ORIGINAL ARTICLE

Increased expression of α_2 (CD49b), α_4 (CD49d) and β_1 (CD29) integrin subunits on peripheral blood T lymphocytes in clinically stable mild-to-moderate persistent asthma

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KEY WORDS

adhesion molecule, asthma, collagen, collagen receptor, integrin

ABSTRACT

INTRODUCTION Adhesive molecules, particularly selectins and integrins, are critical for the inflammatory cell trafficking from blood to the lungs. Among integrins, the most important for cell infiltration are those containing α_4 and β_2 subunits.

OBJECTIVES The aim of this study was to evaluate the expression of α_1 and α_2 integrin subunits on peripheral blood T cells in asthmatic subjects, because previously we showed evidence that $\alpha_1\beta_1$ and $\alpha_2\beta_1$ integrins may be found on peripheral blood eosinophils in these subjects. In this study, we also analyzed the expression of α_4 and β_1 subunits as a positive reference.

PATIENTS AND METHODS Expression of α_1, α_2, α_4, and β_1 subunits was analyzed by flow cytometry on $CD4^+$ and $CD8^+$ T lymphocytes obtained from the peripheral blood of 54 clinically stable, asymptomatic, mild-to-moderate persistent asthmatics and 40 healthy controls.

RESULTS The α_1 subunit was not present on peripheral blood T cells in the majority of subjects in both study groups. Expression of α_2 was detectable on $CD8^+$ cells in both groups and was increased on $CD4^+$ in asthmatics. Both types of T cells showed higher expression of α_4 and β_1 in patients with asthma. Expression of α_4 was higher on $CD8^+$ T cells both in asthmatics and controls.

CONCLUSIONS Expression of α_4 and β_1 integrin subunits is increased on peripheral blood T cells in patients with asthma, which confirms the preactivation of blood lymphocytes even in stable and asymptomatic disease. The biological role of α_2 subunit on T cells remains to be elucidated.

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INTRODUCTION Bronchial asthma is a common chronic inflammatory disease of the airways. Its prevalence increases, while the pathogenesis is still poorly understood.[1] The inflammatory response in asthma is localized in the airways, and eosinophils are considered as major effector cells.[2] Allergen challenge results in an increased number of blood and bronchial eosinophils.[3] However, the mechanism of eosinophil recruitment and the pathway of its activation have not yet been fully elucidated. Although anti-interleukin (IL)-5 antibodies distinctly reduce blood eosinophilia, they have no effect on asthma course and severity.[4] On the other hand, helper T lymphocytes appear to be pivotal in driving the disease development and progression. Adoptive transfer of Ag-primed T cells into naive animals induces eosinophilia, bronchial hyperresponsiveness, and late airway response.[5] Moreover, helper T cells are activated in the airways, even when the disease is asymptomatic.[6] Leukocyte migration through the blood vessel wall and into inflammatory site is mediated by cell-surface receptors and their specific ligands localized on the vascular endothelium and in the extracellular matrix (ECM). Among these receptors, integrins play a key role. Integrins present on leukocyte surface belong to a large family of heterodimeric glycoproteins, which in

TABLE 1 Clinical and laboratory characteristics of the subjects

	Asthmatics n = 54	Healthy controls n = 40	*P*
sex, men/women	18/36	16/24	NS
age, y	43 ±14.1	38 ±10.1	NS
duration of asthma, y	10.2 (9.4)	–	–
FEV_1, % predicted	83 ±17	–	–
blood eosinophilia, /mm^3	225 (159)	106 (66)	<0.05
total IgE, IU/l	562 (265)	45.8 (48.5)	<0.05
serum ECP, µg/l	19 (12.8)	8.8 (6.9)	<0.05

Data are presented as mean ± standard deviation or median (interquartile range).

Abbreviations: ECP – eosinophil cationic protein, FEV_1 – forced expiratory volume in 1 second, IgE – immunoglobulin E, NS – nonsignificant

the active conformation are composed of 2 noncovalently associated α and β subunits. Currently, 18 α and 8 β subunits are identified, which are associated in a restricted manner to create 24 heterodimers for specific ligand binding.[7] By regulating the cell-cell and cell-matrix interactions, they modify cell growth, migration, activation, and survival.[7] Firm adherence of leukocytes to the endothelial cells is supported mainly by interaction of β_2 and α_4 integrins. α_4 associates in vivo with β_1 or β_7. $\alpha_4\beta_1$ mediates adherence to vascular cell adhesion molecule-1, while $\alpha_4\beta_7$ to mucosal addressin cell adhesion molecule-1. Only the former plays an important role in asthma pathogenesis.[8]

Previously, we showed evidence that collagen receptors, $\alpha_1\beta_1$ and $\alpha_2\beta_1$ integrins, can be found upregulated on peripheral blood eosinophils of asthmatic subjects.[9] Increased expression of $\alpha_2\beta_1$ integrin on T lymphocytes has been also documented during severe asthma exacerbation.[10] $\alpha_1\beta_1$ and $\alpha_2\beta_1$ integrins are structurally very homologous but their role in the physiology and disease development displays many differences. $\alpha_1\beta_1$ integrin is a selective receptor for basement membrane collagen type IV, whereas $\alpha_2\beta_1$ is more specific for fibrillar collagens types I–III.[13] Collagen I (and III) is a major component of ECM in the lungs and, for this reason, it could be important in bronchial asthma-dependent airway remodeling.[14] Beneficial effects of anti-$\alpha_1\beta_1$ monoclonal antibodies have been described in certain animal models of immunologically mediated diseases, including inflammatory bowel disease, arthritis, and allergen-induced leukocyte recruitment to the lungs associated with late airway response in sheep.[11,12] However, the role of both these collagen receptors in asthma pathology has not been comprehensively studied so far. For this reason, in our study, we analyzed the expression level of α_1 and α_2 integrin subunits on peripheral blood $CD4^+$ and $CD8^+$ T lymphocytes of asthmatic subjects and healthy controls. Moreover, we also assessed the expression of α_4 and β_1 as a positive reference because the pathological role of $\alpha_4\beta_1$ integrin on T cells in asthma has already been well documented.[15]

PATIENTS AND METHODS

Patients The study was performed in 54 adult atopic asthmatics and 40 healthy controls. All asthma patients were in stable clinical condition with mild (n = 29) to moderate (n = 25) persistent asthma, according to the Global Initiative for Asthma guidelines.[1] Atopic status of all asthma patients was confirmed by a positive skin prick testing for at least 1 standard inhaled allergen (Allergopharma, Germany). All patients had good asthma control and were treated with low or medium dose of inhaled glucocorticosteroids with (moderate asthma) or without (mild asthma) long-acting β_2-agonists. Smokers and patients suffering from heart failure, diabetes mellitus, renal or hepatic diseases, as well as other chronic diseases were excluded from the study. The control group consisted of nonatopic and nonsmoking volunteers without any chronic disease. Our study was approved by the Jagiellonian University Ethical Committee and all subjects gave informed consent to participate in the study.

Antibodies Monoclonal mouse antihuman antibodies: PerCP-conjugated anti-CD3 (clone SK7), FITC-conjugated anti-CD4 (clone SK3), FITC-conjugated anti-CD8 (clone SK1), PE-conjugated anti-α_1 (clone SR84), PE-conjugated anti-α_2 (clone 12F1), PE-conjugated anti-α_4 (clone 9F10), PE-conjugated anti-β_1 (clone HUTS-21) were purchased from BD Pharmingen, (San Diego, California, United States). The isotype control staining was performed using appropriate (PE- or FITC-labeled) mouse isotype antibodies (BD Pharmingen). Control staining was performed for each subject to standardize median fluorescence intensity (MFI) values.

TABLE 2 Comparison of expression of integrin subunits on 2 subsets of T lymphocytes present in asthma patients and healthy controls; values are presented as standardized median fluorescence intensity obtained by subtraction of a nonspecific staining of isotype control

Subunits	$CD4^+$ T cells			$CD8^+$ T cells		
	asthma	control	*P*	asthma	control	*P*
α_1	0.00 (–0.9; 0.22)	0.1 (–0.12; 0.52)	NS	0.04 (–0.06; 0.28)	0.03 (–0.07; 0.23)	NS
α_2	2.31 (1.24; 2.88)	1.59 (0.77; 2.48)	0.02	1.51 (1.02; 2.91)	1.37 (0.54; 2.27)	NS
α_4	7.49 (4.74; 9.7)	5.01 (4.13; 7.06)	0.008	12.4 (9.3; 14.4)	9.00 (7.99; 11.2)	0.002
β_1	11.9 (6.31; 15.1)	6.16 (3.88; 9.11)	0.0002	9.8 (6.33; 14.3)	7.23 (2.3; 9.2)	0.006

Data are presented as median (25th and 75th percentile).

Abbreviations: see TABLE 1

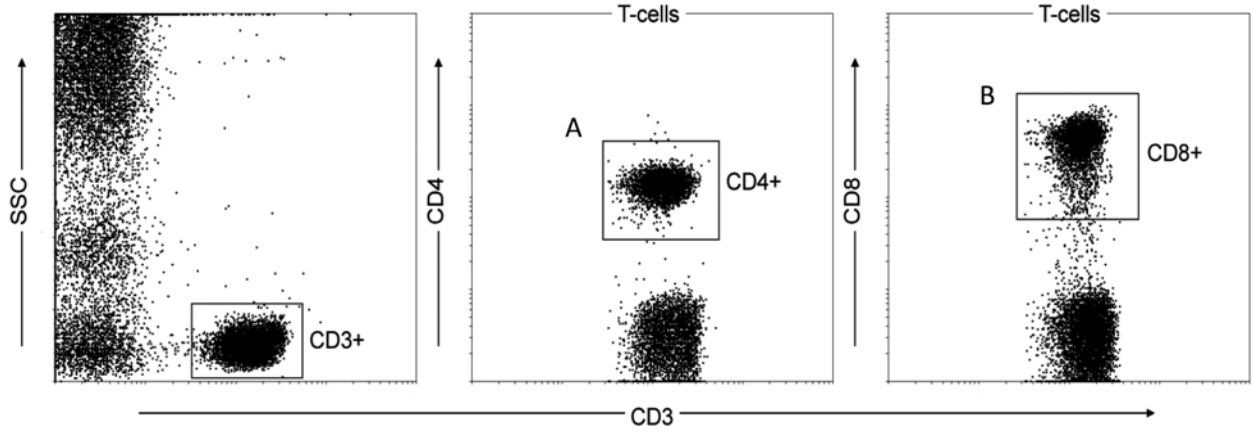

FIGURE 1 Gating strategy used in flow cytometry; fluorescence of the studied integrin subunits (PE-labeled) was analyzed in a cell population presented in gates A ($CD3^+CD4^+$) and B ($CD3^+CD8^+$)

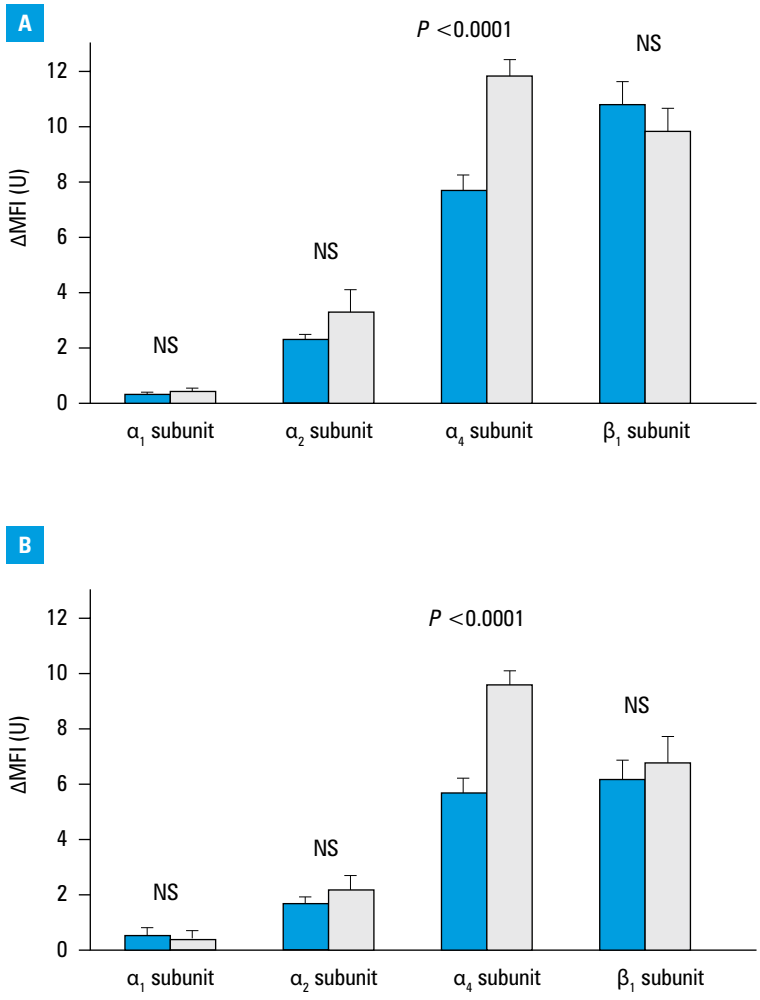

FIGURE 2 Expression of integrin subunits on $CD4^+$ T cells (blue bars) and $CD8^+$ T cells (grey bars) in asthmatics (A) and controls (B); values were obtained by subtraction of nonspecific staining intensity from the fluorescence of integrin subunits (standardized median fluorescence intensity [ΔMFI] expressed in units [U]); data are presented as mean and a standard error of the mean
Abbreviations: see TABLE 1

Eosinophil cationic protein and immunoglobulin E levels Serum levels of eosinophil cationic protein (ECP) and immunoglobulin E (IgE) were measured using the UniCAP System, Pharmacia, Sweden.

Flow cytometry The expression level of α_1, α_2, α_4, and β_1 integrin subunits on $CD4^+$ and $CD8^+$ peripheral blood T lymphocytes was analyzed by flow cytometry (Epics XL, Beckman Coulter International, Nyon, Switzerland). Briefly, 100 µl of EDTA-anticoagulated venous blood was incubated for 30 minutes with saturating concentration (10 µl) of specific mouse monoclonal antibodies. Then, samples were fixed for 10 minutes with 2 ml of BD FACS lysing solution (Becton Dickinson, San Diego, California, United States) and washed twice with 2 ml of phosphate buffered saline supplemented with 0.1% azide. Cells were suspended in 0.5 ml of 1% paraformaldehyde and analyzed by flow cytometry.

Statistical analysis Normally distributed results are presented as mean ± standard deviation. Values that were not normally distributed are presented in tables as median with interquartile range (TABLE 1) or with 25th and 75th percentile (TABLE 2) and in figures as mean with a standard error of the mean. A comparison between the studied groups was done using the Mann-Whitney *U* test; relationship by the Spearman rank correlation test. In all instances, two-sided 5% level of significance was used. All statistical testing was performed by Statistica StatSoft (Tulsa, Oklahoma, United States).

RESULTS

The clinical and laboratory characteristics of the subjects selected for flow cytometry analysis are presented in TABLE 1. Asthmatic and control subjects were similar in sex and age. Blood analysis revealed a significant difference in eosinophilia, ECP, and total IgE levels between asthmatics and controls.

Gating strategy for flow cytometry is presented in FIGURE 1. The expression of integrin subunits (PE-labeled) was analyzed separately in $CD3^+CD4^+$ and $CD3^+CD8^+$ cell populations (gates A and B). MFI of a given marker was standardized by subtraction of a nonspecific staining of isotype control (ΔMFI values are presented in TABLE 2 and FIGURE 2).

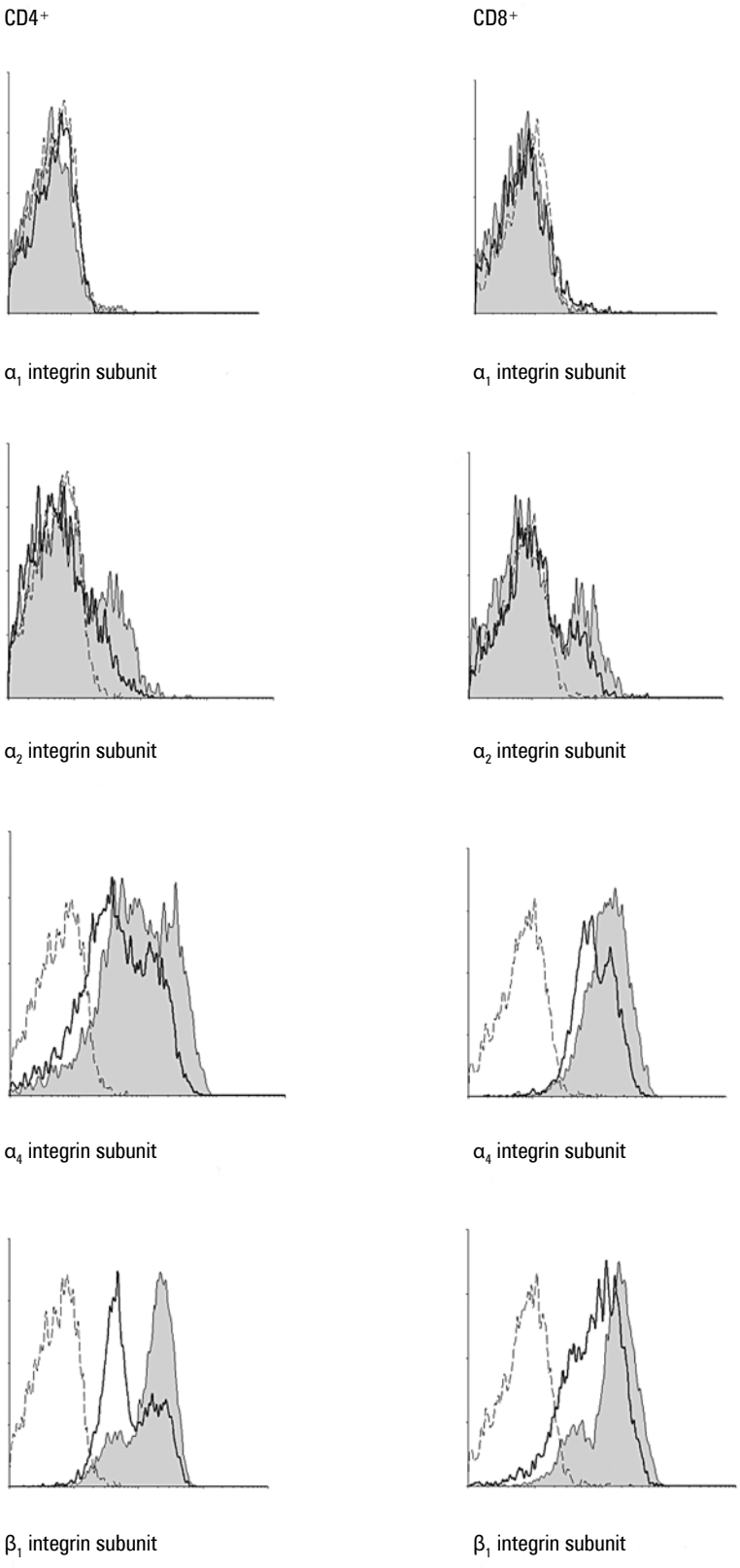

FIGURE 3 Representative flow cytometry patterns of the expression of integrin subunits on T lymphocyte populations; asthma subjects are represented by a thin line with shape shadow, healthy controls by a bolded line, and isotype control by a dotted line

A flow cytometry analysis revealed significant differences between the expression of different integrin subunits on T lymphocytes (TABLE 2, FIGURES 2 and 3). Among the 2 investigated collagen receptors, α_1 integrin subunit was not present on peripheral blood $CD4^+$ and $CD8^+$ T cells of the majority of asthma patients and healthy controls, showing no difference between the asthma and control groups. Only a few subjects from both groups showed clearly detectable expression of α_1 subunit. On the other hand, the expression of α_2 was present on both $CD4^+$ and $CD8^+$ T cells, although its significantly higher level was observed only for $CD4^+$ T cells in asthmatics. Expression of α_4 and β_1 subunits on both T cell subtypes was also increased in asthma. In both groups, we observed a strong positive correlation between α_4 and β_1 subunits ($P < 0.00\,001$, $r = 0.67$ for $CD4^+$; $P < 0.00\,001$, $r = 0.57$ for $CD8^+$ T cells). Moreover, in both groups, we observed significantly higher α_4 expression on $CD8^+$ compared with $CD4^+$ T cells (TABLE 2, FIGURE 2).

DISCUSSION In our study, the expression of α_4 and β_1 integrin subunits on $CD4^+$ and $CD8^+$ as well as α_2 on $CD4^+$ blood T cells was increased in asthmatic subjects. We also observed a tendency for higher expression of α_2 subunit on $CD8^+$ T cells in asthma, but the difference did not reach significance. This observation confirms preactivation of T cells in the peripheral blood of asthma subjects and determines readiness of these cells for migration into the inflammatory site in the airways, even if disease is clinically stable and asymptomatic. The biological role of $CD4^+$ and $CD8^+$ T cells in asthma pathology is controversial but seems to be redundant. In a recent study, Machure et al.[16] found an increased number of both $CD4^+$ and $CD8^+$ blood T cells with highly positive intracellular staining for IL-4 and IL-13 in children with atopic asthma, suggesting a similar function of both these T-cell subtypes.

Our results indicated that α_1 integrin subunit, in contrast to α_2, was not present on peripheral blood T cells in mild-to-moderate persistent asthma and healthy controls in the majority of subjects. Similar observation was made in a group of healthy controls by Goldstein et al.,[17] who found this collagen receptor on $CD4^+$ T cells only in a few subjects and showed that it was restricted to a subset of memory cells mediating T helper 1-type immune response in peripheral tissue. There are no reports concerning expression of $\alpha_1\beta_1$ integrin on T lymphocytes in asthma.

The biological role of increased basal levels of α_2 integrin subunit on peripheral blood $CD4^+$ T cells in asthma remains to be elucidated. Collagens are the major structural matrix proteins, which were abundantly found in the majority of human tissues. Therefore, their receptors could be involved in the pathology of numerous chronic diseases, especially those leading to the architectural changes, e.g., asthma remodeling.[18] Rahmount et al.[19] evaluated the presence of $CD18^{high}CD49b^+$ T lymphocytes in peripheral blood and confirmed an increased number of these cells in severe asthmatics when compared with mild asthmatics and healthy controls. Overexpression of $\alpha_2\beta_1$ integrin

on T lymphocytes has been documented also during severe asthma exacerbation.[10] We obtained similar results in asymptomatic subjects, but only for $CD4^+$ T cells. However, the biological role of $\alpha_2\beta_1$ integrin in asthma remains unknown. Kuijpers et al.[20] reported that $\alpha_2\beta_1$ integrin is involved in eosinophil migration through membranes covered with human umbilical vein endothelial cells. We also showed that inhibition of $\alpha_1\beta_1$ and $\alpha_2\beta_1$ integrins diminished eosinophils, but had no effect on peripheral blood mononuclear cell transmigration through human microvascular endothelial cell monolayer.[21] Therefore, these collagen receptors appeared not to be involved in lymphocyte infiltration. Ligands for $\alpha_2\beta_1$ integrin, such as collagen type I , collagen type IV , and laminin, are important components of the lung ECM, and participation of this integrin in tissue remodeling during asthma development is considered.[22] This hypothesis is supported by a previous report which demonstrated $\alpha_2\beta_1$ integrin as a stimulator of collagen and fibronectin accumulation in the airways.[23] Based on our results, one could speculate that in this aspect the function of $CD4^+$ is more important (with basal upregulation of α_2 integrin subunit) than that of $CD8^+$ T lymphocytes. Current chronic asthma therapy markedly attenuates allergic inflammation, but has no direct effect on the remodeling process.[24] In a murine asthma model, both effects could be achieved by imatinib – a tyrosine kinase inhibitor that inhibits collagen deposition.[24] It is possible that inhibition of β_1 integrins, leading to the blockage of integrin-linked kinase, may also influence airway remodeling, a goal which cannot be achieved by current asthma treatment, including antileukotriene agents.[25,26] It is tempting to speculate that integrin collagen receptors could become a new therapeutic target in the treatment of asthmatic airway remodeling.

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REFERENCES

1 O'Byrne PM. Global guidelines for asthma management: summary of the current status and future challenges. Pol Arch Med Wewn. 2010; 120: 511-517.

2 Mastalerz L, Kasperkiewicz H. Effect of inhaled corticosteroids on small airway inflammation in patients with bronchial asthma. Pol Arch Med Wewn. 2011; 121: 264-268.

3 Flood-Page P, Menzies-Gow A, Phipps S, et al. Anti-IL-5 treatment reduces deposition of ECM proteins in the bronchial subepithelial basement membrane of mild atopic asthmatics. J Clin Invest. 2003; 112: 1029-1036.

4 Leckie MJ, ten Brinke A, Khan J, et al. Effects of an interleukin-5 blocking monoclonal antibody on eosinophils, airway hyper-responsiveness, and the late asthmatic response. Lancet. 2000; 356: 2144-2148.

5 Ohtomo T, Kaminuma O, Yamada J, et al. Eosinophils are required for the induction of bronchial hyperresponsiveness in a Th transfer model of BALB/c background. Int Arch Allergy Immunol. 2010; 152 Suppl 1: 79-82.

6 Gibson PG. What do non-eosinophilic asthma and airway remodelling tell us about persistent asthma? Thorax. 2007; 62: 1034-1036.

7 Hynes RO. Integrins: bidirectional, allosteric signaling machines. Cell. 2002; 110: 673-687.

8 Bazan-Socha S, Bukiej A, Marcinkiewicz C, Musial J. Integrins in pulmonary inflammatory diseases. Curr Pharm Des. 2005; 11: 893-901.

9 Bazan-Socha S, Bukiej A, Pulka G, et al. Increased expression of collage receptors: α1β1 and α2β1 integrins on blood eosinophils in bronchial asthma. Clin Exp Allergy. 2006; 36: 1184-1191.

10 Corrigan CJ, Hartnell A, Kay AB. T lymphocyte activation in acute severe asthma. Lancet. 1988; 1: 1129-1132.

11 Krieglstein CF, Cerwinka WH, Sprague AG, et al. Collagen-binding integrin α1β1 regulates intestinal inflammation in experimental colitis. J Clin Invest. 2002; 110: 1773-1782.

12 Abraham WM, Ahmed A, Serebriakov I, et al. A monoclonal antibody to α1β1 blocks antigen-induced airway responses in sheep. Am J Respir Crit Care Med. 2004; 169: 97-104.

13 Tulla M, Pentikäinen OT, Viitasalo T, et al. Selective binding of collagen subtypes by integrin α1 I, α2 I, and α10I domains. J Biol Chem. 2001; 276: 48206-48212.

14 Eble JA. Collagen-binding integrins as pharmaceutical targets. Curr Pharm Des. 2005; 11: 867-880.

15 Banerjee ER, Jiang Y, Henderson WR Jr, et al. α4 and β2 integrins have nonredundant roles for asthma development, but for optimal allergen sensitization only α4 is critical. Exp Hematol. 2007; 35: 605-617.

16 Machura E, Mazur B, Rusek-Zychma M, Barć-Czarnecka M. Cytokine production by peripheral blood CD4+ and CD8+ T cells in atopic childhood asthma. Clin Dev Immunol. 2010; 2010: 606139.

17 Goldstein I, Ben-Horin S, Li J, et al. Expression of the α1β1 integrin, VLA-1, marks a distinct subset of human CD4+ memory T cells. J Clin Invest. 2003; 112: 1444-1454.

18 Wójcik K, Koczurkiewicz P, Michalik M, Sanak M. Transforming growth factor-β_1-induced expression of connective tissue growth factor is enhanced in bronchial fibroblasts derived from asthmatic patients. Pol Arch Med Wewn. 2012; 122: 326-332.

19 Rahmoun M, Foussat A, Groux H, et al. Enhanced frequency of CD18- and CD49b-expressing T cells in peripheral blood of asthmatic patients correlates with disease severity. Int Arch Allergy Immunol. 2006; 140: 139-149.

20 Kuijpers TW, Mul EP, Blom M, et al. Freezing adhesion molecules in a state of high-avidity binding blocks eosinophil migration. J Exp Med. 1993; 178: 279-284.

21 Bazan-Socha S, Zuk J, Plutecka H, et al. Collagen receptors $\alpha_1\beta_1$ and $\alpha_2\beta_1$ integrins are involved in transmigration of peripheral blood eosinophils, but not mononuclear cells through human microvascular endothelial cells monolayer. J Physiol Pharmacol. 2012; 63: 373-379.

22 Fernandes DJ, Bonacci JV, Stewart AG. Extracellular matrix, integrins, and mesenchymal cell function in the airways. Current Drug Targets. 2006; 7: 567-577.

23 Arora PD, Fan L, Sodek J, et al. Differential binding to dorsal and ventral cell surfaces of fibroblasts: effect on collagen phagocytosis. Exp Cell Res. 2003; 286: 366-380.

24 Rhee CK, Kim JW, Park CK, et al. Effect of imatinib on airway smooth muscle thickening in a murine model of chronic asthma. Int Arch Allergy Immunol. 2011; 155: 243-251.

25 Mastalerz L, Kumik J. Antileukotriene drugs in the treatment of asthma. Pol Arch Med Wewn. 2010; 120: 103-108.

26 Kupczyk M, Dahlén B, Dahlén SE. Which anti-inflammatory drug should we use in asthma? Pol Arch Med Wewn. 2011; 121: 455-459.

ARTYKUŁ ORYGINALNY

Zwiększona ekspresja podjednostek integrynowych α_2 (CD49b), α_4 (CD49d) i β_1 (CD29) na powierzchni limfocytów T krwi obwodowej u stabilnych chorych na przewlekłą łagodną i umiarkowaną astmę oskrzelową

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SŁOWA KLUCZOWE

astma oskrzelowa, cząsteczka adhezyjna, integryna, kolagen, receptor kolagenowy

STRESZCZENIE

WPROWADZENIE W przechodzeniu komórek zapalnych z krwi do płuc w astmie istotne są cząsteczki przylegania komórkowego, w szczególności selektyny i integryny. Spośród integryn najważniejsza rola przypada tym, które posiadają podjednostki α_4 i β_2.

CELE Celem pracy było zbadanie ekspresji podjednostek α_1 i α_2 na powierzchni limfocytów T krwi obwodowej u chorych na astmę, ponieważ poprzednio wykazaliśmy, że integryny $\alpha_1\beta_1$ i $\alpha_2\beta_1$ mogą być obecne na powierzchni eozynofilów krwi obwodowej w tej grupie chorych. W pracy analizowano także ekspresję podjednostek α_4 i β_1, jako kontrolę pozytywną badania.

PACJENCI I METODY Ekspresję podjednostek integrynowych α_1, α_2, α_4 i β_1 badano za pomocą cytometrii przepływowej na powierzchni limfocytów T $CD4^+$ i $CD8^+$ krwi obwodowej u 54 chorych na astmę oskrzelową przewlekłą łagodną i umiarkowaną, w stabilnym okresie choroby i bez objawów oraz u 40 osób zdrowych.

WYNIKI Podjednostka α_1 była nieobecna na limfocytach T krwi obwodowej u większości osób z obu badanych grup. Ekspresja α_2 była wykrywalna na komórkach $CD8^+$ w obu grupach, natomiast podwyższona na limfocytach $CD4^+$ u chorych na astmę. U pacjentów z astmą wykazano także na obu typach limfocytów T zwiększoną ekspresję podjednostek α_4 i β_1. Ekspresja α_4 była większa na komórkach $CD8^+$ zarówno u chorych na astmę jak i w grupie kontrolnej.

WNIOSKI Ekspresja podjednostek integrynowych α_4 i β_1 jest większa na limfocytach krwi obwodowej u chorych na astmę, co potwierdza aktywację tych komórek nawet w stabilnym i bezobjawowym okresie choroby. Biologiczna rola podjednostki α_2 obecnej na limfocytach T pozostaje do wyjaśnienia.

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