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Effect of pharmacological intervention on MIP-1 α , MIP-1 β and MCP-1 expression in patients with psoriasis vulgaris

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ABSTRACT

Objective: To detect the expression level of macrophage inflammatory protein-1 (MIP-1) α , MIP-1 β and monocyte chemoattractant protein-1 (MCP-1) in with psoriasis vulgaris and explore the role in the pathogenesis of psoriasis vulgaris. **Methods:** The level of MIP-1 α ,MIP-1 β and MCP-1 in peripheral blood from 50 patients with psoriasis vulgaris and 50 normal controls were measured by enzyme linked immunosorbent assay. The correlation with psoriasis area and severity index (PASI) was analyzed. The level of MIP-1 α , MIP-1 β and MCP-1 was compared between psoriasis vulgaris patients at active stage and resting stage. And the change in MIP-1 α , MIP-1 β and MCP-1 before and after therapy was also observed. **Results:** The content of MIP-1 α , MIP-1 β and MCP-1 in patients with psoriasis vulgaris was (1342.78±210.30), (175.28±28.18) and (266.86±32.75) ng/L, respectively, significantly higher than those in control group (P<0.05). The expression level of MIP-1 α , MIP-1 β and MCP-1 in peripheral blood of patients with psoriasis vulgaris was positively correlated with PASI (P<0.01). After acitretin therapy, expression level of MIP-1 α , MIP-1 β and MCP-1 in peripheral blood of patients with psoriasis vulgaris was significantly decreased. **Conclusions:** Chemokine factor MIP-1 α , MIP-1 β and MCP-1 may be involved in the pathogenesis of psoriasis vulgaris.

1. Introduction

Psoriasis is a chronic inflammation induced by various stimuli, such as inherit factors, cell apoptosis, immunological factors, inflammation and neurotransmitters, etc. The pathogenesis is still unclear. It is reported that the morbidity of psoriasis is about 3% in Asian. Its physiopathological mechanism includes proliferation of epidermic cells and activation of immunological system. There are 4 types of psoriasis: psoriasis vulgaris, psoriasis pustulosa, psoriasis arfhropathica and psoriatic erythroderma, and psoriasis vulgaris is the commonest[1]. Chemokines comprises of 50 kinds of low molecular weight polypeptide. It can induce leukocytes such as lymphocyte, monocyte, neutrophil, etc to aggregate in inflammatory area. It mediates infiltration, location and activation of immunological cells. Besides, it can induce formation of lymphoid follicle from lymphocyte. Chemokines plays a important key in development of autoimmune diseases[2]. Macrophage inflammatory protein-1 (MIP-1) α , MIP-1 β and monocyte chemoattractant protein-1 (MCP-1) are important chemokines. It is proved that they participate in various autoimmune diseases[3]. This study aims to explore the correlation between MIP-1 α , MIP-1 β and MCP-1 psoriasis area and severity index (PASI), and to observe the effect of oral administration of acitretin and external application of tacrolimus on expression of MIP-1 α , MIP-1 β and MCP-1 in patients of psoriasis vulgaris.

2. Materials and methods

2.1. Objective

A total of 50 cases of psoriasis vulgaris visiting between

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June 2012 and December 2013 were selected, including 29 males and 21 females, aged 20-50 years old, with average age as (29.60±8.29) years. Patients had no history of corticoid, immunosuppressor etc in 4 weeks, and all were in accord with diagnosis of psoriasis vulgaris. Patients with other autoimmune diseases, systematical chronic diseases, incompetent hepatorenal function, administration of glucocorticoids, immunosuppressor, macrolides in 1 month were excluded. They comprised of 35 cases at active stage and 15 cases at resting stage. PASI score was performed. Another 50 healthy persons were selected, including 30 males and 20 females, aged 25-53 years old, with average age as (30.14±8.52) years. There was no significant difference in gender and age between two groups.

2.2. Sampling

Five mL venous blood of patients with confirmed psoriasis vulgaris and without any treatment was extracted, centrifugated to obtain supematant. It was preserved in liquid nitrogen. Serum of experiment group was also collected 4 weeks after treatment.

2.3. Reagent

Mouse anti-human monoclonal antibody, ELISA of MIP-1 α, MIP-1 β and MCP-1 were purchased from R&D System. Enzyme mark detector type Elx800 was from USA BIO-TEK Company.

2.4. Methods

MIP-1 α, MIP-1 β and MCP-1 was detected by ELISA strictly according to instruction.

2.5. Medical invention

Patients in experimental group had external application of tacrolimus and oral administration of acitretin (Huabang Pharma Co Ltd, Chongqing) after lunch, 30 mg/d for 4 weeks. Side effect was observed. The administration was discontinued as soon as skin allergy or neurological symptoms occurred.

2.6. PASI score

To guarantee the uniformity and reliability, the PASI score was performed by the same physician.

2.7. Statistical analysis

All data were analyzed by SPSS19.0. The difference in MIP-1 α, MIP-1 β and MCP-1 between two groups, and the difference between those before and after treatment were analyzed by t test and χ^2 test. The correlation between PASI and MIP-1 α, MIP-1 β and MCP-1 was analyzed by Person test.

3. Results

3.1. PASI score

The PASI score was 18.25±5.56 in 50 patients of psoriasis vulgaris before treatment.

3.2. MIP-1 α, MIP-1 β and MCP-1 level between experimental group and control group

The result showed that MIP-1 α, MIP-1 β and MCP-1 were significantly higher in experimental group than those of control group (P<0.01) (Table 1).

Table 1

MIP-1 α, MIP-1 β and MCP-1 level between experimental group and control group.

Group	MIP-1 α (ng/L)	MIP-1 β (ng/L)	MCP-1 (ng/L)
Experimental group	1342.78±210.30	175.28±28.18	266.86±32.75
Control group	756.82±166.62	93.75±19.27	158.90±25.36
t value	15.442	16.887	18.430
P value	<0.001	<0.001	<0.001

3.2. MIP-1 α, MIP-1 β and MCP-1 level between patients at active stage and resting stage

The result showed that MIP-1 α, MIP-1 β and MCP-1 level of patients at active stage were significantly higher than those of patients at resting stage (P<0.01) (Table 2).

Table 2

MIP-1 α, MIP-1 β and MCP-1 level between patients at active stage and resting stage.

Group	MIP-1 α (ng/L)	MIP-1 β (ng/L)	MCP-1 (ng/L)
Experimental group	1 389.26±225.23	182.56±28.85	275.47±33.54
Control group	1 195.35±208.67	160.84±27.55	242.60±32.04
t value	2.849	2.472	3.217
P value	0.006 4	0.017 1	0.002 3

3.3. MIP-1 α, MIP-1 β and MCP-1 level before and after medical intervention

Four weeks after treatment, MIP-1 α, MIP-1 β and MCP-1 were significantly decreased (P<0.01), but the levels were still significantly higher than those in control group (P<0.01) (Table 3).

Table 3

MIP-1 α, MIP-1 β and MCP-1 level before and after medical intervention.

Group	MIP-1 α (ng/L)	MIP-1 β (ng/L)	MCP-1 (ng/L)
Before treatment	1 342.78±210.30	175.28±28.18	266.86±32.75
After treatment	1 025.65±180.53▲	131.75±22.35▲	195.67±28.91▲

▲P<0.01 *vs*. before treatment.

3.4. Correlation between PASI and MIP-1 α, MIP-1 β and MCP-1 level

Person analysis showed that MIP-1 α (r=0.652, P<0.01), MIP-1 β (r=0.436, P=0.0031) and MCP-1 (r=0.585, P<0.01) were positively correlated with PASI score.

Beside no side effect occurred in experimental group.

4. Discussion

Chemokines includes 50 kinds of low molecular weight polypeptide which comprise of 60-100 amino acids. The front end of molecular structure is composed of 4 kinds of cysteine. They are divided into 4 subfamilies according to the existence of amino acid between the first two cysteines: C, CC, CXC and C3XC4 (X means amino acid)[4,5]. MIP-1 α, MIP-1 β and MCP-1 mentioned in our study all belong to CC subfamily, which can induce chemotaxis of T cell and monocytes, activate and assemble monocyte-macrophage to participate in immune-mediated inflammation process[6]. Chemokines and their receptors play important role in migration of leukocyte under both normal and ill condition. They can induce directed migration of lymphocytes, monocytes and along with concentration gradient of chemokine. Besides, they also take part in various physiological regulation of tissues and cells, and play a key role in development of many diseases[7,8].

Many researches showed obvious infiltration of lymphocytes and monocytes in skin lesion of psoriasis patients, especially infiltration of T lymphocytes in dermis, which is important pathological character of psoriasis. There are various immunological factors such as IL-8, IL-10, IL-12, TNF-α, INF-γ *etc* in serum of skin lesion, which indicate that T cell-mediated immune reaction is important mechanism for development of psoriasis[9]. Ekman *et al*[10] reported that expression of CSCL9 and CXCL10 mRNA in some patients are significantly higher than those of healthy persons. It may be because of activation of STAT1, NF-kappa B, JAK2 and MEK/ERK pathway, which induce keratinocytes to produce CSCL9 and CXCL10.

This study shows that expression of MIP-1 α, MIP-1 β and MCP-1 in psoriasis vulgaris patients are higher than those of healthy people, and it is positively correlated with PASI score. It may be because during repair duration, various damage factors stimulate the secretion of MIP-1 α, MIP-1 β and MCP-1. It causes directed migration of responsive T lymphocyte to tissue of skin lesion, then leads to immunological inflammation, which induced skin lesion. In this study it is found for the first time that 4 weeks after external application of tacrolimus and oral administration of acitretin, the levesl of MIP-1 α, MIP-1 β and MCP-1 are significantly decreased. Besides, levels of MIP-1 α, MIP-1 β and MCP-1 of patients at active stage are significantly higher than those of patients at resting stage. It indicates that MIP-1 α, MIP-1 β and MCP-1 may participate in pathogenesis of psoriasis vulgaris, and expressions of MIP-1 α, MIP-1 β and MCP-1 are associated with its development and prognosis. Furthermore, levels of MIP-1 α, MIP-1 β and MCP-1 are significantly increased in peripheral blood of psoriasis vulgaris patients, and intervention with tacrolimus and acitretin can significantly reduce the expression level. It may provide new pathway for treatment of psoriasis vulgaris.

Conflict of interest statement

We declare that we have no conflict of interest.

References

[1] Boruah D, Moorchung N, Vasudevan B, Malik A, Chatterjee M. Morphometric study of microvessels, epidermal characteristics and inflammation in psoriasis vulgaris with their correlations. *Indian J Dermatol Venereol Leprol* 2013; **79**(2): 216-223.

[2] Bellelis P, Barbeiro DF, Rizzo LV, Baracat EC, Abrão MS, Podgaec S. Transcriptional changes in the expression of chemokines related to natural killer and T-regulatory cells in patients with deep infiltrative endometriosis. *Fertil Steril* 2013; **99**(7): 1987-1993.

[3] Venkatesha SH, Astry B, Nanjundaiah SM, Yu H, Moudgil KD. Suppression of autoimmune arthritis by Celastrus-derived Celastrol through modulation of pro-inflammatory chemokines. *Bioorg Med Chem* 2012; **20**(17): 5229-5234.

[4] Jamali Z, Nazari M, Khoramdelazad H, Hakimizadeh E, Mahmoodi M, Karimabad MN, et al. Expression of CC chemokines CCL2, CCL5, and CCL11 is associated with duration of disease and complications in type-1 diabetes: a study on Iranian diabetic patients. *Clin Lab* 2013; **59**(9-10): 993-1001.

[5] Jawa RS, Quist E, Boyer CW, Shostrom VK, Mercer DW. Mesenteric ischemia-reperfusion injury up-regulates certain CC, CXC, and XC chemokines and results in multi-organ injury in a time-dependent manner. *Eur Cytokine Netw* 2013; **24**(4): 148-156.

[6] Curran CS, Bertics PJ. Lactoferrin regulates an axis involving CD11b and CD49d integrins and the chemokines MIP-1 α and MCP-1 in GM-CSF-treated human primary eosinophils. *J Interferon Cytokine Res* 2012; **32**(10): 450-461.

[7] Nakasone Y, Fujimoto M, Matsushita T, Hamaguchi Y, Huu DL, Yanaba M, et al. Host-derived MCP-1 and MIP-1 α regulate protective anti-tumor immunity to localized and metastatic B16 melanoma. *Am J Pathol* 2012; **180**(1): 365-374.

[8] Martin G, Guérard S, Fortin MM, Rusu D, Soucy J, Poubelle PE, et al. Pathological crosstalk in vitro between T lymphocytes and lesional keratinocytes in psoriasis: necessity of direct cell-to-cell contact. *Lab Invest* 2012; **92**(7): 1058-1070.

[9] Zakka LR, Fradkov E, Keskin DB, Tabansky I, Stern JN, Ahmed AR. The role of natural killer cells in autoimmune blistering diseases. *Autoimmunity* 2012; **45**(1): 44-54.

[10] Ekman AK, Sigurdardottir G, Carlström M, Kartul N, Jenmalm MC, Enerback C. Systemically elevated Th1-, Th2- and Th17-associated chemokines in psoriasis vulgaris before and after ultraviolet B treatment. *Acta Derm Venereol* 2013; **93**(5): 527-531.