

reported wheezing in the last 12 months. A total of 7.5% of the males and 2.2% of the females had persistent wheezing complaints. Wheezing symptoms were found to be significantly high among males and smokers.

The prevalence of allergic rhinitis and dermatitis were 24.1% and 6.8% respectively. Rhinitis rates were 16.5% among males and 7.6% among females. The eczema rate was 5.2% among males and 1.6% among females. Prevalence of having a pet at home was 11.7% and family history of atopy was 11.9%. Pet ownership [OR: 1.25 (0.94–1.65)] and family history of atopy [(OR: 3.77(2.88–4.94)] were significantly associated with rhinitis.

Smoking rate was 23.3% in the whole group, 20.3% in males and 3.0% in females. Wheezing, asthma-like symptoms, cumulative asthma, current asthma and rhinitis were less common related in students who did not smoke. The rates of asthma, and asthma-like symptoms were found to be higher among smoking students than in non-smoking students, statistically.

The low prevalence of asthma in our low-income population may depend on geographical and climatic variation, as well as to the low socioeconomic status of our population. The higher prevalence of rhinitis may depend on that some students may have confused the question about rhinitis and some with sinusitis or other nonallergic rhinitis complaints may have answered the same question with 'yes', because nonallergic rhinitis patients may have the same complaints like allergic rhinitis patients (5).

In conclusion, asthma and/or asthma-like symptoms among university students in the eastern region of Turkey are lower than the developed countries, and habitual smoking is an important risk factor for allergic diseases.

*Department of Internal Medicine and Immunology
Yüzüncü Yıl University Hospital
İskele Cad. Altungöl Blokları
A Blok, No. 84, Daire:10
Van 65040
Turkey
Tel.: 90 432 214 7836
Fax: 90 432 214 7836
E-mail: onbasi@yahoo.com

Accepted for publication 31 July 2008
Allergy 2008; 63:139–140
© 2007 The Authors
Journal compilation © 2007 Blackwell
Munksgaard
DOI: 10.1111/j.1398-9995.2007.01541.x

References

1. Wang DY, Niti M, Smith JD, Jeoh KH, Ng TP. Rhinitis: do diagnostic criteria affect the prevalence and treatment. *Allergy* 2002;**57**:150–154.
2. Kay AB. Allergy and allergic diseases. *N Engl J Med* 2001;**344**:30–37.
3. Asher IM, Montefort S, Björkstén B, Lai CKW, Strachan DP, Weiland SK et al. Worldwide time trends in the prevalence of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC phases one and three repeat multicountry cross-sectional surveys. *Lancet* 2006;**368**: 733–743.
4. ECRHS. Variations in the prevalence of respiratory symptoms, self-reported asthma attacks, and use of asthma medication in the European Community Respiratory Health Survey (ECRHS). *Eur Respir J* 1996;**9**:687–695.
5. Ciprandi G. Treatment of nonallergic rhinitis patients. *Allergy* 2004;**59**:16–23.

Mast cell activation after adenosine inhalation challenge in patients with bronchial asthma

G. Bochenek, E. Niżankowska, A. Gielicz, A. Szczeklik*

Key words: adenosine; asthma; mast cell; prostaglandin D₂; tryptase.

Adenosine is a naturally occurring purine nucleoside playing an important role in asthma. It is believed to provoke bronchoconstriction indirectly, via activation of A_{2B} adenosine receptors expressed on airway mast cells (1). However, contribution of alternative mechanisms cannot be ruled out.

A prostaglandin D₂ metabolite (9 α ,11 β -PGF₂) is a sensitive marker of

mast cell activation, being almost entirely synthesized by these cells. We reported a sig-

nificant increase of plasma 9 α ,11 β -PGF₂ levels in asthmatic subjects after either oral aspirin (2) or inhaled allergen (3) challenges, reflecting an active involvement of mast cells in bronchoconstriction precipitated by both these agents. We wondered whether adenosine challenge would induce a similar response.

We therefore measured the blood levels of 9 α ,11 β -PGF₂ and tryptase before and after adenosine inhalation challenge in 18 stable mild asthmatics (9 M, 9 F; 11 allergic and seven nonallergic). The groups were well matched in terms of baseline forced expiratory volume in one second (FEV₁) and inhaled corticosteroid therapy. Allergic asthmatics had higher total immunoglobulin E levels. Inhalation challenge with 5'-adenosine monophosphate was carried out by five-breath technique, in line with the European Respiratory Society (ERS) Task Force recommendations. Blood samples were taken at baseline and at 5, 30, 60 and 120 min after completion of the challenge (fall in FEV₁ $\geq$ 20%). 9 α ,11 β -PGF₂ was measured in plasma by gas chromatography-negative ion chemical ionization-mass spectrometry (Hewlett Packard, Palo Alto, CA, USA). Tryptase was measured in serum by a fluoroenzyme immunoassay using UniCAP100 Tryptase System (Pharmacia & Upjohn, Uppsala, Sweden). Comparisons were carried out with the Friedman's analysis of variance (ANOVA) repeated-measure ANOVA for dependent variables, followed by Wilcoxon's signed rank test.

In patients with allergic asthma the bronchial reaction was followed by a mild but significant ($P < 0.01$) early mean 1.4-fold increase in plasma 9 α ,11 β -PGF₂ level (Table 1). This rise appeared already 5 min after the challenge, tended to continue 30 min later ($P = 0.06$), and then declined to baseline values. In nonallergic asthmatics the levels of 9 α ,11 β -PGF₂ did not differ significantly at baseline or at any time points after the challenge. Adenosine challenge had no effect on the serum

Mast cells are activated after adenosine challenge in allergic but not in nonallergic asthmatics.

Table 1. Mean (SD) values of plasma prostaglandin D₂ metabolite (9 α ,11 β -PGF₂) and serum tryptase at baseline and after adenosine challenge

	<i>n</i>	Baseline	5 min	30 min	60 min	120 min
9 α ,11 β -PGF ₂ (pg/ml)						
Allergic asthma	11	4.1 (0.78)	5.65 (1.65)	5.29 (1.95)	4.53 (1.1)	4.18 (0.76)
Mean difference† (95% CI)			-1.55 (-2.54 to -0.55)*	-1.19 (-2.46 to 0.07)	-0.43 (-0.95 to 0.09)	-0.08 (-0.38 to 0.21)
Nonallergic asthma	7	4.27 (1.48)	4.56 (0.68)	4.6 (1.17)	4.23 (0.55)	4.46 (1.07)
Mean difference† (95% CI)			-0.29 (-1.53 to 0.96)	-0.33 (-1.94 to 1.28)	0.43 (-1.01 to 1.09)	-0.19 (-1.28 to 0.9)
Tryptase (μg/l)						
Allergic asthma	11	5.45 (2.81)	5.27 (2.86)	5.34 (2.94)	5.24 (2.79)	5.28 (2.66)
Mean difference† (95% CI)			0.19 (-0.21 to 0.59)	0.12 (-2.9 to 0.52)	0.22 (-0.2 to 0.63)	0.17 (-0.26 to 0.59)
Nonallergic asthma	7	5.34 (1.7)	5.14 (1.67)	5.41 (1.7)	5.23 (1.54)	5.33 (1.34)
Mean difference† (95% CI)			0.19 (-0.27 to 0.42)	0.74 (-0.33 to 1.18)	0.11 (0.4 to 0.62)	0.01 (-0.51 to 0.52)

**P* < 0.01.

†Difference between baseline and postchallenge value.

tryptase levels in either allergic or nonallergic asthmatics.

The results obtained suggest that atopy may be relevant to mast cell degranulation in asthma. This corroborates the previous observations, whereby adenosine enhanced the release of inflammatory mediators when human mast cells were immunologically 'primed' *in vitro* (4). It was demonstrated recently that adenosine-induced effects on urinary 9 α ,11 β -PGF₂ levels were enhanced during repeated low-dose allergen challenge in allergic asthmatics (5).

A similar extent of bronchoconstriction occurring after adenosine challenge in nonallergic asthmatics, despite a lack of a significant rise of 9 α ,11 β -PGF₂ in plasma, might suggest mechanisms other than mast cell activation in the airway response to this nucleoside; possibly a cholinergic reflex component or the release of contractile neuropeptides from sensory nerve endings. The possible factors might also include: the different density of A_{2B} receptors on the surface of mast cells, their different expression, or different mast cell localization in the airways. It was demonstrated that allergic asthmatics had a more pronounced mast cell infiltration of the bronchial smooth

muscles than nonallergic ones. A growing body of evidence suggests that, once activated, the response of mast cell is further regulated by the balance of positive and negative intracellular molecular events that determine whether cells become active during the challenge (6). The lack of simultaneous release of tryptase may suggest that only systemic mast cell degranulation may precipitate its increase in serum.

In conclusion, mast cells are involved in adenosine-precipitated bronchoconstriction in allergic asthmatics but not in nonallergic ones. In this study 9 α ,11 β -PGF₂ is a more sensitive marker of mast cell activation than tryptase.

*Department of Medicine
Jagiellonian University School of Medicine
31-066 Cracow, Skawińska 8, Poland
Tel: +48 12 4305169
Fax: +48 12 4305203
E-mail: mmszczek@cyf-kr.edu.pl

Accepted for publication 11 September 2007
Allergy 2008; 63:140–141
© 2008 The Authors
Journal compilation © 2008 Blackwell
Munksgaard
DOI: 10.1111/j.1398-9995.2007.01565.x

References

- Polosa R. Adenosine-receptor subtypes: their relevance to adenosine-mediated responses in asthma and chronic obstructive pulmonary disease. *Eur Respir J* 2002;**20**:488–496.
- Bochenek G, Nagraba K, Nizankowska E, Szczeklik A. A controlled study of 9 α , 11 β -PGF₂ (a prostaglandin D₂ metabolite) in plasma and urine of patients with bronchial asthma and healthy controls after aspirin challenge. *J Allergy Clin Immunol* 2003;**111**:743–749.
- Bochenek G, Nizankowska E, Gielicz A, Swierczyńska M, Szczeklik A. Plasma 9 α ,11 β -PGF₂, a PGD₂ metabolite, as a sensitive marker of mast cell activation by allergen in bronchial asthma. *Thorax* 2004;**59**:459–464.
- Peachell PT, Columbo M, Kagey-Sobotka A, Lichtenstein LM, Marone G. Adenosine potentiates mediator release from human mast cells. *Am Rev Respir Dis* 1988;**138**:1143–1151.
- Ihre E, Gyllfors P, Gustafsson LE, Kumlin M, Dahlén B. Early rise in exhaled nitric oxide and mast cell activation in repeated low-dose allergen challenge. *Eur Respir J* 2006;**27**:1152–1159.
- Rivera J, Gilfillan AM. Molecular regulation of mast cell activation. *J Allergy Clin Immunol* 2006;**117**:1214–1225.