (skin lesion assessment), points	4,75±0,13		**3,00±0,33** [1]		**0,82±0,29** [1, 2]	
NAPSI (nail lesion assessment) hand scores	10,50±5,77		11,27±6,16		6,45±3,84	
NAPSI feet (nail lesion score), points	18,45±6,94		18,36±6,96		**11,91±4,67** [1, 2]	
Neutrophil and monocyte extracellular traps	Spontaneous formation (n=12)	Upon activation of IgG (n=8)	Spontaneous formation (n=9)	When activated by IgG (n=9)	Spontaneous formation (n=9)	When activated by IgG (n=8)
NEL, %	5,87±1,43	**13,83±2,33***	5,50±2,18	**10,55±1,41***	7,87±2,57	**18,35±5,38***
NEL dimensions, µm	28,08±6,22	53,98±9,37	74,10±25,50	133,42±36,71	61,12±12,75	115,19±26,76
EMAIL, %	0,00±0,00	0,70±0,47	0,00±0,00	0,00±0,00	0,00±0,00	0,21±0,20

Note: 1 - p <0.05 compared to the values at point 1;
2 - p <0.05 compared to the values at point 2;
** - p <0.05 for extracellular traps compared to spontaneous formation at the corresponding points*

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found

- between the number of NELs, %, and the skin lesion index sPGA: R=0.76 (p <0.05),

- between the number of MELs with IgG activation, %, and the asthenia index MFI-20: R=0.76 (p <0.05).

After 2 months from the start of treatment (point 3), Spearman correlations were found

- between the sizes of NELs with IgG activation, µm, and the indices of nail bed lesion of the hands (NAPSI hands) and feet (NAPSI feet): R = 0.88 (p < 0.05) and R = 0.85 (p < 0.05), respectively.

Discussion

During treatment with netakimab, there is a decrease in the PASI, MFI-20, DLQI, sPGA, NAPSI (hands, feet) tests. There is also a slight decrease in the mPEST tests, which can be explained by an inappropriate dosage of the drug due to the likely presence of concomitant psoriatic arthritis.

Accordingly, neutrophil extracellular traps reduce the number of activated T-lymphocytes. In the samples of the studied peripheral blood, the number of neutrophil traps before treatment is small, which is explained by their localization in the inflammation focus. During treatment with netakimab, the number of NELs in the peripheral blood increases, which is manifested by a decrease in the inflammatory process and clinical manifestations of the disease, as also evidenced by a decrease in clinical tests.

Conclusions

Accordingly, in patients with vulgar psoriasis, a negative correlation was found between the PASI, MFI-20, DLQI, sPGA, NAPSI (hands, feet), mPEST and the number of spontaneously formed NELs, which confirms the effectiveness of netakimab.

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