LETTER TO THE EDITOR

Altered metabolism of prostaglandin E_2 in asthma patients with aspirin hypersensitivity

To the Editor A specific regulatory role of prostaglandin E_2 (PGE_2) was postulated in aspirin-induced asthma.[1] Indeed, in this distinct asthma phenotype, several observations have accumulated pointing to depressed PGE_2 production by peripheral blood cells, nasal polyps, and bronchial fibroblasts; diminished EP_2 receptor expression on the inflammatory cells; and the association of EP_2 gene polymorphism with aspirin hypersensitivity.[2]

We performed inhalation challenge with increasing doses of lysine aspirin[2] in 14 patients with aspirin-induced asthma and 11 asthmatics who tolerated aspirin well. The mean age of the patients was 44.3 years, and the groups did not differ in their main clinical characteristics. In all subjects, exhaled breath condensates (EBC) were collected at baseline.[3] The collection was repeated at the time of appearance of the bronchial symptoms in subjects with aspirin-induced asthma, and when the cumulative dose of 182 mg of aspirin was reached in aspirin-tolerant asthmatics. In EBC samples, PGE_2 and its main metabolite (tetranor-PGEM) were measured using gas chromatography / mass spectrometry (GC/MS) and high-performance liquid chromatography/tandem mass spectrometry (HPLC/MS/MS), respectively. The results were expressed as raw concentration per 1 ml and as parts per million palmitic acid.[3]

Aspirin precipitated bronchial reactions in all subjects with aspirin-induced asthma, but in no subjects from the aspirin-tolerant group. At baseline, mean PGE_2 values did not differ between the groups, while tetranor-PGEM was higher in subjects with aspirin-induced asthma compared with the other group (P <0.001). Following aspirin challenge, the mean values remained unchanged (**TABLE**). The dose of aspirin had no effect on the response of PGE_2 and its metabolite. There was a positive correlation between the levels of PGE_2 and tetranor-PGEM following aspirin challenge only in aspirin-tolerant subjects (r = 0.93, P <0.001).

Our results add to the observations on the changes in prostaglandin production in aspirin-induced asthma[2,4-6] and indicate a rapid catabolism of PGE_2 in the lungs – its rate is 4-fold higher in aspirin-induced than in aspirin-tolerant asthma. The upregulation of the enzymes metabolizing PGE_2 might be related to a specific proinflammatory milieu operating in the bronchi of patients with aspirin-induced asthma.

TABLE Prostaglandin E_2 and tetranor-PGEM values at baseline and following aspirin challenge in patients with aspirin-induced asthma and aspirin-tolerant asthma

	Aspirin-induced asthma		Aspirin-tolerant asthma	
	baseline	challenge	baseline	challenge
PGE_2, pg/ml	0.79 (0.59 ±1.17)	0.93 (0.76 ±1.37)	1.06 (0.44 ±3.03)	0.641 (0.55 ±2.32)
PGE_2, parts/million of PA	3.49 (2.47 ±5.81)	3.97 (3.50 ±6.59)	2.79 (1.31 ±12.13)	2.104 (1.45 ±12.22)
tetranor-PGEM, pg/ml	67.84 (63.25 ±122.50)	89.70 (59.46 ±133.60)	25.46 (17.60 ±36.76)	12.03 (9.82 ±31.98)
tetranor-PGEM, parts/million of PA	435.40[a] (212.40 ±681.50)	357.40 (218.0 ±502.40)	92.74[a] (47.81 ±106.10)	50.00 (24.23 ±101.30)

Data are presented as median (25% and 75% percentiles).

a significant differences between the groups at baseline (P <0.05)

Abbreviations: PA – palmitic acid, PGE_2 – prostaglandin E_2

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